



Kaunas University of Technology

Mathematics and natural sciences

**Measurement and analysis of radiation doses to the tumour
and healthy tissues during intensity-modulated treatment
procedures**

Master's Final Degree Project

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Kaunas University of Technology
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Summary

Prostate cancer (PCa) is the most prevalent malignancy among men worldwide. The PCa incident and mortality rates in the European Union are significantly lower than in the Baltic states, with rates more than twice as high in the latter. However, advancements in radiology and radiotherapy led to create more individualized treatment, improving life expectancy after the treatment. Despite the improved treatment planning approaches, dose calculation algorithms of the treatment planning systems (TPS) tend to underestimate the dose and insufficiently compute out-of-field doses beyond the in-field edge.

During this study the reliability of the dose calculation algorithms used in a daily clinical practice was checked, paying special attention to the out-of-field region. The four different treatment plans: 2 intensity-modulated radiotherapy (IMRT) and 2 volumetric arc therapy (VMAT) technique plans were planned with the treatment planning system *Eclipse* for each technique using different dose calculation algorithms (AAA or Acuros XB). Comparison of the calculated doses with the treatment planning system was additionally measured with 2D radiochromic films *RTQA2* dosimetry.

The main study results showed that the highest difference (up to 51.4%) of four planned treatment plans was observed between different treatment planning techniques (IMRT vs. VMAT) since just a slight difference (up to 4.6%) between dose calculation algorithms was registered. Treatment planning system (TPS) calculations versus 2D dosimetry measurements revealed miscalculations of TPS by 30%. Due to the lack of accuracy, TPS not always can be trusted for the evaluation of out-of-field doses (or doses for critical organs or healthy tissues).

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Santrauka

Prostatos vėžys (PCa) yra labiausiai paplitęs piktybinis navikas tarp vyrų visame pasaulyje. Europos Sąjungoje sergamumo ir mirtingumo nuo PCa rodikliai yra gerokai mažesni nei Baltijos šalyse, o pastarosiose – daugiau nei du kartus didesni. Tačiau radiologijos ir spindulinės terapijos pažanga leido sukurti labiau individualizuotą gydymą ir pagerinti tikėtiną gyvenimo trukmę po gydymo. Nepaisant patobulintų gydymo planavimo metodų, gydymo planavimo sistemų (TPS) dozės apskaičiavimo algoritmai paprastai nepakankamai įvertina dozę, ir ribotai apskaičiuoja už taikinio ribų esančias dozes.

Šio tyrimo metu buvo patikrintas kasdienėje klinikinėje praktikoje naudojamų dozės apskaičiavimo algoritmų patikimumas, ypatingą dėmesį skiriant už lauko ribų esančias sričiai. Keturi skirtingi gydymo planai: 2 moduliuto intensyvumo spindulinės terapijos (IMRT) ir 2 tūrinės arkinės spindulinės terapijos (VMAT) planai buvo suplanuoti naudojant gydymo planavimo sistemą „Eclipse“ kiekvienai teknikai taikant skirtingus dozės apskaičiavimo algoritmus (AAA arba „Acuros XB“). Gydymo planavimo sistemos apskaičiuotos apšvitos dozės buvo palygintos su papildomai išmatuotomis dozėmis naudojant 2D radiochrominių filmų RTQA2 dozimetriją.

Pagrindiniai tyrimo rezultatai parodė, kad didžiausias keturių suplanuotų gydymo planų skirtumas (iki 51.4%) nustatytas tarp skirtingų gydymo planavimo metodų (IMRT ir VMAT), nes tarp dozės apskaičiavimo algoritmų užfiksuotas tik nedidelis skirtumas (iki 4.6%). Gydymo planavimo sistemos (TPS) skaičiavimai, palyginti su 2D dozimetrijos matavimais, atskleidė, kad TPS skaičiavimai buvo klaidingi iki 30%. Dėl nepakankamo tikslumo TPS ne visada galima pasitikėti vertinant už lauko ribų gaunamas apšvitos dozes (kritinių organų ar sveikų audinių apšvitos dozes).

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List of abbreviations and terms

Abbreviations:

PCa – Prostate cancer

IARC – International Agency for Research on Cancer

SNPs – Single nucleotide polymorphisms

SCNAs – Somatic copy number alterations

DNA – Deoxyribonucleic acid

EBRT – External beam radiotherapy

IGRT – Image-guided radiotherapy

3D – Three-dimensional

GTV – Gross Tumour Volume

CTV – Clinical Target Volume

PTV – Planning Target Volume

ITV – Internal Target Volume

PRV – Organs at Risk Volume

DVH – Dose volume histogram

3D-CRT – Three-dimensional conformal radiotherapy

VMAT – Volumetric-modulated arc therapy

IMRT – Intensity-modulated radiation therapy

MU – Monitor units

AAA – Anisotropic analytical algorithm

PB – Pencil beam

CCC – Collapsed-cone convolution

PBC – Pencil beam convolution

MC – Monte Carlo

EGS – The Electron Gamma Shower

SLAC – Stanford Linear Accelerator

LINAC – Linear accelerator

AXB – Acuros XB

BTE – Boltzmann transport equations

HU – Hounsfield Unit

TPS – Treatment planning system

LBTE – Boltzmann transport equation

ICRP – The International Commission on Radiological Protection

TLD – Thermoluminescence dosimetry

SPM – Secondary primary malignancy

1D – One-dimensional

IC – Ionisation chambers

2D – 2-dimensional

IAEA – International Atomic Energy Agency

PMMA – Polymethylmethacrylate

VHP – The Visible Human Project

FFF – Flattening filter-free

RPM – Rotations per minute

QA – Quality assurance

SSD – Source-surface distance

RT – Radiotherapy

OARs – Organs at risk

CT – Computed tomography

PET/CT – Positron emission tomography/computed tomography

MRI - Magnetic resonance imaging

CBCT – Cone-beam computed tomography

MLC – Multi-leaf collimator

CPE – Charge particle equilibrium

TCPE – Transient charged particle equilibrium

Introduction

Radiation therapy is receiving an increased interest concerning the selection of the most suitable treatment technique and algorithms to optimize the precision of dose delivery. This precision is fulfilled by conformal dose distribution/ avoiding “cold spots” of the tumour through image-guided radiotherapy, treatment planning system (TPS), and beam intensity modulation [1-3]. TPS is a crucial tool for creating optimal radiation treatment plans, assessing radiation doses, and ensuring the safe and efficient delivery of the treatment [4].

Nevertheless, healthy tissue exposure is a growing concern due to out-of-field doses. This has highlighted the importance of assessing the risk of developing secondary cancers, which result from exposure to healthy tissues that are not directly targeted during treatment [6]. Consequently, anthropomorphic phantoms are constantly utilized for the evaluation of out-of-field doses. These phantoms contribute an important part in validating and preserving the quality of radiotherapy systems by providing a realistic representation of the human body for dosimetry measurements and verification. By inserting dosimeters into the phantom and exposing it to a known radiation beam, the precision and reliability of the TPS can be confirmed. Anthropomorphic phantoms enable the evaluation of dose distributions and the comparison of TPS-calculated doses with measured doses of the dosimetry tool in specific areas of the body, a process that cannot be performed on real patients.

The aim of this study is to analyse and compare irradiation doses based on treatment planning system *Eclipse* calculations and 2D radiochromic film dosimetry measurements, imitating irradiation of the prostate cancer case.

The tasks:

1. To analyse dosimetry data of the planned treatment plans, for the planning using two distinct treatment planning techniques (IMRT and VMAT) each calculated utilising different algorithms (AAA and Acuros XB).
2. To evaluate and compare in-field and out-of-field doses of 2D radiochromic films dosimetry with the calculated treatment planning system irradiation doses.
3. To evaluate limitations of the dose calculation with the treatment planning system and provide possible recommendations for the constraints of organs at risk.

1. Literature review

1.1. Prostate cancer

The most frequently registered cases of cancer are breast (530,000 only the cases involving women), colorectum (520,000 cases), lung (480,000 cases), and prostate (470,000 cases). Half of all the diagnosed cancer cases in Europe are caused by these four localisations [1]. As it is observed prostate cancer (PCa) is a widespread malignancy and the leading cause of fatalities due to cancer for men globally [2, 3]. According to the statistics of the International Agency for Research on Cancer (IARC), the Baltic States have one of the highest incident rates per one hundred thousand inhabitants (Estonia (86.8), Latvia (82.4), and Lithuania (122.4)) (Fig. 1), while the average incident rate of the European Union countries is equal to 52.1. The highest mortality rate is in Latvia (11.9), lower one in Estonia (10.3), and the lowest is in Lithuania (9.7), while in the European Union, the mortality is equal to 4.7 [4].

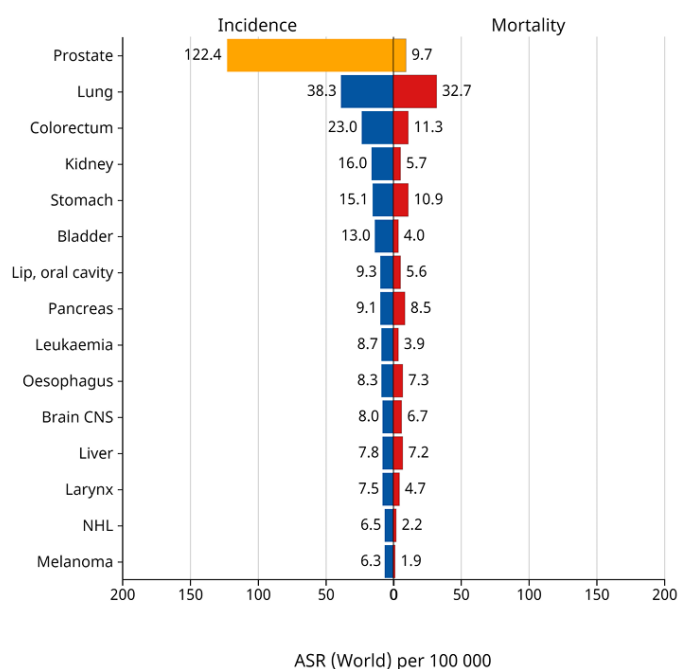


Fig. 1. Age-Standardized Rate per 100 000 inhabitants in Lithuania in 2022 [4]

The main cause of cancer is deoxyribonucleic acid (DNA) sequence variations resulting from the point mutations, variations in a single nucleotide (SNPs), and changes in the number of copies of a particular gene in somatic cells (SCNAs). It is known that these mutations can activate oncogenes and shut down tumour suppressor genes, which can cause prostate cells to divide uncontrollably [5, 6]. Germline mutations, race, age, anamnesis of family history, and other non-changeable threat factors are some characteristics of PCa. Conversely, smoking, obesity, and metabolic syndrome are the risk factors that can be changed. The aetiology of PCa may also be influenced by dietary, behavioural, viral, and environmental risk factors, though the evidence for this is limited [7, 8]. Depending on the clinical risk, men newly diagnosed with PCa can be treated with radiotherapy (brachytherapy and external beam radiotherapy), surgery (radical prostatectomy), chemotherapy, hormonal therapy, immunotherapy, cryotherapy, or any other combination of the mentioned ways of treatment [5, 9-12]. The most commonly utilized treatment strategy for handling cancer is radiation therapy (RT), which can be used either on its own or in conjunction with other procedures (e.g.

surgery, chemotherapy, etc.). Innovative technologies have improved patients' survival rates and achieved a greater level of local tumour control, making radiation therapy (RT) more effective [13, 14].

