INVESTIGATION OF GAMMA INDEX PARAMETERS IN PATIENT SPECIFIC QUALITY ASSURANCE (PSQA) FOR RADIOTHERAPY TREATMENT PLANNING TECHNIQUE: RETROSECTIVE STUDY

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by

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CERTIFICATE

This is to certify that the dissertation with the title of Investigation of Gamma Index Parameters in Patient Specific Quality Assurance (PSQA) in Radiotherapy Treatment Planning Technique: Retrospective Study is the bona fide record of research work done by Siti Yuni Sara during the period of November 2023 to June 2024 under my supervision.

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DECLARATION

I hereby declare that this dissertation is the result of my own investigations, except when otherwise stated and acknowledge by myself. I would also like to declare that this work has not been previously or concurrently submitted for any other degrees in Universiti Sains Malaysia or other institution. Lastly, I shall grant Universiti Sains Malaysia the right to use the dissertation for teaching, research, and promotional purposes.

Siti Yuni Sara Binti Mukhtar

Date: _____

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LIST OF SYMBOLS

a-si	Amorphous silicon
cGy	Centi gray
cm	Centimeter
R^2	Coefficient of determination
ΔD	Criteria of the dose deviation
R^2	Coefficient of determination
cm^3	Cubic centimeter
$\left\vert \vec{r}_{ref} - \vec{r}_m \right\vert$	Distance difference between the reference point and the evaluated point
$\left\vert D(\vec{r}_{ref}) - D(\vec{r}_m) \right\vert$	Dose difference between the reference point and the evaluated point
$\gamma\ (\vec{r}_{ref}, \vec{r}_m)$	Gamma Index
kV	Kilovoltage
MV	Megavoltage
mm	Millimeter
%	Percentage
n	Sample size

LIST OF ABBREVIATIONS

1D	One-dimensional
2D	Two-dimensional
3D	Three-dimensional
3D-CRT	Three-dimensional conformal radiation therapy
AAA	Analytical anisotropic algorithm
AAPM	American Association of Physicist in Medicine
BED	Biologically Effective Dose
BEV	Beam's eye view
CBCT	Cone-bean computed tomography
CNS	Central Nervous System
CT	Computed tomography
DD	Dose difference
DNA	Deoxyribonucleic acid
DTA	Distance-to-agreement
DVH	Dose volume histogram
EBRT	External beam radiation therapy
EPID	Electronic portal imaging device
EPI	Electronic portal imaging
FIF	Field-in-Field
GI	Gamma index
GPR	Gamma passing rate
GTV	Gross tumor volume
HN	Head and neck
HUSM	Hospital Universiti Sains Malaysia

IMAT	Intensity-modulated arc therapy
IMRT	Intensity-modulated radiation therapy
JEPeM	Human Research Ethics Committee USM
LINAC	Linear Accelerator
MLC	Multi-leaf collimator
MU	Monitor unit
MV	Megavoltage
OBI	On-board imaging
OAR	Organs at risk
PSQA	Patient-specific quality assurance
QA	Quality assurance
RT	Radiotherapy or Radiation therapy
SAD	Source-to-axis distance
SBRT	Stereotactic body radiation therapy
sMLC	Segmental multi-leaf collimator
SNC	SunCHECK
SRS	Stereotactic radiosurgery
SPSS	Statistical Package for Social Sciences
TG-119	Task Group 119
TG-218	Task Group 218
TPS	Treatment Planning System
VMAT	Volumetric modulated arc therapy

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PENYIASATAN PARAMETER INDEX GAMMA DALAM JAMINAN KUALITI KHUSUS PESAKIT (PSQA) BAGI TEKNIK PERANCANGAN RAWATAN RADIOTERAPI: KAJIAN RETROSPEKTIF

ABSTRAK

Jaminan kualiti khusus pesakit (PSQA) ialah prosedur pra-rawatan yang dilakukan untuk menilai kesahihan pelan rawatan terbalik, sebelum rawatan radioterapi yang sebenar diberikan, ini untuk memastikan rawatan yang tepat akan deberikan untuk menjamin keselamatan pesakit. Kaedah semasa yang digunakan untuk penilaian PSQA di Jabatan Hospital Universiti Sains Malaysia (HUSM), adalah dengan kaedah pengukuran berasakan fantom dengan mengunakan analisis index gamma (GI). Matlamat kajian ini adalah untuk menyiasat aplikasi parameter GI (3%/3mm,3%/2mm,2%/2mm, 2%/1mm and 1%/1mm) kedalam terapi arkus isipadu termodulat (VMAT), rawatan modulasi keamatan radiasi (IMRT) dan terapi radiasi tubuh stereotaktik (SBRT), merentasi pelbagai kawasan pengrawatan, secara retrospektif. Kadar lulus gamma (GPR) sebanyak 95% ialah had toleransi sejagat yang direkomendasikan oleh American Association of Physicist in Medicine Task Group 218 (AAPM TG-218). Keputusan GPR menunjukkan kes PSQA mampu memenuhi had toleransi 95% apabila 3%/3mm, 3%/2mm and 2%/2mm parameter GI digunakan, dengan mencatatkan keputusan lulus sebanyak 92.5% (99 kes), 100% (29 kes) dan 87.5% (14 kes) bagi 3%/3mm, 82 kes (82.8%), 18 kes (62.1%) dan 8 kes (57.1%) bagi 3%/2mm, manakala bagi 2%/2mm sebanyak 46 kes (46.5%), 6 kes (20.7%) dan 6 kes (42.9%) masing-masing bagi VMAT, IMRT dan SBRT. Selanjutnya, Had toleransi GPR juga dinilai dan keputusan menunjukan 3%/2mm (≥95%), and 2%/2mm (>90%) mampu diaplikasikan bagi teknik IMRT, VMAT dan SBRT disebakan toleransi yang

tercatat sejajar dengan cadangan yang diberikan oleh kajian yang lepas. Seterusnya, had toleransi GPR untuk teknik rawatan yang berbeza menunjukkan perbezaan yang ketara ($p<0.05$) pada had toleransi antara IMRT dan VMAT apabila diaplikasikan menggunakan 3%/2mm (≥97.19%) dan (≥94.85%), 2%/2mm (≥93.74%) dan (≥90.39%). Tambahan pula, had toleransi GPR bagi kawasan perawatan yang berbeza mencerminkan perbezaan yang ketara ($p<0.05$) apabila VMAT 3%/2mm digunakan untuk HN (≥97 %), Pelvis (≥ 96%) dan Dada (≥ 98%). Kesimpulannya, kajian ini membuktikan bahawa selain daripada 3%/3mm (≥95%), 3%/2mm (≥95%) dan 2%/2mm (>90%) juga adalah sesuai untuk digunkan bagi teknik IMRT, VMAT dan SBRT untuk semua kawasan perawatan di HUSM, kecuali bagi IMRT dan VMAT apabila digunakan pada kawasan HN, serta untuk VMAT apabila 3%/2mm diaplikasikan pada kawasan HN, pelvis dan dada.