1.2. External beam radiotherapy

As it is known, in radiotherapy, the primary goal is to induce DNA damage, stopping the cell cycle, genetic damage, programmed cell death, and the process of aging, ultimately halting their capability to multiply, promoting cell death [13]. This outcome can be easily achieved by external beam radiotherapy (EBRT), using high-energy photons (e.g. X-rays) or charged particles (e.g. protons) [15]. Also, external beam radiotherapy is known as the exterior cancer treatment method. In this treatment procedure, a linear accelerator is used to irradiate tumours inside the patient. External beam radiotherapy for deep-seated cancers, for example, prostate cancer, usually are treated with high-energy X-ray photon beams (≥ 6 MeV). Prostate cancer irradiation is challengeable due to the movements, and elasticity (possible volume changes) of the bladder and rectum. Furthermore, it is significant to consider the other processes as some anatomy changes such as weight loss, tumour progression, and shrinkage, causing movements between sessions of the treatments [16]. Also, they can affect the position of the prostate gland which challenges the accurate dose delivery. These changes can result in an under-dose of the tumour and/or overexposure of nearby healthy tissues. One of the ways to minimize the negative impact of the mentioned variations/movements is the use of image-guided radiotherapy (IGRT).

1.2.1. Image-guided radiotherapy

Image-guided radiotherapy (IGRT) is used to ensure more accurate dose delivery to the tumour, minimizing irradiation of surrounding healthy tissues [17]. IGRT provides not only accurate information on the patient and tumour position, nonetheless, it also permits verifying the consistency of actual treatment geometry and plan adjustments to daily changes to achieve better dose delivery [18]. Usually, cone-beam computed tomography (CBCT) is among the imaging techniques routinely used for IGRT. Generally, it permits a reduction in the set-up margins, which lowers toxicity for critical organs with observable, measurable, and fixable movement within or between treatment sessions. [18]. Thus, IGRT consists of an imaging system (e.g. CBCT), which is usually used for a comparison boundary of tumours and organs at risk (OARs) of the images taken before the treatment procedure and images (computed tomography (CT)) used for the treatment planning [18, 19].

1.2.2. Treatment planning

Treatment planning is one of the main steps for the volumetric calculation of dose distribution, using various three-dimensional (3D) treatment planning systems. Basically, CT diagnostic information is used for radiotherapy planning, which could be fused with magnetic resonance images (MRI), or/and positron emission tomography-computed tomography (PET/CT) images [20, 21]. The fusion of various imaging modalities usually leads to improved diagnostic information about the patient's distribution of the internal organs and even changes in physiological functions [22]. For example, MRI can offer a higher resolution of soft tissue data (very valuable information for prostate tumour) (Fig. 2 a)), however, this is not the case for CT images (Fig. 2 b)). Nevertheless, the fusion of CT and MRI scans improves the distinguishability of the soft tissues and bone structures (Fig. 2 c)).

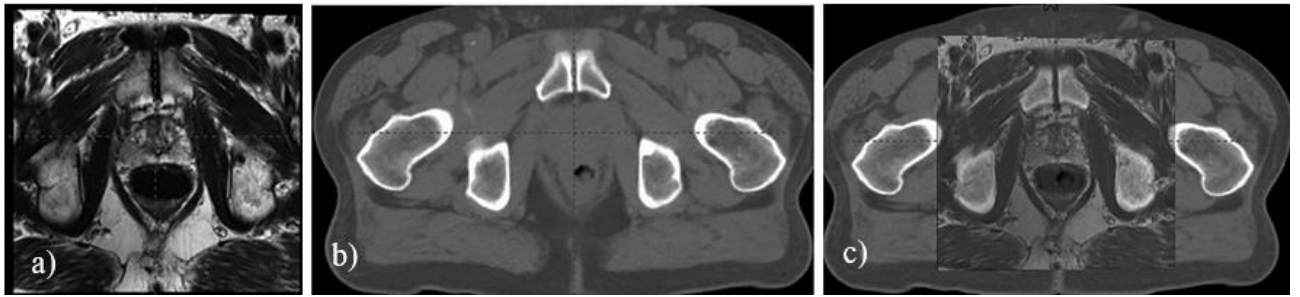


Fig. 2. Diagnostic images representing soft tissues of a) MRI T2WI, b) CT and c) Fused CT and MRI scans [22]

Therefore, multimodal medical image fusion systems are gaining more attention for their important clinical uses, tumour identification, cell categorization, and, of course, treatment planning [23]. In this way radiation oncologist combines modern treatment planning and imaging techniques to provide individualized treatment plans, maximizing tumour control and lowering organs toxicity [24]. Nonetheless, the main parts of the target volume can be distinguished which is an essential delineation step (Fig. 3).

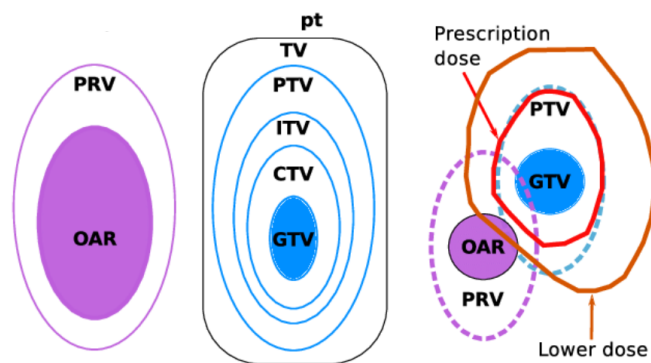


Fig. 3. Schematic view of various target volumes and organs at risk [25]

The main delineated structures for the treatment planning are known as:

1. Gross Tumour Volume (GTV) which represents the apparent range with the greatest concentration of malignant growth and requires treatment for local tumour control.
2. Clinical Target Volume (CTV) including GTV and microscopic expansions at a probability level (also requires irradiation).
3. Planning Target Volume (PTV) is added due to unplanned situations (e.g. organ motion). A treated volume takes into account differences in dimension, form, and location concerning the treatment beam and is defined as the volume receiving a dose important for local cure or palliation.
4. The determination of the Internal Target Volume (ITV) and the Organs at Risk Volume (PRV) are the steps in the planning process. Overlapping volumes may have an impact on both volumes, which could result in unwanted dosage levels in OAR or inadequate PTV coverage [23, 25, 26].

In the case of PCa, the volumes are hardly delineated due to the bladder and rectum possibilities to alter their volume holding or releasing metabolite wastes. This phenomenon leads to possible inaccuracies. The ideal method to lessen these variables may be the usage of the protocol for filling the bladder and emptying the rectum [27].

All the mentioned criteria are very important in choosing a treatment planning technique.

1.2.2.1. Types of the treatment planning

There exist two main sorts of treatment planning: forward and inverse [28]. The main stages of forward treatment planning (Fig. 4 a)) are: 1) setting of planning parameters (dose constraints and limitations); 2) calculation of dose distribution; 3) evaluation of treatment plan, which is generally presented as evaluation of dose volume histogram (DVH). An example of forward treatment planning is known as static three-dimensional conformal radiotherapy (3D-CRT).

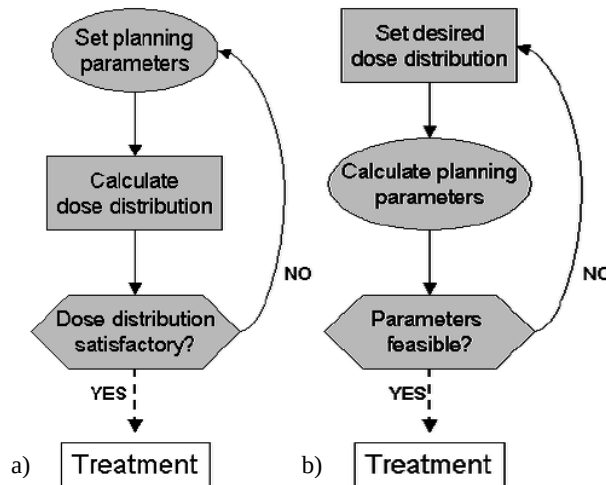


Fig. 4. Schemes of a) forward treatment planning technique; b) inverse treatment planning technique [29]

The second approach, known as the inverse treatment planning, includes several actions to optimize the delivery process (Fig. 4 b)): 1) definition of preferred dose distribution; 2) calculation of planning parameters; 3) review of the parameters. This comprehensive technique is commonly utilized in intensity-modulated radiation therapy (IMRT) and volumetric-modulated arc therapy (VMAT).

Intensity-modulated radiation therapy. IMRT uses tiny beamlets, whose intensity is adjusted to a better fit to the target volume dose coverage, reducing the radiation to the nearby structures (organs at risk). The geometry of multiple beam angles can be used to provide treatment and to optimize dose delivery following predetermined goals (Fig. 5) [30, 31].