INVESTIGATION OF GAMMA INDEX PARAMETERS IN PATIENT SPECIFIC QUALITY ASSURANCE (PSQA) FOR RADIOTHERAPY TREATMENT PLANNING TECHNIQUE: RETROSPECTIVE STUDY.

ABSTRACT

The patient specific quality assurance (PSQA) is a pre-treatment procedure performed to evaluate the validity of the inversed treatment plans, before the actual radiotherapy (RT) treatment delivery, to ensure the patient's safety. The current method applied for the PSQA assessment in Hospital Universiti Sains Malaysia (HUSM) department is the ArcCHECK phantom based measurement using 3%/3mm gamma index (GI) analysis and currently, there is no standard procedure to perform the PSQA assessment. The aim of this study is to investigate the GI parameters (3%/3mm, 3%/2mm, 2%/2mm, 2%/1mm and 1%/1mm) in Volumetric modulated arc therapy (VMAT), intensity-modulated radiation therapy (IMRT) and Stereotactic body radiation therapy (SBRT) across various treatment regions retrospectively. The gamma passing rate (GPR) of 95% is the universal tolerance limit provide by the American Association of Physicist in Medicine Task Group 218 (AAPM TG-218). The GPR result indicated the PSQA cases were able to fulfill the 95% limit when 3%/3mm 3%/2mm and 2%/2mm GI parameter were applied with the result of 92.5% (99 cases), 100% (29 cases) and 87.5% (14 cases) for 3%/3mm, 82 cases (82.8%),18 cases (62.1%) and 8 cases (57.1%) for 3%/2mm, meanwhile for 2%/2mm, 46 cases (46.5%), 6 cases (20.7%) and 6 cases (42.9%) respectively for VMAT, IMRT and SBRT. Consequently, the GPR tolerance limit were also evaluated and reflected that 3%/2mm (≥95%), and 2%/2mm (>90%) is applicable for IMRT, VMAT and SBRT as the tolerance limit aligns with the suggestion by the previous study. Subsequently, The

GPR tolerance limit for different treatment technique indicates a significant difference ($p<0.05$) in tolerance limit between IMRT and VMAT when applied using 3%/2mm (≥97.19%) and (≥94.85%), 2%/2mm (≥93.74%) and (≥90.39%). Moreover, The GPR tolerance limit for different treatment region reflect a significant different ($p<0.05$) when VMAT 3%/2mm is applied for HN (≥97 %), Pelvic (≥ 96%) and Chest (≥ 98%). In conclusion this study proves that apart from 3%/3mm (≥95%), 3%/2mm (≥95%) and 2%/2mm (>90%) are suitable for IMRT, VMAT and SBRT cases for all treatment region to be applied in HUSM, except for IMRT and VMAT when applied on HN region, as well as for VMAT when applied on HN, pelvic and chest region using 3%/2mm.

CHAPTER 1

INTRODUCTION

1.1 Background of the study

Through a recent statement mentioned by the minister of health Malaysia, there has been an increment of cancer statistic in Malaysia from 10.5% in 2021 to 12.6% in 2022, making cancer to be the fourth leading cause of death in the government hospitals in 2023. Coincidently, 50% of the cancer patients may require radiation therapy as part of their cancer treatment regime (malaymail, 2024; Yahya et al., 2019). In general, Radiation therapy is one of the various types of cancer treatment option available. It involves the application of directed X-rays beams or subatomic particles beams such as electron, to generate a beam of ionising rays, for both curative and palliative purpose of cancer treatments.

Additionally, radiation therapy treatment can be administered externally or internally (Elizabeth and Christopher V. Maani, 2022). The radiation therapy treatment is delivered externally, by exposing the target site from the outside of patient body with high-energy radiation beams, generated from the linear accelerator (LINAC). It is commonly known as the external beam radiation therapy (EBRT). Internal radiation therapy on the other hand, is delivered through the implantation of radioactive source adjacent to the target site within the patient body, commonly known as Brachytherapy (Wang et al., 2019). Regardless of the type of treatment delivered the aim of the treatment is to provide a sufficient dose to cause damage to the tumour deoxyribonucleic acid (DNA) and triggers the subsequent cell death (Lu et al., 2022).

The process of delivering the radiation therapy treatment begins with patients' assessment by the oncologist. Once the treatment technique has been decided, the

patient would undergo CT simulation procedure to acquire CT images for the treatment planning and to simulate the delivery procedure before treatment delivery. The treatment plan is required for radiation therapy treatment delivery and would be planned by the physicists, through a software known as the treatment planning system (TPS). It will be tailored specifically according to each patient's condition and anatomy. Where the dose of the ionizing radiation beams to be administered to the patient will be calculated as well (F.I. Osman, 2019).

For conventional radiation therapy treatment plans, such as three-dimensional conformal radiation therapy (3D-CRT), no verification of plan is required. However, for a more advanced technique such as IMRT, VMAT and SBRT, the verification of treatment plan is a standard procedure. Due to the high complexity of the techniques, that is contributed by the multi-leaf collimator (MLC) configuration and gantry head movements. After the treatment plan is created and verified accordingly, treatment would be delivered exactly as the CT simulation procedure (F.I. Osman, 2019; Tang et al., 2020)

The plan verification process, better known as the patient specific quality assurance (PSQA), is an important step and has become a standard practice in assessing the validity of the advanced treatment plans according to the American Association of Physicist in Medicine (AAPM) TG No-218 protocol. It is the assessment of every treatment plan before treatment delivery, which is commonly assessed via a dosimetry evaluation method known as the gamma index (GI) analysis. Through the GI analysis method, the calculated treatment plan would be compared with the measured treatment plan in terms of the dose difference (DD: %) and distance-to-agreement (DTA: mm) of the compared dose distribution. The dose difference (DD) and distance-to-agreement (DTA) are the components of the GI parameter, which is a

unitless tolerance level chosen to evaluate the dose distribution. The outcome of the comparison will be assessed by the gamma passing rate (GPR) that would reflect the percentage of the assessed points that lies within the GI parameter set. As well as the passing and failing threshold for the GPR (Mohamed et al., 2018; Stella et al., 2022).