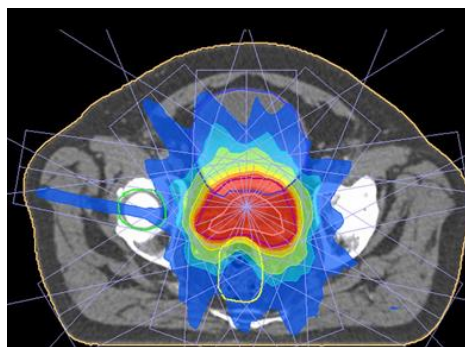


Fig. 5. Dose distribution of IMRT [32]

In comparison with 3D-CRT, IMRT demonstrates decreased toxicity and local disease control with minimal adverse side effects [30].

Volumetric-modulated arc therapy. VMAT is the improved radiation technique that utilizes an ongoing modification of MLCs with dose-rate adjustment and gantry rotation to give the whole dose volume coverage in a specific rotation of set degrees (e.g. half, partial, and/or full arcs) [33]. It is dependent on localization/ cancer type, but for some of the cases, VMAT is more effective at sparing OARs than IMRT, due to enhanced uniformity of dose distribution (Fig. 6).

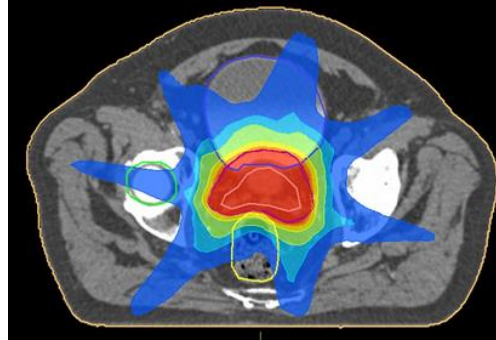


Fig. 6. Dose distribution of VMAT [32]

It is known that for open-design linear accelerators, VMAT has some benefits, such as shorter treatment times and fewer monitor units (MU) [30]. On the other hand, increased low-dose irradiation to the nearby tissues' structures and organs at risk for VMAT treatment plans could be related to a higher risk of developing secondary cancers [34].

A comparison of VMAT and IMRT techniques used for prostate cancer treatment planning showed that VMAT treatment plans (with 1 or 2 arcs) had a better result in rectum sparing than the IMRT plans with a geometry of 8 beams [31]. However, increasing beams number per IMRT plan (from 12 up to 18 gantry angles), the quality of such treatment plans started to be comparable to the VMAT treatment plans [31].

Summarizing inverse treatment planning techniques (IMRT and VMAT), it could be said that today they provide more accurate dose delivery to the target while simultaneously ensuring the sparing of the surrounding healthy tissues in comparison with the 3D-CRT treatment planning technique. Regardless of whether a forward or/and inverse treatment technique is used, the dose distribution could be calculated using various dose calculation algorithms, which guarantee the accuracy of the dose delivery and evaluate the main interaction with matter processes.

1.3. Interactions of photons with matter

The dose distribution in the patient's body is calculated by utilizing an appropriate dose calculation algorithm. An ideal algorithm takes into account all possible physical processes. These processes can be observed during the beam's interaction with the irradiation media [35, 36]. It is known that the photon interaction model with the matter highly depends on photon energy, atomic number, and density of the material. The main types of interaction include photoelectric effect, Compton scattering, and pair creation (Fig. 7).

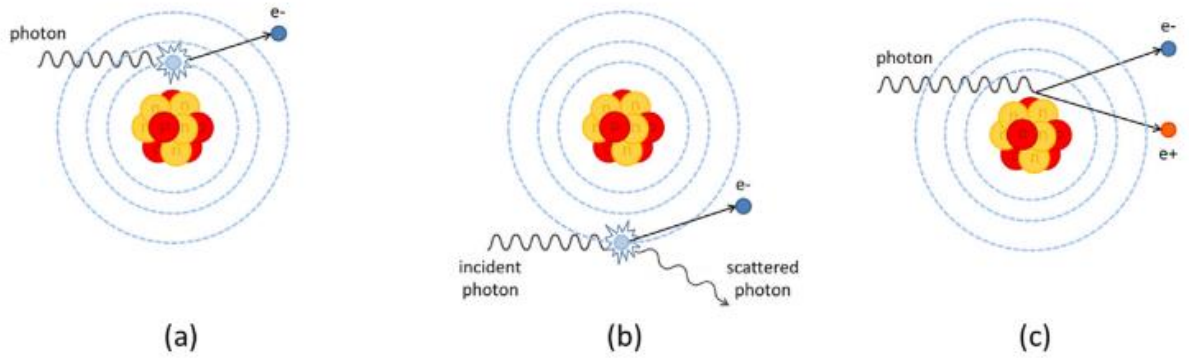


Fig. 7. Radiotherapy's main interaction processes: (a) photoelectric effect, (b) Compton effect, and (c) pair production [37]

When a photon (up to 500 keV) delivers total energy into an electron in the inner shell, the latter is ejected and replaced by a higher shell electron (Fig. 7 (a)). The excess energy is emitted as a characteristic radiation or an Auger electron. The photoelectric effect only happens when the photon's energy is greater than the electron's binding energy. The probability of this effect relies on atomic number Z^3 and energy E^{-3} [37].

When a photon interacts with an electron in an outer shell, the photon loses energy and shifts its path (Fig. 7 (b)). The emitted electron will have the energy transferred from the photon minus the binding energy of the shell. The photon that has been scattered will exhibit a wavelength different from the original photon. The energy given to the electron causes the incident photon to change course and lose some energy. The decrease in energy results in a greater wavelength for the photon, as they both are inversely related [37]. The Compton effect is the most frequent interaction in radiotherapy at energy levels from 6 to 20 MeV [37, 38]. The likelihood of this outcome is dependent on an energy E^{-1} .

When a photon with an energy >1.022 MeV interacts with the nucleus of an atom, it leads to the creation of an electron-positron pair (Fig. 7 (c)). These new particles move through the tissues and release energy. The positron will eventually combine with an electron, resulting in the emission of a photon pair annihilation at the opposite angles. This effect is highly dependent upon Z and E [37].

Moreover, photons' interaction with the biological tissues plays a crucial part in radiotherapy. During the treatment, these interactions can generate $4 \cdot 10^5$ electrons per MeV of incident radiation. Generated electrons typically have energy distributions up to 100 eV, with a peak at 20 eV [38]. The main electron interaction processes are represented in Fig. 8.

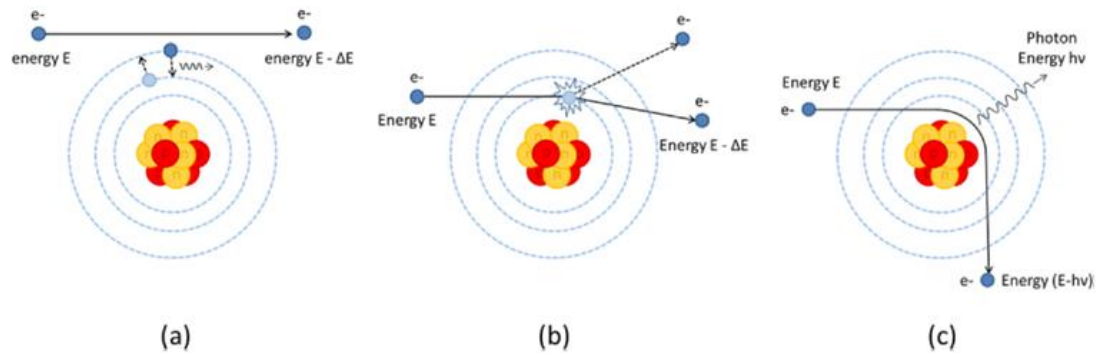


Fig. 8. Main electron interactions in radiotherapy (a) excitation, (b) ionisation, and (c) bremsstrahlung [40]

The excitation (Fig. 8 (a)) – incident electron first raises the atomic electron to a greater energy level, before the electron eventually goes back to its initial state and emits a photon.

Ionization (Fig. 8 (b)) – the incident electron may also dislodge an inner shell electron, and these electrons are capable of dose deposition through subsequent interactions.

Bremsstrahlung (Fig. 8 (c)) – the interaction of the incident electron with the nucleus's electric field results in rapid deceleration and the emission of Bremsstrahlung photons [40].

Thus, knowing and understanding the photon and electron interactions with a matter are crucial steps for determining the dose to the patient during the treatment. The understanding of how photons, and electrons interact with different materials (for example, soft tissues, bones, etc.) is essential for the usage of the dose calculation algorithms.

1.3.1. The dose calculation algorithms

The dose calculation algorithms are classified into three main groups which represent their working principles (Table 1).