However, each institution has a vary take on which GI parameters that are suitable to be used, depending on the equipment, operation processes, and treatment types available within the institution (Lu et al., 2022). The variation in the equipment is associated with the different utilisation of the LINAC machine modality, the PSQA detector, the gamma analysis software as well as the modality of the TPS used. Naturally, will contribute to the variation of the operation process. In addition to the difference in the clinical policy, the experience of the physicist and commissioning process. Furthermore, GI analysis permeates ambiguity in the choice of GI parameter, GPR threshold, local or global comparison as well as the dimension of dose distribution to be applied for the analysis which further complicates the standardisation of the PSQA process (Anetai et al., 2022).

This becomes the main factor to the non-standardised application of GI analysis for the PSQA process across different institution. Conclusively, all institution is free to follow any guidelines available or to apply any PSQA method deemed suitable, as long as the PSQA result fulfil the GPR threshold, the treatment can be proceeded accordingly (Chan et al., 2021; Park et al., 2018). Which allows for the exploration on the application of a more stringent GI parameter of 3%/2mm, 2%/2mm, 2%/1mm and 1%/1mm within the department. In conjunction to the re-evaluation of the current PSQA standard in the department. Provided that the 3%/3mm GI parameter is currently being applied, it will be used as a benchmark to compare with the outcome of the stringent GI parameters, when it is applied for the advanced treatment techniques

of VMAT, SBRT and IMRT across various treatment regions. Including the HN, pelvis, chest, Central Nervous System (CNS) and Abdomen. As it is the autonomous responsibility for each institution to re-evaluate the suitable GI parameter to be applied based on their operation system using available formalism as a guideline (Park et al., 2018)

1.2 Problem statement

The PSQA is the assessment of every treatment plan of the radiation therapy treatment before treatment delivery, to evaluate the dose distribution point between calculated plan and measured plan. It is assessed through the GI analysis by setting a certain GI parameter of DD/DTA. However, the main issue in PSQA is that there are no fixed GI parameters to be used in assessing the PSQA outcome and it has remained facility dependent (Anetai et al., 2022; Chan et al., 2021; Miften et al., 2018; Park et al., 2018). As per stated via Task Group 218 (TG-218) formalism, the acceptance criteria for PSQA are more difficult to establish because of large variations among treatment planning systems, delivery systems, the measurement tools as well as the analysis tools used to interpret the QA results. The calculations and measurements are compared and approved or rejected using the institution's criteria for agreement. If the agreement is deemed acceptable, then one will infer that the delivered patient plan is accurate within the clinically acceptable tolerances (Miften et al., 2018).

Despite the variation, as long as the treatment plan is passed then treatment shall be proceeded accordingly regardless of the GI parameters used (Lu et al., 2022). Moreover, a local author (Hizam et al., 2023) found that the treatment delivery is dependent the planner as well, adding to variation in the treatment delivery from facility to facility which contributes to variation in PSQA outcomes. Naturally, due to

this variation existed in the PSQA practice, it adds up to a significant burden to the facility as it complicates the PSQA condition and acceptability (Anetai et al., 2022; Chan et al., 2021). Making it challenging to evaluate the clinical accuracy of PSQA outcome via GI analysis, when it permeates ambiguity not only in the treatment set up, but also in all of the gamma analysis aspects that includes the GI parameter itself, the GPR, dose threshold and type of dose normalization point used (Anetai et al., 2022). Making it necessary to develop an institute-specific protocol, as the GI will depend on the planning and treatment setup of each institute (Das et al., 2022).

Therefore, (Chan et al., 2021) aims for a more consistent PSQA process and result, to streamline their workflow for the improvement of the treatment quality. In which is achievable by increasing the confidence level of the PSQA result, through the exploration of a stricter GI parameter such as 3%/2 mm or even 2%/2 mm (Pan et al., 2019). Including the assessment of the current GI parameter used in HUSM which is 3%/3mm. As it clarifies the state of PSQA practice in HUSM, enabling the identification of the areas for potential improvement, and facilitate the continued improvement in standardization, consistency, efficacy, and efficiency of PSQA, further elevating the confidence level of the PSQA outcome in the department (Chan et al., 2021).

1.3 Research Questions

1. What is the average GPR for 3%/3mm, 3%/2mm, 2%/2mm, 2%/1mm and 1%/1mm GI parameter?
2. Is there a significant difference between the GPR of 3%/3mm with 3%/2mm, 2%/2mm, 2%/1mm and 1%/1mm GI parameter respectively?

3. Is there a correlation between the GI parameter used with the type of RT treatment technique used and the treatment region?

1.4 General objective

The main objective of this retrospective study is to investigate the significance of the GI parameters in pre-treatment PSQA for advanced RT treatment planning techniques of various treatment regions in HUSM.

1.4.1 Specific objective

1. To assess the GPR for the IMRT, VMAT and SBRT treatment planning technique using standard 3%/3mm GI parameter for all treatment regions.
2. To evaluate the effective GI parameter for IMRT, VMAT and SBRT technique with treatment region and GPR of various GI parameters.
3. To correlate between the GI parameters of 3%/2mm, 2%/2mm, 2%/1mm and 1%/1mm for IMRT, VMAT and SBRT techniques of various treatment region on GPR outcome

1.4.2 Research Hypothesis

a) H_0: there is no significant relationship between GI parameters and GPR for advanced RT technique of IMRT, VMAT and SBRT in HUSM

b) H_A: there is a significant relationship between GI parameters and GPR for advanced RT technique of IMRT, VMAT and SBRT in HUSM

1.5 Significance of the study

GI parameter is a tolerance limit set for GI analysis to allow for the spatial and dosimetry shift of evaluated point dose distribution in terms of DD for dosimetry shift and DTA for spatial shift (Das et al., 2022). Currently, there is no fixed GI parameter value to be used when evaluating the PSQA. Therefore, it is the responsibility of each institution to determine the suitable GI parameter to be applied according to their respective operational system (Park et al., 2018). Hence it allows for the exploration of a stricter GI parameter. As recommended by the current protocols and previous studies, along with assessing the GI parameter that is currently being used in the HUSM department which is 3%/3mm (Miften et al., 2018).

Exploring the stricter GI parameter provided by the AAPM, as per TG NO-218 such as 3%/2mm would provide an insight on the compatibility of the stricter GI parameter with the clinical setting of the HUSM RT department. Which can be implemented permanently or as an option in the future when deemed necessary. On the other hand, assessing the current GI parameter would provide a better clarification of the current PSQA standard in the department. As an effort to stay updated with the current standards and contribute to the overall improvement of the PSQA standard within this field and in the department. Increasing the confidence level in the accuracy of PSQA outcome and therefore the quality of the treatment, for the enhancement of the patient's safety in the HUSM department.

CHAPTER 2

LITERATURE REVIEW

2.1 Radiation Therapy for Cancer Treatment

Radiation therapy is a type of cancer treatment which specializes in destroying the cancerous cells in the body by exposing them to ionizing radiation, such as X-rays, gamma rays, high-energy electrons or heavy particles. Depending on the type and location of cancer, radiation oncologists may use two types of radiation therapy, alone or in combination of both external known as the external beam radiation therapy (EBRT) and internal radiation therapy known as brachytherapy (Zaorsky et al., 2017)

The EBRT is delivered from a LINAC machine that directs radiation in the form of photon or electron beams at the cancerous area. The most common form of ionizing radiation used in clinical practice is the photon beam. While the electrons beam is commonly used for treating the superficial tumor. The LINAC machine, although large and potentially noisy, does not come into physical contact with patient. It can maneuver around the patient, delivering radiation to a specific part of the body from various angles. This form of therapy is considered a local treatment, targeting a specific area of the body. For instance, when treating for breast cancer, the radiation will be focused solely on the breast, rather than the entire body (Elizabeth V. Maani and Christopher V. Maani, 2022).

2.1.1 Linear Accelerator (LINAC)

A LINAC is a machine used for radiation therapy treatment, utilizing high radio-frequency electromagnetic waves to accelerate electrons along a linear path within an accelerator waveguide. Generally, a typical LINAC machine could generate low energy

photon of 4 to 8 megavoltage (MV) energy, medium energy photon and electron of 10 to 15 MV and high energy photon and electron of 18 to 25 MV. Both high energy photons and electrons are generated with multi-leaf collimator (MLC) to create an intensity modulated beam. The main component of LINAC consists of a drive stand, gantry, modulator cabinet, treatment table and control console. The drive stand functions to house the Magnetron, Klystron and water-Cooling System. The magnetron provides the microwaves to accelerate the electrons, where the klystron helps to amplify the microwaves generated by the magnetron. As for the water-cooling system helps in maintaining a constant temperature so that the components in the drive stand and gantry function properly (Mallick and Benson, 2020)

The gantry is responsible for generation of beams and directing the beams towards patient for treatment, as it comprises of the electron gun, accelerator guide and treatment head. The accelerator guides are the evacuated, or gas filled structures and are used in the transmission of microwaves generated by magnetron, where the electron gun produces electrons into the guide and the bending magnets along the guide enable the change of direction of electron and bends it towards the X-ray target to produce a photon beam that will be used to target patient (Mallick and Benson, 2020)

The other components located in the treatment head of LINAC includes the beam directing, modifying, monitoring devices, bending magnet, target, and primary collimator, beam flattening filter, ion chambers, secondary collimators, wedges, blocks, and compensators. Are used to shape the photon beam, monitor the radiation, and adjust the field size as well as reducing the generated beam intensity. Modulator cabinet basically is the support or auxiliary system to the LINAC machine, as for the control console, it is for controlling the LINAC machine and monitor patient from the outside of the treatment room. (Mallick and Benson, 2020) Several of the common LINAC

modalities that have been established and available in the market for radiation therapy treatment includes, TrueBeam, Halcyon and Edge (Varian Medical Systems Inc., Palo Alto, CA). As well as the Infinity and Synergy (Elekta Oncology Systems Inc., Crawley, UK)

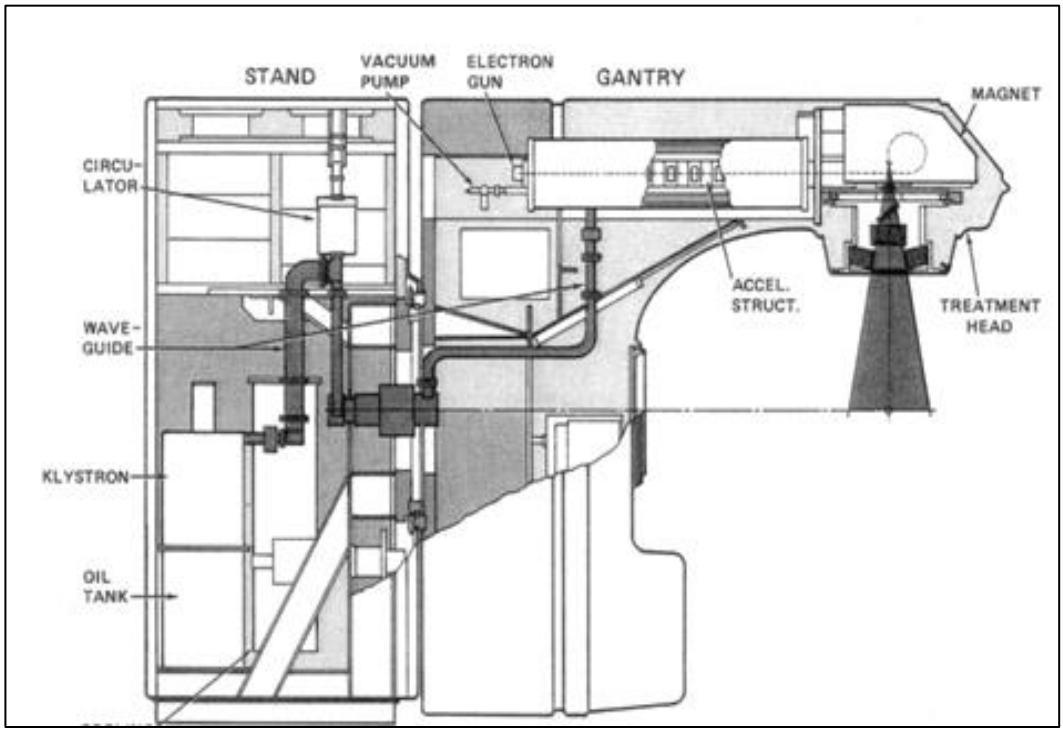

Figure 2.1: The image of LINAC components with (Karzmark and Morton, 2017)

2.1.2 RT workflow

Radiation therapy or RT treatment begins with consultation by the oncologist, followed by computed tomography (CT) simulation, regardless of the type of RT treatment. The CT simulation is carried out to simulate the actual RT treatment procedure where the patient will be in their treatment position on the couch. The radiation therapist will then mark the patient's body as a reference point and note down the patient's position on the treatment couch, along with their immobilization devices if any is involved. From the simulation procedure, the CT image acquired would be used to create a treatment plan for the patient (Courtney Misher, 2022).