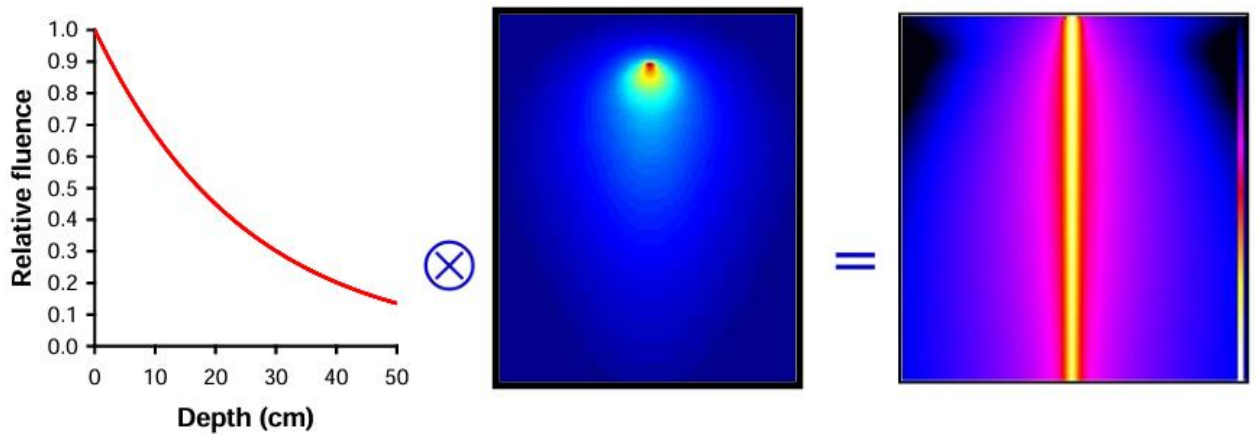
Table 1. The main types of the dose calculation algorithms [35, 41-43]

Classification			
	Type A	Type B	Type C
Definition	Models that neglect to take electron transport variations into account	Models that roughly account for variations in electron transit along the lateral side	Algorithms that rigorously account for the physics causing the dose absorption pathway
Working principle	To transform the dose from a known (calibration) to a current scenario (charge particle equilibrium/transient charged particle equilibrium), applying correction factors.	Convolution superposition modelling (TERMA with kernel) is used to represent dose deposition. Dose modelled separately and in a combined way from a primary beam, head scatter photons, electron contamination	Particle tracks are modelled individually
Advantages	Fast, and accurate in a uniform medium	Sufficiently quick and has acceptable accuracy in every type of medium	The most precise estimator of dosage to heterogeneities

Table 2. The main types of the dose calculation algorithms [35, 41-43] (continued)

Classification			
	Type A	Type B	Type C
Disadvantages	Unreliable in heterogenous medium	The accuracy of measurements is imprecise near the intersections of materials with the significantly different densities	Time-consuming
Algorithm	Pencil beam convolution	anisotropic analytical algorithm (AAA); collapsed-cone convolution;	Acuros XB; Monte Carlo simulation; Linear Boltzmann Transform Equation Solvers

Type A. Type A model inhomogeneities in a patient's body are handled by the pencil beam (PB) convolution algorithms, which adjust for them throughout the single-dimensional journey length along the fan lines. One way to improve the calculation speed and make it clinically viable is by using pencil beam kernels (Fig. 9).

**Fig. 9.** Pencil beam creation (TERMA convolution with point kernel) [44]

This method reduces the complexity of dose calculations from 3D to 2D convolution. By combining point kernels in the depth direction, a 2D representation of the dose distribution is obtained (Fig. 9) [44].

When this type of algorithm encounters areas of different densities or materials within the patient's body, it adjusts the dose delivery to account for these variations. This correction helps to ensure that the dose is accurately delivered to the intended target area within the patient's body [41, 45]. The dose of radiation is spread evenly in all directions. However, non-uniformity correction is necessary to account for differences in density or composition within the irradiated tissue. This correction is simply applied in the longitudinal direction, or depth of the tissue, as opposed to laterally. The correction factor is calculated by converting the mass attenuation coefficient of the material to an equivalent path length. It allows for the adjustment of the dose based on the electron density of the tissue [35, 42].

The pencil beams are often parametrized, and their actual values are determined through a fitting procedure to the measured data [44]. The pencil beam convolution is represented by the equation:

$$D(x, y, z) = \iint \Psi(x', y') \cdot P(x - x', y - y', z) dx dy, \quad (1)$$

here $\Psi(x', y')$ – fluence distribution at a certain specified plane; $P(x - x', y - y', z)$ – pencil beam kernel (Fig. 10).

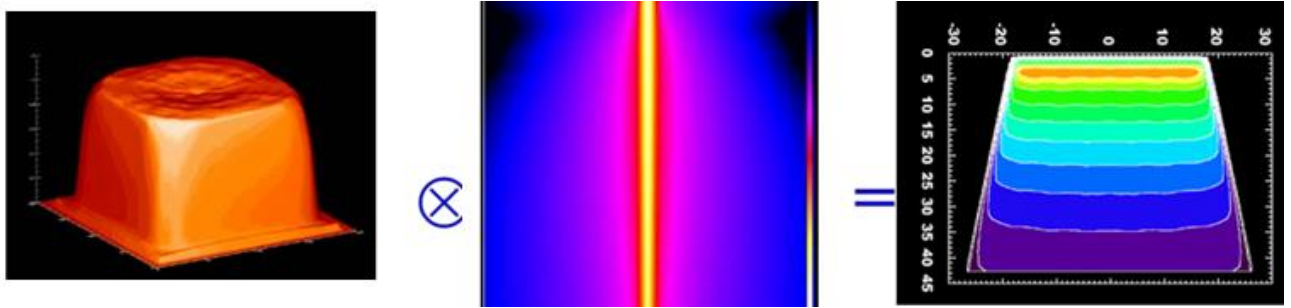


Fig. 10. Dose distribution creation (2D fluence distribution convolved with pencil beam) [44]

In heterogeneous media, the pencil beam kernel is adjusted along the propagation direction by taking into account the density of the voxels through which the beam is passing [44]. This helps to verify that the dose of radiation delivered is accurate and effective for the target area [35].

PBC determines the homogeneity of the lateral dispersion and ensures that all interaction locations are on the pencil beam's central axis. As a result, inhomogeneity correction is only taken into account in the longitudinal direction. The difference in electron density between tissue and water in a mixed environment is considered to scale the path length and determine the value of TERMA. The radiological path length is calculated along the central axis of a pencil beam using kernel values in water [36].

Traditional techniques for calculating dosage, e.g. pencil beam algorithm, perform well in areas of homogeneous tissue, such as the brain. However, greater accuracy is needed for treatments in the head and neck or thorax, that is, in areas with bone, soft tissue, and air cavities. For the treatment of tiny lung cancers, for instance, it is widely acknowledged that the pencil beam method overestimates the dose in the target volume [46].

In initial implementations, there is no scaling performed perpendicular to the propagation direction, making it a type A algorithm. However, nowadays there is a pencil beam model that includes lateral scaling of the kernel, such as in the analytical anisotropic algorithm (AAA) – Type B [35, 44].

Type B. The Type B model considers the heterogeneous influence in both the lateral and longitudinal directions. In four lateral directions, AAA describes the mean heterogeneous impact using Gaussian functions. To simplify and shorten the computation time in collapsed-cone convolution (CCC), a specific number of discrete elements are used in place of the kernel, and the average for every component is employed. When applying an inhomogeneity correction, CCC is more accurate than AAA. It suggests that in a diverse setting, CCC manages lateral scattering better than AAA [35]. Therefore, these algorithms take into account the non-uniform impact of both the longitudinal and lateral positions [36].

The AAA features the distinct creation of a model for primary photons, dispersed extra-focal photons, and contaminated electrons. It uses spatially variable MC-derived convolution scatter kernels. The AAA adjusts scatter kernels based on electron density in the lateral direction and dose buildup in the beamlet direction to address inhomogeneities. The dose deposition of the photon and electron combination are superposed to yield the dosages. The advantage of the AAA algorithm is that it

calculates very quickly and has an accuracy that is superior to the pencil beam convolution (PBC) method and comparable to the CCC algorithm [36]. Nonetheless, considering the excellent computation efficiency, it has been noted that the dose estimation error utilizing AAA may surpass 5 % for heterogeneous tissue margins [47]. This is partly due to the transmitting energy since the dosage kernel does not take into account the physical interactions between individual particles [48].

At every given calculation point in the patient, the final dose $D(\tilde{X}, \tilde{Y}, \tilde{Z})$ is obtained by superimposing the individual dose contributions [49].

$$D(\tilde{X}, \tilde{Y}, \tilde{Z}) = \sum_{\beta} (D_{ph1,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z}) + D_{ph2,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z}) + D_{cont,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z})), \quad (2)$$

here $D_{ph1,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z})$ – dose contribution from the primary photons; $D_{ph2,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z})$ – extra-focal photons; $D_{cont,\beta}(\tilde{X}, \tilde{Y}, \tilde{Z})$ – contaminating electrons.

Since the scatter kernels have Gaussian shapes and the photon and electron fluences, as well as the energy deposition functions, can be treated as uniform across the beamlets' cross-sections without significantly altering the eventual dose distribution, most of the convolutions that appear in superposition can essentially be completed analytically [49].

It is known that the CCC algorithm uses an archive of mono-energetic kernels to calculate energy kernels which deposited by a spectrum beam that contains multiple types of energy. The kernel, consisting of a finite number of polar angles for the primary beam, is analytically expressed in polar coordinates. Each radially oriented line represents an axis of a cone, and the point of interaction is located at the apex of these lines [36]. Discretising the point kernel is another approximation to manage inhomogeneities and performance. The kernel is discretized into around 100 directions, with each direction denoting a cone whose centre is the point at which all energy is crushed [44]. The inverse square dependence is eliminated when the energy in a cone collapse into the central ray. With larger density employed in the forward direction for high-energy beams, the cone distribution is not isotropic. A small number of cones control backscatter, guaranteeing a large energy deposit [44].

Since the convolution integral is commutative, altering the order of the functions does not affect the outcome:

$$D(r) = \int T(r') \cdot P(r - r') dr, \quad (3)$$

$$D(r) = \int P(r') \cdot T(r - r') dr, \quad (4)$$

here $T(r')$ – TERMA at specified plain; $P(r - r')$ – beam kernel.

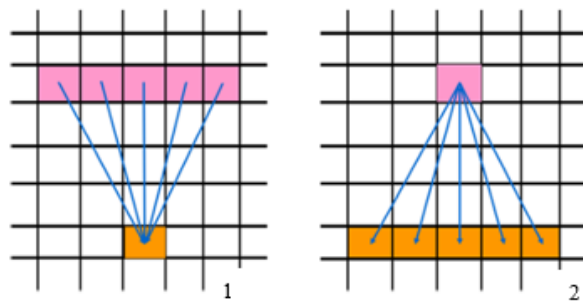


Fig. 11. 1 dose delivery, 2 representation of interactions [44]

The deposition voxel receives an accumulation of energy, or TERMA, from the surrounding voxels (Fig. 11. 1). The total amount of radiation in the voxel is found by adding up all the contributions. Fig. 11.2 A voxel's TERMA extends to its neighbouring voxels, and every contribution from interaction points must be considered.