Once the CT image is acquired, the medical physicist will design a suitable treatment plan based on the dose and treatment technique prescribed by the oncologist, via the treatment planning software (TPS) available from various vendors such as Pinnacle **(**Phillips healthcare Inc, Andover, MA), Eclipse (Varian Medical Systems Inc, USA), Monaco and OnCentra (Elekta Oncology Systems, Crawley, UK) (Taschetta-Millane, 2016). Consequently, once the treatment plan is ready, its viability will be checked by conducting a quality assurance (QA) procedure known as the pretreatment PSQA. This is carried out mainly by measuring the treatment plan using either a 2D detector such as the electronic portal imaging device (EPID) or PSQA 3D phantom such as the ArcCheck (Sun Nuclear Corporation) and Octavious 3D phantom (PTW dosimetry company) that represent the patient, along with the dosimeters to measure the radiation dose received by the patient. After exposing the PSQA phantoms, the QA result will be compared between the calculated plan in TPS and measured dose in PSQA phantom (Courtney Misher, 2022).

The differences between the calculated and measured dose will be analysed through the phantom software. This process is also known as the GI analysis. Typically, the difference between the calculated treatment plan and the measured plan should not be higher than ±5%, only then the assessment is considered as a passed within the 95% of the universal tolerance limit. The treatment plan that has passed the assessment, can be proceeded using the calculated treatment plan. After the patient had undergo their RT treatment and completed their treatment regime, their oncologist will follow up with their treatment progress accordingly (Courtney Misher, 2022).

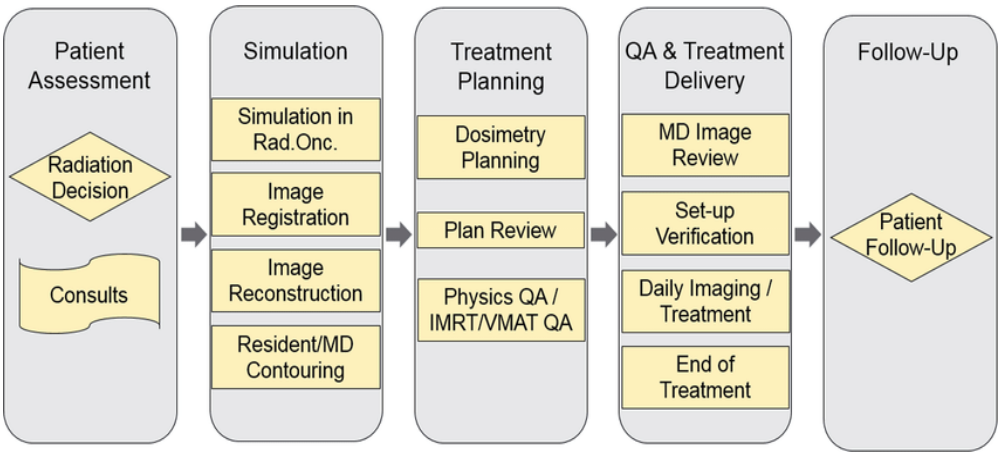

Figure 2.2: The representation of radiation therapy workflow (F.I. Osman, 2019)

2.2 RT treatment planning technique

Generally, the calculation algorithm available in the treatment planning for RT are for both forward and inverse planning techniques. Forward planning is an iterative trial-and-error approach used in planning, where the planner has to manually specify and adjust the plan parameters. However, with the current improved computing advances, inverse planning has become the common method. Through this method, the planner would only require defining the dose constraints for target volume and OARs, along with framework conditions. These treatments use non-uniform intensity beams to better conform to the target volume and to avoid the organ at risk involved. Allowing these advanced RT techniques to provide a better target volume coverage and higher dose homogeneity, when compared to 3D-CRT (Lizar et al., 2021). The optimization algorithm incorporated in the TPS will also determine the best plan parameters using an objective function. The planner could also influence the optimization by modifying the penalty weight of each constraint. Making the inverse planning to be a more time-efficient method as much of the trial-and-error time is removed. (Ebert et al., 2018).

2.2.1 Forward planning technique

Forward planning technique is a technique that involves creating the treatment plan step by step through a series of process including adjusting the field size, field weightage dose calculation and more, manually until the desired treatment plan is achieved. Forward planning uses the field-in-field technique to achieve a simple intensity-modulated dose distribution. With forward planning, a planner must manually adjust the block shape, the beam intensity of each field and subfield through a trial-and-error process (Shang et al., 2015).

Forward planning, also known as Field in Field planning (FiF), involves in dose homogenization using the static multi-leaf collimator (sMLC) segments which is included in the planning after the initial dose calculation, with equally weighted and open tangential fields. These segments block high dose regions and deliver more radiation to lower dose regions. Their weights are defined considering that the dose values are blocked, and non-uniform intensity beams are used to better conform to the target volume and avoid involvement of the organ at risk (OARs). Generally, this approach still provides superior target volume coverage and a higher dose homogeneity as compared to 3D-CRT (Lizar et al., 2021).

2.2.2 Inverse Planning technique

Inverse planning technique is a technique that requires the planner to specify their desired treatment plan goals and constraints prior to planning. This is done by inserting the plan parameters and allowing the software to generate the best possible outcomes. Which is only possible through the employment of customized optimization algorithms in the treatment planning software to shape the desired dose distributions, ensuring that the treatment is tailored to the specific needs of the patient in terms of

radiation beam shapes and intensities to meet those goals, ultimately enhancing the precision and effectiveness of radiation therapy. This technique is often used for IMRT and VMAT as both techniques comprise of variation in beam intensity (Azharuddin et al., 2022).

Unlike forward technique, the Inverse planning technique uses non-uniform beams generated after an inverse optimization process, based on the goals of the plan which resulted in a more significant dose reduction to the organs at risk (OARs). As the use non-uniform intensity beams aids in the better conformity to the target volume and to avoid the organ at risk involved. This way, providing a better target volume coverage and higher dose homogeneity. (Lizar et al., 2021). Additionally, the computer algorithm enables users to adjust the beam weighting and blocking, to achieve an optimal plan based on dose objectives applied to the tumor targets and critical organs.