The CCC algorithm has a computational resource-saving benefit over conventional convolution algorithms. In conventional convolution algorithms, each voxel is calculated individually, which increases the computational time. Meanwhile, CCC groups neighbouring voxels into cones and process them together. Thus, it reduces the number of operations required and significantly speeds up the computation. In an inhomogeneous medium, the computation time is proportional to MN^3 where M represents the quantity of cones and N is the quantity of voxels on a single side of the computation volume. This is a much more efficient method compared to traditional convolution algorithms, which have a computation time proportional to N^3 [36]. Nevertheless, it becomes less accurate when there are significant variations in density and when is calculated the lateral beam spread. It was proved that it is not as accurate as the Monte Carlo (MC) algorithm. They agree that there is a difference between CCC and Monte Carlo algorithms, the CCC algorithm provides a higher overestimation of the average tumour dose for the gross tumour volume or planning target volume for the gross tumour volume (GTV) or planning tumour volume (PTV) by ~3 %, even if when employing 3D conformal radiation therapy (3D-CRT), it closely resembles the MC simulation [50]. The other study [51] showed that there could be a big clinical impact from the discrepancies between the CCC and Monte Carlo algorithms. However, with 4-dimensional dosages, variations in dosimetry amounts become less significant.

Type C. The most advanced method that incorporates practically all physical characteristics known for microscopic radiation–tissue interactions is the principle-based algorithm. The accuracy of alternative dosage calculation algorithms is compared to the Monte Carlo (MC) approach. It can even measure almost incalculable amounts, such as the dosage contribution from various photon scattering orders [36]. Dose calculation algorithms, which are the gold standard, take into account the physical interactions between particles by utilizing empirical formulas and experimental data. Nevertheless, because it must model each particle interaction, MC calculation takes a long time [47, 52]. By modelling particle tracks using probability distributions, the statistical simulation method makes it possible to calculate parameters, for example, beam intensity, energy range, and distribution of absorbed doses [53]. However, it is complicated to solve statistical random sampling which consists of multi-dimensional integral equations. Due to this reason, it is implemented into digital computers to help solve problems using various programs and codes. In the majority of cases for applications involving radiation and medical imaging, the Monte-Carlo EGSnrc code is utilized. The Electron Gamma Shower (EGS) code created at the Stanford Linear Accelerator (SLAC) serves as its foundation. Nonetheless, the EGSnrc code can simulate electron, positron, and gamma transport with kinetic energies between 1 keV and 10 GeV. The package consists of user scripts with intuitive graphical user interfaces that make it easier to calculate patient doses and simulate the treatment heads of medical linear accelerators. The DOSXYZnrc code made possible the computation of dose deposited in voxelized geometries, including models of patients created from CT data [54, 55]. Decomposing radiation into photons, electrons, and positrons solves the problem of ionizing radiation transport. Several elements in each voxel are taken into consideration while simulating the transport of quantum particles through the linear accelerator (LINAC) head and into the human body. Particles interact with atomic shell electrons and the electromagnetic field of atomic nuclei to create ionization

events [46]. Two main steps in the Monte-Carlo simulation procedure are: a) a randomly generated number of seeds in the target, which starts the simulation process, both the accelerator gantry head and the collimator system are traversed by the radiation beams; b) the patient's body receives a dose distribution from the collimated beam particles as they pass through the head of gantry. The correctness of the events is mostly based on how many events it generates; statistical uncertainty is inversely proportional to the square root of the quantity of events that are evaluated [35].

Similar to the Monte-Carlo approach, the algorithm Acuros XB (AXB) uses Boltzmann transport equations (BTE) to simulate every physical process involved in beam particle creation [56]. Acuros XB mathematical problems are solved using numerical techniques, which yield outcomes that are similar in accuracy to those of the Monte-Carlo algorithm [52]. The AXB patient's dosage calculation involves three steps: 1) transporting fluence from the source model, 2) computing fluence for scattered photons and electrons, and 3) determining the eventual dose received to the patient. The cross-section of each element in the calculation grid is required by the AXB [57].

The dose D_i in grid voxel i is calculated by equation [58]:

$$D_i = \int_0^\infty dE \int_{4\pi} d\hat{\Omega} \frac{\sigma_D^e(\vec{r}, E)}{\rho(\vec{r})} \Psi^e(\vec{r}, E, \hat{\Omega}), \quad (5)$$

here the latter includes discretisation of the spatial ($\vec{r}$), energy (E), and angular ($\hat{\Omega}$) variables; σ_D^e – macroscopic electron energy deposition cross section; ρ – the material density; Ψ^e – angular electron fluence.

Acuros XB computes the electron fluence that is dependent on energy by using the patient's body properties – derived from the datasets of Hounsfield Unit (HU) in computed tomography (CT) [58]. The AXB involves the overall cross-section of all elements within the calculation grid. AXB used in the treatment planning system (TPS) *Eclipse* uses a lookup table to identify material composition and density of every single voxel in the image grid, including five biological and sixteen non-biological materials [57].

The use of the linear Boltzmann transport equation (LBTE) provides a more straightforward method of calculating in-patient doses. Also, it characterizes the behaviour of the distribution function of each specific type of particle in the phase space as a result of various processes involving mutual relations [56, 59]. The LBTEs result in a series of integrated kinetic partial integro-differential equations after accounting for species interactions within the radiation beam. These equations require the phase space to be discretized in spatial, angular, and energy ranges to be numerically solved [45, 41].

In addition, evaluating the Møller scattering is the sole method that can genuinely deposit dosage in the medium at the location of interest, whether or not it produces delta rays. The energy from the primary particle is transferred by all other processes to a secondary particle, which then keeps on transporting. The absorbed dose can be calculated using [59, 60]:

$$D(r) = \frac{p_e(r)}{p(r)} \int_{4\pi} \int_{4\pi} \int_0^\infty \int_0^\infty \tilde{\sigma}_M(E'_e, E_e, \Omega'_e \cdot \Omega_e) \Phi_e(r, \Omega'_e, E'_e) \cdot (E'_e - E_e) dE_e dE'_e d\Omega_e d\Omega'_e, \quad (6)$$

here $p_e(r)$ – the electron density at position r ; $p(r)$ – the physical density of the medium; $\tilde{\sigma}_M(E'_e, E_e, \Omega'_e \cdot \Omega_e)$ – The differential Møller scattering cross-section of an electron travelling initially with energy E'_e in direction Ω'_e and finally with energy E_e and direction Ω_e ; $\Phi_e(r, \Omega'_e, E'_e)$ – the electron fluence at position r , with direction Ω'_e and energy E_e .

All Møller scattering events at various initial energies, final energies, and orientations are calculated to determine the radiation dose deposited. Nevertheless, deterministic computations are generally faster than MC simulations and yield comprehensive radiation field distribution data without any problems arising from statistical uncertainty [59].

According to the research [61] on dose calculation accuracy, for all TPS, dosage discrepancies between measurement and computation are often greater for the smaller areas: ~1.5 % in a 12 mm field, versus <1 % in a 60 mm field. Reduced heterogeneous medium density, smaller field size, and deeper heterogeneity often result in greater discrepancies between observed dosage and various estimations of the TPS. For the pencil beam (PB) algorithm, these variations can reach up to 30–40 % for small field sizes. Nonetheless, it was noticed that MC calculations demonstrate a strong agreement with the measured dose for all field sizes and depths analysed. Also, it was found that Acuros XB and Pinnacle algorithms used for the dose distribution calculation inside the lung exhibited the best alignment with the MC code, whereas AAA and PB showed the biggest disagreement [61].

Whatever calculation algorithm will be used for the dose distribution calculation it is known that the algorithms used are accepted and show good agreement for in-field (planning target volume – PTV) dose evaluations, but it becomes challenging for the irradiation doses of out-of-field regions estimation [62].

1.4. Understanding of out-of-field doses

The International Commission on Radiological Protection (ICRP) states that it is crucial to estimate out-of-field doses in order to evaluate the entire stochastic risks and sufficiently justify radiation exposure [63, 64]. Since it is well-known that deterministic effects only are common for high doses, whereas stochastic effects are related to low doses which appear in years after therapy [65, 66]. However, concerns about the late treatment-related side effects have a significant role, especially as modern radiotherapy techniques are commonly used and lead to an increased life expectancy after the treatment [64]. Even the modern treatment planning techniques are used, it is known that the dose calculation algorithms used in treatment planning systems (TPS) do not calculate out of the field edge (Fig. 12) of PTV more than a few centimetres [64], and tend significantly underrate the dose [62]. Also, it consistently understates the out-of-field dose for treatments using CyberKnife, IMRT, VMAT, and 3D-CRT [66]. Due to this reason, estimation of regions outside the treatment field are very important and challenging step, especially evaluating irradiation of healthy tissues and organs at risk (OARs), which usually are in close vicinity to the irradiating volume.

Huang et. al. [69] study showed an underestimation of the out-of-field doses for IMRT treatment plans. Moreover, a mean TPS miscalculation was 50 % (within the range of 1 - 30 cm), and it was observed that the measured value and differences between calculated and measured values increased by expanding the distance from the treatment field edge [69].

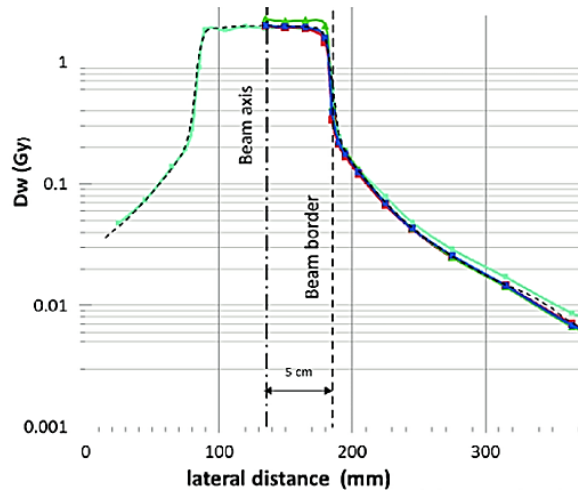


Fig. 12. Out-of-field dose profile [68]

Meanwhile, Howell et al. [70] showed that the treatment planning system miscalculated the dose by a mean of $40\% \pm 20\%$ within the range starting with 3.75 to 11.25 cm from the treatment field edge. The underestimation of the dose by the TPS is more significant as the distance from the treatment field edge expands (Fig. 13).