Thus, as compared with forward planning, the inverse planning technique provides more conformal-dose distributions to the tumor volumes with significantly better sparing of critical structures (Shang et al., 2015). Besides, this technique allows for an improved conformity of the dose to the target areas by allowing for variation in fluence or energy deposited in the target, thereby spatially modulating the intensity of the beam. This technique utilizes multi-leaf collimators to divide the beam into small beamlets, allowing for fluence modification. As a result, it achieves a maximum dose to the target while minimizing the dose to critical organs. (Lizar et al., 2021; Shang et al., 2015)

2.2.2 (a) Intensity Modulated Radiation Therapy (IMRT)

Intensity Modulated Radiation Therapy (IMRT) is a general term to represent different types of advanced RT treatments. The beam intensity is modulated or in

another words changes in a controlled manner to conform the dose distribution shape according to the tumor. This is achieved by dividing each beam into beamlets with adjusted individual intensity, through the help of computerized inverse planning algorithm, to manipulate the Multi-leaf Collimator (MLC) movements through iterative calculation and various algorithms.

Both modulated intensity of beamlets and variable number of fields within each tumor voxel allow better dose conformation through non-uniformity of beam intensity. Producing a variety of dose distribution from within a beam (Rehman et al., 2018). It can generally be divided into two common types according to each delivery technique, fixed and moving gantry. Fixed-gantry IMRT delivery employs step-and-shoot (or segmental), sliding window (dynamic), or compensator-based methods (Miften et al., 2018). The comparison between IMRT and VMAT technique is shown in Figure 2.3 below.

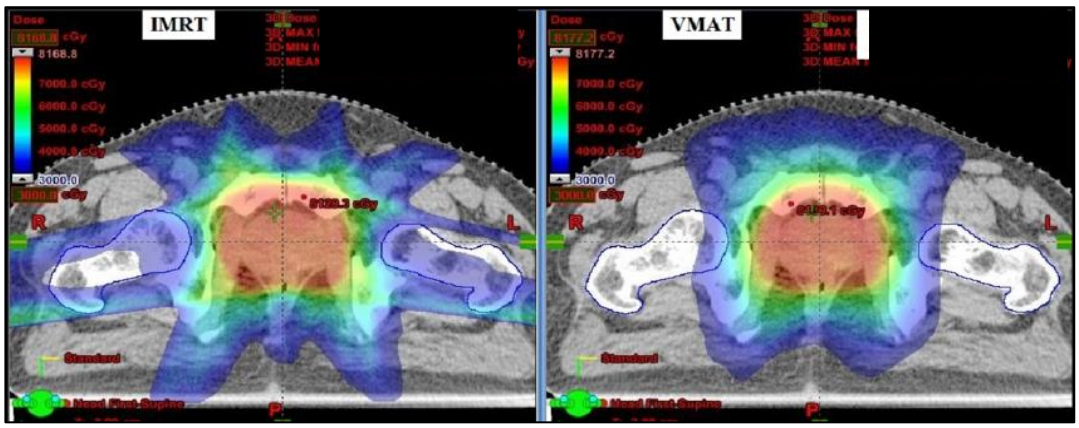

Figure 2.3: Comparison of dose distribution in IMRT and VMAT treatment plan of prostate cancer (M. Ali et al., 2014).

2.2.2 (b) Volumetric Modulated Radiation Therapy (VMAT)

Volumetric Modulated Arch Therapy (VMAT) is one of the many treatment techniques that are available for RT treatment. It is a modified form of Intensity

Modulated Arch Therapy (IMAT) of IMRT whereby it could provide an increased dose conformity through gantry rotation that occurs simultaneously with MLC movements into a series of positions based on a computerized sequence as dose is being distributed continuously (Hunte et al., 2022).

Therefore, requiring a much lesser usage of monitor unit as it enables a more rapid dose delivery that takes minimal time, in comparison to the conventional IMRT (Ohira et al., 2017). With the MLC being on a constant motion with the radiation beam during rotation while the dose rate is with the MLC being on a constant motion with the radiation beam during rotation while the dose rate is reduced as compared to IMRT. (Dieterich et al., 2016; Fraass et al., 2016).

Instead of using a single fixed beam shape and size, the combination of the moving MLC, moving gantry, and variable dose rate allows for the creation of fluence across a full or partial ring, as depicted in image 2.4 below. In this context fluence refers to the amount of radiation passing through a unit area in a specific direction this means that the radiation can be delivered from multiple angles around the patient, as the machine rotates and adjusts the beam shape and intensity continuously. Additionally, it can be adjusted dynamically during treatment, which is achieved by the continuous gantry and MLC movements. During the delivery process the gantry may rotate around patient in either a full 360 degrees or half-arc of 180 degrees depending on the set protocol (Dieterich et al., 2016; Fraass et al., 2016)

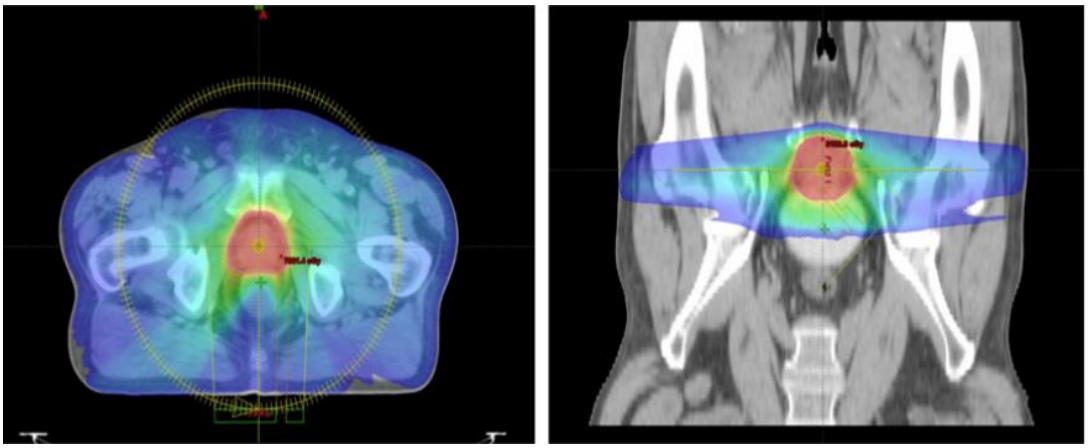

Figure 2.4: Figure 2.4 the image of VMAT treatment plan and dose distribution of prostate cancer (Cakir et al., 2015)

2.2.2 (c) Stereotactic Body Radiation Therapy (SBRT)

Stereotactic Body Radiation Therapy (SBRT) is called stereotactic ablative RT(SABR) when applied to extracranial tumors, which are tumors located outside of the brain. However, when used on the brain, it is often called stereotactic radiosurgery (SRS). Regardless, both terms are used to describe the same RT treatment technique. The SBRT technique destroys tumors by delivering a more precise and intense radiation beam as compared to IMRT and VMAT, which is as shown in Figure 2.5 below, guaranteeing minimal normal tissue complications and maximal tumor destruction (Song et al., 2021).

Several distinctive factors that differentiate SBRT technique than IMRT and VMAT, includes a limited number of high dose-per-fraction treatments with a biologically equivalent dose (BED) of at least 75–100 as a minimum or even higher, smaller treatment field margins which is typically 5 mm or less than 10 mm which is closely similar to the Gross Tumor Volume (GTV) margin. SBRT also enables a sharper dose fall-off gradient. However, due to higher single dose per fraction, a slight patient movement would create a bigger dose impact on the OARs. As this technique only

requires 1 to 5 fractions to complete a single treatment regime. Which is why immobilization devices are crucial for this technique (Kim et al., 2020).

Another interesting and potentially important aspect of SBRT and SRS is that high-dose irradiation of tumors may augment antitumor immunity, thereby leading to a further sustained indirect tumor cell death and inhibition of recurrence and metastatic growth. Customarily, due to its treatment intensity it is often used to treat the brain arteriovenous malformation through SRS (Song et al., 2021). Other treatment regions that commonly utilize the SBRT technique includes prostate, spinal cord and brain (Kim et al., 2020; Song et al., 2021).

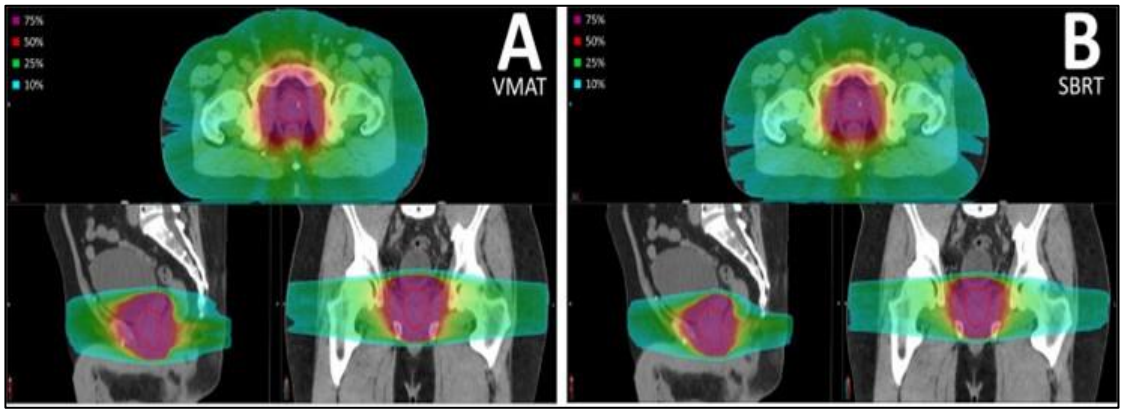

Figure 2.5: The comparison of dose distribution between VMAT and SBRT treatment plan of prostate cancer (Grzywacz et al., 2023).

2.3 Patient Specific Quality Assurance (PSQA)

PSQA in radiation therapy is defined as the QA step in ensuring that each treatment plan that is tailored specifically for each patient is viable to be applied for the actual treatment delivery. Quality assurance is an important step as it emphasizes on providing confidence to patients that the promised quality requirement will be met by the healthcare providers (Klein et al., 2023) The promised quality requirement in this sense, is the treatment planned for the patient, provided by the medical physicists. This

step is strongly recommended by various bodies to provide safety and the detection of possible clinical errors especially for advanced or inversed treatment planning techniques (Pan et al., 2019; Xu et al., 2022)

The PSQA assessment can be categorised into measurement based and calculation based, for the measurement based, the PSQA procedure would involve measuring the radiation dose of a specific treatment plan that is calculated or created with TPS. The measurement is done using 2D or 3D GI analysis by utilising 2D or 3D detectors respectively. In which the diodes arrays or also known as the detector, may come in various kinds such as EPID for 2D and ArcCHECK for 3D GI analysis Then the measured plan obtained will be compared and assessed with the created plan itself through the GPR, to assess the difference in the dosimetry distribution. If the difference is within the pre-set GPR, the planned treatment will be proceeded accordingly (Han et al., 2023).

2.3.1 Types of PSQA

Generally, PSQA can be categorized into two types, measurement-based QA and calculation-based QA. The commonly applied method for measurement based QA is the pre-treatment phantom measurement. In pre-treatment phantom measurement method, a homogenous phantom will be used to deliver the planned dose by placing it on the LINAC treatment couch. This is due to the fact that the phantom is incorporated with a large amount of detectors, capable of measuring the radiation dose delivered onto them (Xu et al., 2024).

On the contrary, for calculation based method, some of the common methods includes the independent dose calculation. In independent dose calculation, the planned dose distribution to be delivered would be calculated. The dose to be calculated can

either be based on plan from TPS or based on plan reconstructed from the treatment delivery log file, where no PSQA phantom or detectors are involved to measure the dose to be delivered, as the calculation would be performed according to patients' geometry. For TPS plan based, the TPS algorithm will perform the calculation, as for the delivery log file based, the calculation will be performed either via manual hand calculations or calculation software (Meijers et al., 2020)

For Software calculation, it involves using independent algorithms outside of the TPS which consist of another software programs such as MCsquare with different algorithms, to re-check the calculated plan. Such algorithms may include Analytical Anisotropic Algorithm (AAA) and electron Monte Carlo (eMC) or even the collapsed Cone Based algorithm (Jiménez-Acosta et al., 2021). Either way, both methods involve in the assessment of GPR outcome by performing the GI analysis (Meijers et al., 2020). The significant difference between delivery log and TPS plan-based methods is that the log file based, relies on the self-reported delivery parameters from the LINAC rather than providing an independent assessment (Chan et al., 2021).

As for the measured based QA although it is quite labor-intensive effort it provides a variety of QA assessment options, which comprises of point dose measurement, 1D dose measurement, planar dose measurement (2D), and 3D dose measurement. Using various measuring devices like ion chamber, film dosimeter, EPID as well as ArcCHECK phantom (Xu et al., 2022). The devices used would be dependent on the kind of GI analysis to be performed, if 3D GI analysis were to be performed ArcCHECK phantom would be typically used. On the other hand, if 2D GI analysis were to be performed then EPID and film dosimeter may be sufficient to be used (Lu et al., 2022)

2.3.2 Workflow for PSQA

The for the measurement based PSQA, the created inverse RT treatment plan will be measured as part of the PSQA evaluation, the measurement will first be taken in the form of point dose using the cylindrical ionization chamber connected to the PSQA phantom, to measure the dose at the center of the plan which coincided with the LINAC isocenter. The cumulative dose would be measured, if VMAT or IMRT plans are involved, the cumulative dose will account for all the arcs in the plan and compared to the dose calculated to the same point. The DD between the plan and the measured plan will be calculated.