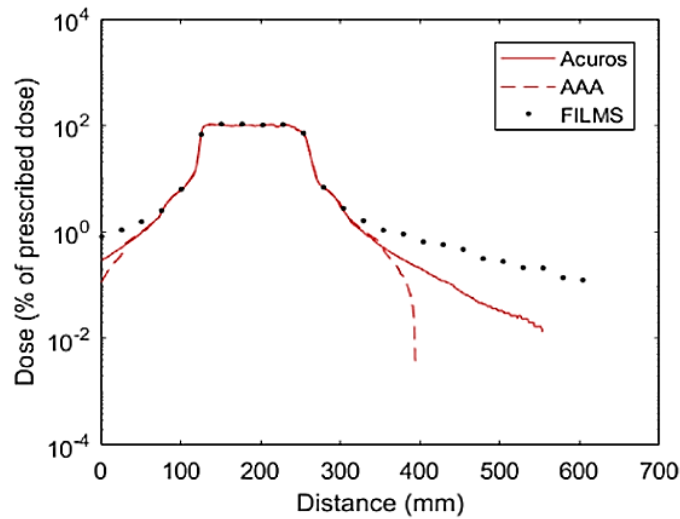


Fig. 13. TPS *Eclipse* VMAT algorithms calculated and radiochromic measured doses [66]

A paediatric phantom-based study revealed (Fig. 13) [66] that in comparison between dose calculation algorithms (Acuros and AAA) and 2D dosimetry radiochromic films the dose distribution for the planning tumour volume (PTV) had the best agreement, while the differences between studied algorithms were observed highest in a few centimetres from the field edge. It can be mentioned that the AAA algorithm does not consider head leakage modelling, due to this reason it could lead to the great miscalculation of out-of-field doses [66]. Another paediatric anthropomorphic phantom study [71] using thermoluminescence dosimetry versus TPS showed that the out-of-field dose values were greater for the experimental measurements with thermoluminescence dosimeters (TLDs). On the other hand, it was observed that the measured out-of-field doses for the IMRT treatment planning technique were approximately 7 times higher in comparison with the 3D-CRT technique planned treatment plans [71].

Another similar study [72] showed that dose calculation with TPS was underestimated in comparison with p-type diode experimental measurements (Fig. 14). It was found that the assessment of dose contribution utilising the treatment planning system (TPS) was inadequate in areas outside the treatment field (for dose calculation algorithm AAA doses were underestimated by 38.80 %) where doses are quite low and gradients are high. The study indicated that the underestimation of out-of-field doses was significant as the range from the field edge increased from 2.5 cm to 7.3 cm and changed from 0.6 % to 39.63 % [72].

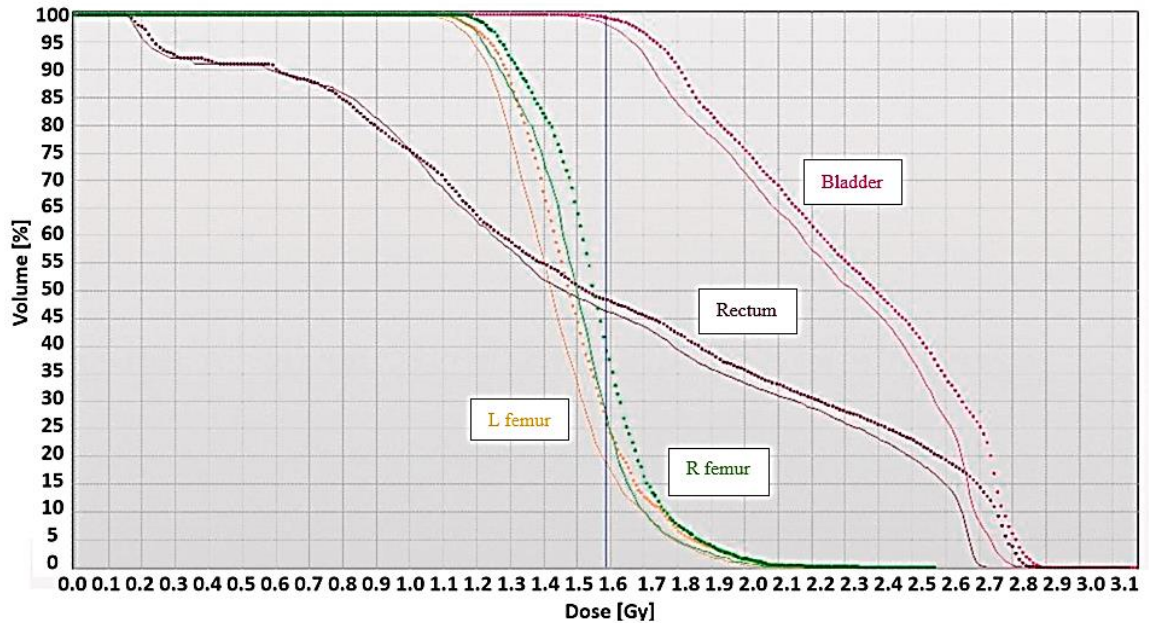


Fig. 14. Dose-volume histogram for the comparison between TPS dose calculation (line) and dose measurements using a p-type diode detector (dotted line) for the organs at risk (OARs): femur, rectum, and bladder [72]

The study of TPS versus thermoluminescence dosimetry (TLD) experimental measurements showed the same tendency that the calculated doses at specific points were underestimated and differed by an average of 35 % [73]. A comparison of two different calculation algorithms (AAA and PBC) calculation with TLD experimental measurements [74] revealed that both algorithms underestimated out-of-field doses, especially using a small (3x3) cm² irradiation field. Analysis of the results showed that the difference between TLD measurements and the PBC algorithm for a (10x10) cm² field was equal to 39.40 %, whereas for the AAA algorithm, the maximum difference was equal to 12.06 %. Therefore, the AAA algorithm demonstrated a better accuracy in predicting doses up to 12 cm from the field edge across all the irradiation fields [74].

Additionally, the assessment of the collapsed cone convolution (CCC) algorithm in prostate cancer treatment revealed increased exposure in the brain, particularly in the hippocampus region, with doses reaching up to 0.080 Gy and 0.099 Gy in the two treatment plans delivering 60 and 66 Gy of the prescribed dose to the tumour. This highlights the importance of monitoring distant out-of-field doses, as measured using TLDs, to ensure patient safety [75].

Even though the out-of-field dose is often less than 4 Gy, there are still unanswered concerns regarding the possible link between the low dose exposure and unfavourable outcomes, especially for radiosensitive tissues/organs [65, 67]. It was represented that the cases of secondary primary malignancy (SPM) can be up to 20 % of radiotherapy patients [69]. It was discovered that SPM

appears near the radiation-exposed edge from 2.5 cm inside to 5.0 cm outside the irradiated volume. Also, it was noticed that secondary cancer could be developed at far locations outside the treatment edge [69, 76]. Nevertheless, the connection between radiation therapy and the risk of developing a second cancer in organs outside of the treatment field is not well-established. The main factors contributing to out-of-field doses include internal patient scattering, apparatus head leakage, collimator, and possible treatment room scattering effects [77]. The main factor remains internal body scattering because it contributes 70 % of the out-of-field doses and lasts up to 25 cm from the field edge for conventional radiotherapy techniques. In the IMRT treatment planning cases, the main contributor of out-of-field doses is machine scatter/leakage, which is equal to 65 % [78].

To improve risk assessment for both stochastic and deterministic effects, it is recommended to incorporate prospective out-of-field treatment planning systems for dosimetry calculations and data collection. It is important to note that the choice of calculation algorithm can have a significant impact on the accuracy of dose calculations in out-of-field areas [72]. Due to this reason, dosimetry measurements could be an essential step for the simulation of possible realistic situations in radiotherapy.

1.5. Dosimetry

Dosimetry is usually known as various experimental measurements, calculations, or computational data usage for radiation dosage quantification.

A variety of significant factors are considered for choosing a suitable dosimeter for the irradiation dose measurements. Precision, variety of absorbance of energy also energy dependence within various ionizing energy as well and simplicity to employ can be considered to be the most important characteristics [79]. Conventional dose testing techniques including the ionization chambers, TLDs, and radiochromic films are still used for the dose measurements by many oncology departments [80]. In addition, various anthropomorphic or computational phantoms could be used for the simulation of irradiation conditions as much as possible realistic.

1.5.1. 1-dimensional dosimetry

One-dimensional (1D) dosimetry refers to the dose distribution at a specific point by measuring ionizing radiation energy deposition. 1D dosimeters (e.g. ion chambers, thermoluminescence dosimeters) are used to determine the absorbed dose at one particular location along a certain axis. It provides the dose distribution in a single dimension [81].

Ionisation chambers (IC). IC are used for absolute and reference dosimetry in clinical radiotherapy [82]. The dosimeters can be classified into three main types: cylindrical, free air, and parallel plate ionization chambers (Fig. 15). Each IC is composed of a chamber containing gas with two electrodes of opposite charge, and an electrometer. The working principle can be explained as the electric field created among the electrodes accelerates the ions produced by radiation towards the electrodes for collection. The electrometer detects and measures this charge, which can then be converted into an absorbed dose [83]. These kinds of dosimeters are used for reference dosimetry [84].