Then, a 3D dose distribution measurement will be taken using PSQA phantom of ArcCHECK, by setting up the phantom onto the couch and connect it to SNC patient software within a personal computer, to measure dose distribution three dimensionally which coincides with better with patient anatomy. The measured and calculated composite dose distributions were compared in SNC Patient software through the GI analysis method using the GI parameter of choice that is presented as DD and DTA. The GPR of the GI analysis will then be assessed, if the passing rate fulfills the predefined tolerance limit, then the treatment plan is passed. Thus, treatment can be proceeded according to the treatment plan that has been created. (Low et al., 2018)

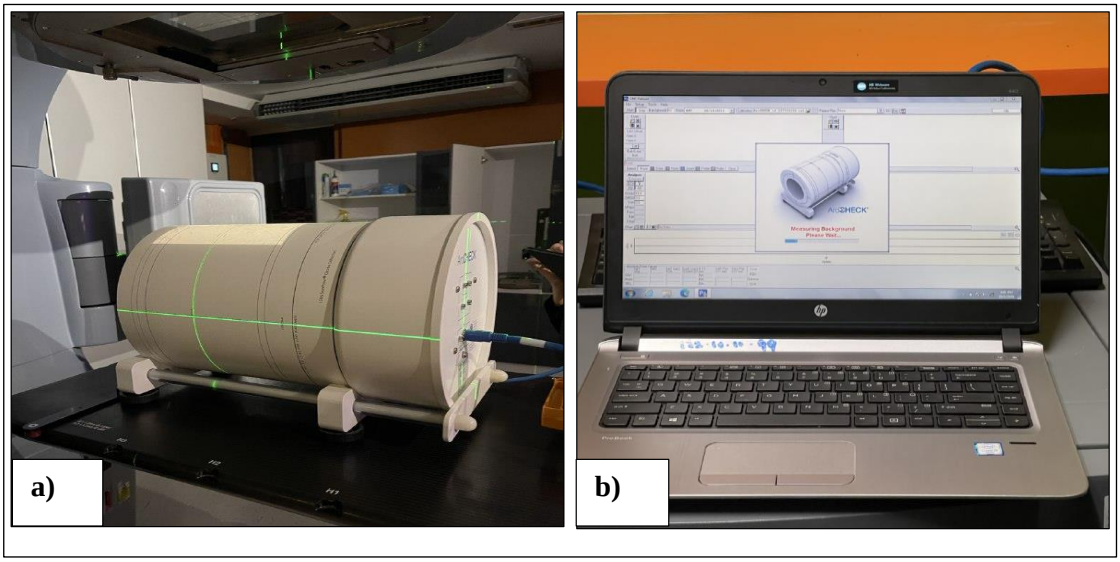

Figure 2.6: The PSQA set-up from the Department of Nuclear Medicine, RTand Oncology of HUSM a) the set-up of the ArcCHECK phantom on the LINAC couch b) the set-up of the SNC patient software to obtain and analyse the reading obtained from ArcCHECK phantom

2.3.3 Tools in PSQA

2.3.3 (a) Treatment planning system (TPS)

The Treatment Planning System (TPS) is computer software used to create a treatment plan, for each of the RT treatments to be carried out on patient by determining the optimal beam arrangements, energies, field sizes, and fluence patterns. Which is necessary to produce a safe and effective dose distribution in RT as part of treatment planning. An example of a TPS is the Eclipsed TPS introduced by the Varian Medical System. Generally, the TPS provides tools needed for radiation oncologists, medical physicists, and treatment planners to create and visualize RT treatments based on available imaging data where the CT image is commonly used. Modern TPS includes the advanced tools for treatment plan optimization, analysis, and visualization, such as the beam's eye view (BEV) technique, enabling the visualization of radiation beams in conjunction with relevant patient anatomy.

TPS allows for the rigid registration of images from various modalities to the treatment planning system, facilitating the examination of anatomic and functional information with respect to the treatment plan. The system enables easy adjustment of beam angles and weighting factors for forward-calculated plans, as well as the alteration of optimization parameters and associated weightage, for inverse planning tasks, streamlining the treatment planning process. Furthermore, advanced TPS analysis tools, such as the dose volume histograms (DVH), provide a comprehensive investigation of the delivered dose to the RT target and surrounding normal tissues. These capabilities allow for accurate and efficient treatment planning, significantly enhancing the quality and precision of RT treatments. (Hegi et al., 2018).

2.3.3 (b) Phantom in PSQA application

The PSQA phantom used for GI analysis are essentially made of commercial diode detector arrays that are arranged differently in a grid format, also referred to as the PSQA detectors. The type of detectors used depends on the dimensions of the GI analysis to be performed, that could either be in 2D planar, 3D planar or 3D volumetric GI analysis (Pal et al., 2021) A diode detector array used in GI analysis is primarily designed to measure the gamma rays. However, depending on the specifications of the diodes and the design of the array, it could be sensitive to other forms of radiation as well, such as X-rays (Marrs et al., 2013)

Normally, Different type of analysis would require different type of phantoms or detector, to better suits the analysis to be performed. For 2D GI analysis, the Commercially available detectors include, MapCheck (Sun Nuclear Corporation) and 2D-Array 1500 detector (PTW-Freiburg, Freiburg, Germany) (Pal et al., 2021). Not to

mention, the detector equipped along with LINAC known as the EPID could as well be used as the PSQA detector (Mohammad Hussein et al., 2013).

ArcCHECK phantom (Sun Nuclear Corporation) on the other hand, is a cylindrical phantom where the diodes are arranged in a cylindrical arrangement around the phantom body. Conveniently designed to accommodate for 3D planar GI analysis. Therefore, is highly recommended by AAPM, that the TG-218 formalism, to be utilized for 3D dosimetry verification in radiation therapy (Sun Nuclear Corporation, 2023)

For 3D volumetric gamma analysis, the commonly utilized phantom would be Octavius 4D phantom system. It is octahedral in shape, equipped with inclinometer and used along with 2D-Array 1500 detector (PTW-Freiburg, Freiburg, Germany). The inclinometer allows for the phantom to rotates synchronically with the gantry and records the gantry angle continuously which is needed for the reconstruction of 3D dose distribution, in combination with the reading captured by the 2D single planar array (Yang et al., 2019). It is used for a more complex dosimetry verification of a 3D (3D) dose matrix, with a volumetric evaluation of composite fields, which is superior to a planar dose value map (Das et al., 2022).