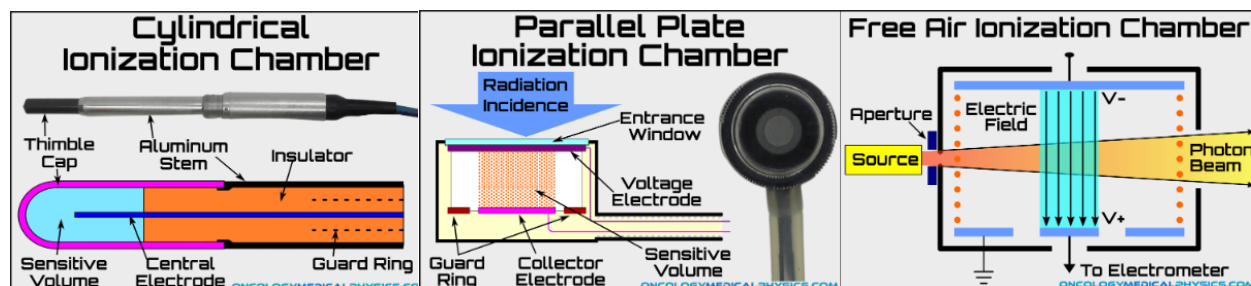


Fig. 15. Types of ionization chambers [84]

For diagnostic radiology reference dosimetry using parallel plate ionization chambers (Fig. 15) that are calibrated to air Kerma is a widely used method for X-ray beams from 40 kV to 300 kV or electrons. This approach enables accurate and real-time dose measurements. A new dosimetry method using IC calibrated to ^{60}Co absorbed dose to water has been suggested, with specific coefficients available for accurate dose assessment [85]. For clinical reference dosimetry where energies are above 6 MeV the Cylindrical ionization chamber is used. This benefit is due to the construction because the effective point of the measurements is in the front of the chamber. The free air IC is essentially linked to the absorbed dose because it serves as the definitional tool for the Roentgen unit [84, 86].

Depending on the design of the ionization chambers, measurable dose intervals differ. One example is the Farmer ionization chamber, which can accurately measure doses per pulse up to 0.91 mGy without reaching saturation and a maximum dose rate of 10 Gy/s with 99% saturation [87]. In comparison, the Advanced Markus IC handles doses per pulse up to 5.56 mGy with 99 % collection efficiency [82].

Dosimetry with IC is widely used in radiotherapy for the reference dosimetry, percent depth dose distributions, and this is highly accurate ($\pm 1\%$), providing real-time dose measurements. Nevertheless, it has limitations, since it requires corrections, and accredited dosimetry calibration [84].

Thermoluminescence dosimetry (TLD). Thermoluminescence dosimeters (TLDs) are another one-dimensional dosimetry approach. Benefits like the small size for measurements inside phantoms, nearly equivalent to tissue, and sensitivity made them extraordinary for dose monitoring and measurements. TLD-100 (LiF:Mg,Ti) can accurately measure doses ranging from 1 mGy to 10 Gy with a precision better than 3 %. However, at doses above 10 Gy, TLD-100 shows a supralinear response [85]. TLDs are small crystals that after the irradiation store the energy. It is a passive dosimeter because it needs to be heated to release energy in the form of light, which is measured to determine the dose of radiation received [83]. TLDs are favoured because they can measure radiation exposure cumulatively over an extended period, which makes them appropriate for brachytherapy, and individual dosimetry.

LiF:Mg,Ti is the common material used for TLD measurements and is available in a variety of forms and dimensions, including rods with a dimension of 1 mm and chips with a cross-sectional area of 3.2 mm by 3.2 mm. CaF₂:Mn, LiF:Mg,Cu,P is more often used in research laboratories for individual and environmental dosimetry due to the better replicability linearity of the registered data [88]. Every TLD dosimeter with different compounds has its own characteristics (Table 2).

Table 3. TLD dosimeters [89]

TLDs	Density ρ , g/cm ³	Z_{eff}	Glow peak temperature, °C	Emission, nm	Sensitivity (TL vs LiF)	Fading off at normal temperature
LiF:Mg,Ti	2.6	8.31	235	410	Reference	3-12 months (5 %)
LiF:Mg,Cu,P	2.5	8.31	200	370	30	3 months (2 %)
CaF ₂ :Mn	3.18	16.90	300	495	10	Up to 4 weeks 25 %

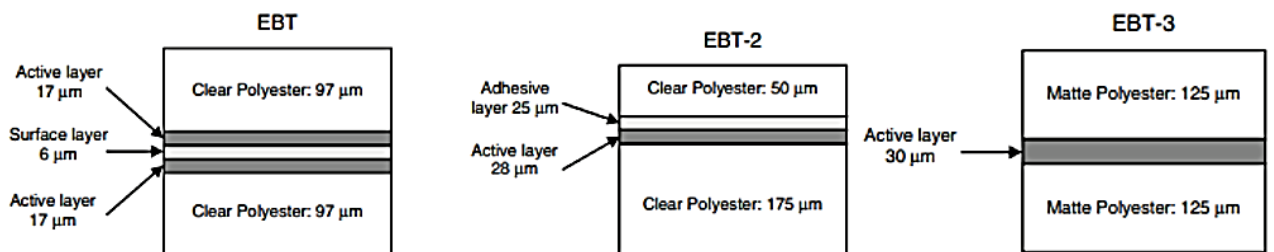
Each, LiF:Mg,Ti and LiF:Mg,Cu,P are based on LiF, nevertheless, there is a significant variation in sensitivity due to the differing dopants. The LiF:Mg,Cu,P possesses an extremely high sensitivity and responds effectively in low-dose applications. Thermoluminescence dosimeters utilizing calcium are particularly effective in detecting low levels of radiation in the mGy range. However, these dosimeters are not widely used in regular medical practices due to their substantial energy dependency [89].

1D dosimetry measures radiation dose in a single dimension, providing high-resolution depth information but lacking accuracy for the complex dose distribution. On the other hand, 2-dimensional (2D) dosimetry offers a more accurate representation of dose distribution for the complex geometry of the treatment fields but may have lower resolution and potential inaccuracies in small-scale dose variations.

1.5.2. 2-dimensional dosimetry

2-dimensional (2D) dosimetry provides the ability to analyse and measure the 2D dose distribution. It mainly utilizes radiochromic films which play a key role in quality assurance, dose verification, and treatment planning processes within the field [90]. Radiochromic films are particularly desirable for radiation dosimetry and quality assurance because they exhibit a mild reliance on energy, good spatial image resolution, and close resemblance of tissues. They change the colour by polymerization of the active layer (Fig. 16, which results in the formation of dyes inside the film, eliminating the demand for an extra chemical manufacturing process [91, 92].

Therefore, the high degree of spatial resolution, nearly equivalent to tissue, insignificant energy dependence, angle independence, constant response in extended doses, brief water immersion, and inexpensive cost of radiochromic films make them practical for two-dimensional dosimeters in radiation oncology [91].

**Fig. 16.** Examples of the radiochromic films (EBT, EBT-2, and EBT-3) used for external beam therapy [83]

The dose ranges from 0.01 to 20 Gy could vary for the EBT series films (Fig. 16) [91, 93]. It is known that every film must be read out no earlier than eight hours after irradiation because of the rather sluggish polymerization reaction. However, because polymerization is still ongoing and the films are continuing to darken, they must be read out within twenty-four hours. They should be kept

at the same temperature through irradiation and reading as they are also temperature-sensitive. Keeping the film calibration and readout steady to this minimizes inaccuracy by up to 10 %. Thus, due to the high spatial resolution, strong energy sensitivity radiochromic films, and convenience of usage during experiments, they can be applied to various fields from radiotherapy plan verification to various dosimetry methods (e.g. micro dosimetry) [83, 91, 94].

The main characteristics of 1D and 2D dosimetry are depicted in a Table 3. The highest observed accuracy is related to ionization chambers usage. However, the smallest number of limitations are represented by radiochromic films.

Table 4. 1D and 2D dosimeter comparison [83, 84, 85, 89, 91, 93]

Characteristics	1D dosimetry		2D dosimetry
	Ionization chambers	Thermoluminescence dosimeters	Radiochromic films
Accuracy	± 1 %	± 3 %	$\pm(2-5)$ %
Utilization	Reference, absolute dosimetry; Percent depth dose measurements; Beam calibration	Personnel dosimeters; Point measurements	Planar dose distributions; Phantom measurements; Quality control; Portal imaging
Advantages	Easy to use; Instant readout; Low energy dependence	Small size; Various forms; Linear response up to 10 Gy	Best spatial resolution; Large area measurements; Tissue equivalent; Very thin
Limitations	Size limitations; Accredited Dosimetry calibration is required; Corrections are required; Cables for connections are needed; High high-voltage source is necessary	Delayed readout; Signal loss over time; Thermal suffering; Total erosion after reading; Time-consuming (readout and calibration)	Delayed readout; Requires calibration

Regardless of which dosimetry method is used, the environment in which the measurements are performed is one of the key steps, as a result of which efforts are made to reproduce and simulate real exposure conditions as much as possible. Various phantoms are commonly used for this purpose.

1.6. Phantoms

In general phantoms are made to improve the accuracy of radiation dosimetry measurements by creating a ‘model’ that as much resembles the human body as feasible. The main classifications of phantoms are known as: 1) Physical phantoms (water phantom, solid-state phantoms, anthropomorphic phantoms) are actually used to mimic the anatomy of tumours and/or the body to solve the particular imaging or therapy problems, and 2) computational individual phantoms, which are program-based representations of the patient's body or specific body components [95].

Water phantoms are used for the beam profile acquisition, dose assessment, commissioning, and quality assurance tests of linear accelerators, machines, and treatment planning system stems (TPS) because they are widely available, accurate, and reasonably priced [96]. Also, it is known that water is the gold standard for dosimetry analyses for the photon and electron beams. Moreover, it is feasible to measure the amount of ionizing radiation at particular depths as the density of water during treatment is similar to that of the soft tissues. Usually formed like a cube (Fig. 17), the phantom has a paper-thin polymer surface in which a dosimeter can be inserted [97].



Fig. 17. Water phantom for measuring the distribution of dose [98]

The main recommendations for the water phantoms are 1) recommended size of more than (30 x 30 x 30) cm; 2) the phantom should be expanded to the maximum field used on the measurement depth by at least 5 cm by each of the four corners; 3) the window needs to be at least 10 cm x 10 cm and have a thickness ranging from 0.2 cm and 0.5 cm [97].

Solid-state phantoms (Fig. 18) in comparison with a water phantom could be said to be easier to use. These phantoms are recommended in radiotherapy for routine quality assurance testing [99]. The International Atomic Energy Agency (IAEA) initially recommended polymethylmethacrylate (PMMA) as an alternative to water replacement, which is quite frequently used in radiation dosimetry. These solid-state phantoms are associated with the attenuation and scattering properties of water, making them useful for dosimetry applications [96, 97].



Fig. 18. Solid-state phantoms usually are represented as slab phantoms [101]

These phantoms could be used for the energies up to 10 MeV, while for low-energy radiotherapy measurements, the measured dose uncertainty is up to 1 %. Slabs can be made from different materials such as PMMA, polystyrene, and plastic. The main point is to achieve equivalent to water characteristics [97, 102].

Even it seems that water phantoms and solid-state phantoms have their own advantages, however, the main lack of these phantoms is that they do not simulate different densities environment, and hardly recreate the real irradiation environment. Due to this reason instead of simplified water and solid-state slab phantoms are used anthropomorphic phantoms.

Anthropomorphic phantoms. The first example of the anthropomorphic phantom was fabricated with many polyethylene components, including cross sections with circles and ellipses. Many polyethylene tubes have been considered along the axis of the body. Each section has been compared to an equivalent anatomical part, such as the abdomen and limbs. Theoretically, for an object to be tissue equivalent in terms of both photon absorption and scattering, it should have a comparable

atomic number, inhomogeneity of the tissues, and electron density like the human body tissues. There are multiple categories for this type of phantom, including physical and computational anthropomorphic phantoms [103, 104].

Physical anthropomorphic phantoms are formed by creating anatomic geometric structures and simulating biological characteristics, including dimension, form, density, and radiation interaction with matter. The phantom is a perfect model for radiation therapy treatment testing since it mimics the features of the human body and was built from an anonymized CT scan. Data collection, structure segmentation, tweaking of visualizations, and additive manufacturing using materials that are comparable to tissues are all steps in the process [105, 106]. The complexity of producing a perfect phantom is related to tissue or organ structures because some of the organs have many different surrounding small enough tissues that are hard to mimic (e.g. ligament, tendons).

Traditionally fabricated anthropomorphic phantoms for radiology are quite costly and usually are constructed from acrylic or ceramic materials. Today as an alternative is widely used 3D printing technology for human anatomy and organ shape imitation and anthropomorphic phantom fabrication [102, 107, 108]. Several studies that considered the movement of inter-fraction organs showed that the anthropomorphic phantoms that were used to scan and apply image-guided radiotherapy (IGRT) scenarios were suitable. The focus is on the actual movement and interaction between various organs, just as it occurs within the patient's receiving treatment. Other multimodal phantoms are less common than deformable lung phantoms, especially those involving the pelvic area (Fig. 19) [109-111].

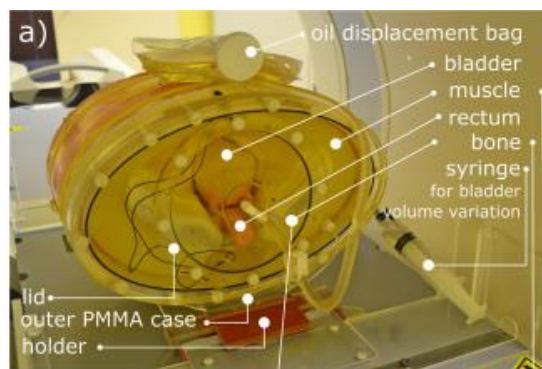


Fig. 19. The ADAM-pelvis phantom was placed in a CT table and measured using a 3D-printed holder [110]

The polymethylmethacrylate ADAM-pelvis phantom is fully assembled, ready for testing, and intended to treat actual people. It has a bladder that is externally attached by a tube, enabling manual volume adjustments with a syringe. The interior of the rectum is accessible through a second opening at the lower end. By increasing the volume of the silicon balloon, the rectum size can be increased by injecting it with liquid or air [110]. Measuring organ doses within physical anthropomorphic phantoms offers major advantages over computational methods since it does not require observation of a specific photon's spectrum energy range or irradiation geometry [111].

Computational anthropomorphic phantoms. There is known three primary types of computational anthropomorphic models accessible (Fig. 20.).

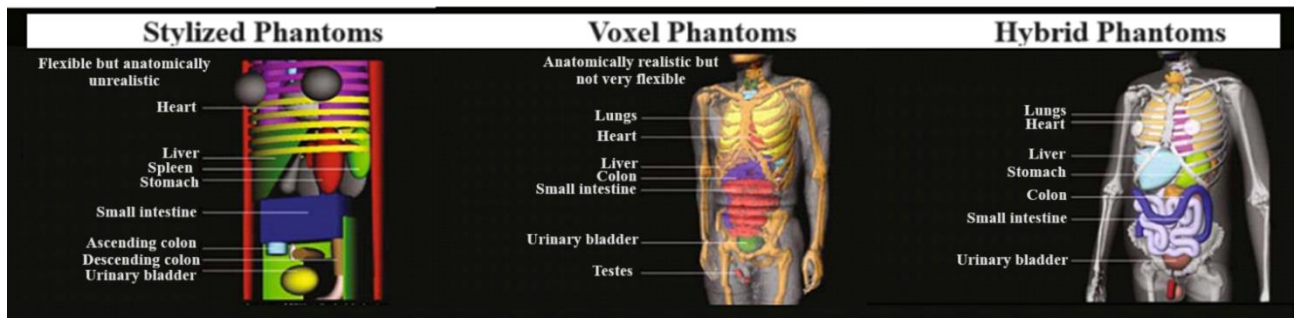


Fig. 20. Examples of stylized, voxel, hybrid male phantoms [112]

Stylized phantoms are utilized in many standard datasets for dosage and risk levels and are essential to radiation dosimetry. These 3D geometric areas represent organ and body regions, but because they may be adjusted to account for differences in organ terms of size, body shape, and extremities positions, they frequently lack anatomical realism. While three-dimensional matrices of voxels with unique organ identities, appearances, and densities are known as voxel phantoms. Because the CT or magnetic resonance imaging (MRI) slices are segmented, they provide a high level of morphological realism [112, 113]. A combination of voxel and mathematical models provides hybrid phantoms, which are more accurate simulations of biological elements such as organs and blood vessels. They provide faster computation since they require fewer voxels than voxel phantoms. Additionally, hybrid phantoms provide greater flexibility in adjusting organ position, size, and shape to accommodate to a certain anatomical variation. They can mimic imaging modalities like CT and MRI, which increases the accuracy of diagnosis and treatment planning [114, 115].

1.7. Literature review summary

Radiotherapy treatment planning is a complicated process that requires the use of dosimetric tools such as ionizing chambers, radiochromic films, and thermoluminescence dosimeters. These tools can be used for both in vivo and in vitro dosimetry, but when it comes to in vivo applications in external beam radiotherapy, phantoms are often used. The most frequent types of dosimetric phantoms are water, solid-state, and anthropomorphic phantoms. Anthropomorphic phantoms are considered to be the most effective as they closely mimic the organ density of actual patients, helping to ensure that critical organs are avoided and that the required dosage is accurately delivered to the target volume. In addition to the use of dosimetric tools and phantoms, advanced algorithms are utilized in cancer treatment planning software such as *Eclipse* to figure out the most efficient course of action for each patient. These algorithms take into account the patient's specific condition and the precise location of the tumour, as well as any potential side effects of radiation therapy.

2. Materials and methods

The experiment of this study was performed at the Hospital of Lithuanian University of Health Sciences Kaunas Clinics, Oncology Hospital, Department of Radiotherapy. Phantom-based study for analysis and measurements of out-of-field doses was performed.

2.1. Phantom

Out-of-field dose evaluation and analyses were carried out utilizing adolescent male pelvic anthropomorphic phantom CIRS model 801-P-A (USA, CIRS) (Fig. 21).

This phantom is tissue equivalent and designed for radiotherapy dosimetry applications. The whole physical makeup of the phantom is derived from data sets from The Visible Human Project (VHP), which is a resource for studying human anatomy. The phantom is constructed from patented epoxy materials that replicate the density and radiation attenuation characteristics of human tissue. It includes anatomically accurate bone, cartilage, muscles, intestines, bladder, prostate, rectum, spinal cord, and interstitial fat. This type of phantom is sectional without holes with a 25 mm slice thickness [116].

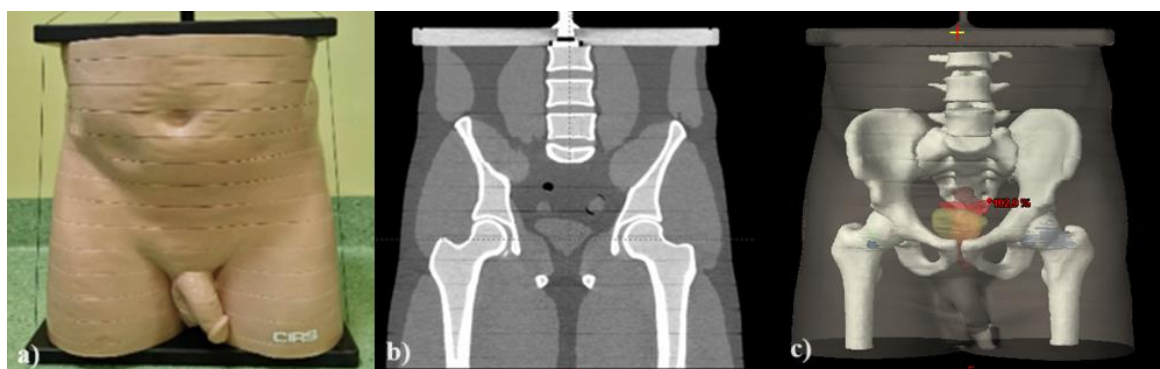


Fig. 21. a) Anthropomorphic phantom CIRS model 801-P-A, b) its inner structures scanned and c) visualised with computed tomography imaging modality

2.2. Computed tomography imaging and contouring

Computed tomography (CT) is an imaging technique that creates cross-sectional scans. Using an appropriate mathematical procedure, the 3-dimensional data about the measured object found in this set of images is retrieved and made available as a voxel image [117, 118].

Computed tomography (CT) unit GE Bright Speed was used for the scanning of the phantom. The phantom was scanned every 0.06 cm using pelvis protocol (Fig. 22 and Table 4).

Table 5. The main parameters of the pelvis protocol [119]

Clinical CT pelvis protocol	
Coverage	600 mm
Rotation	0.5 s
Mode	16 x 0.625 mm
Pitch	1
mA	420
kV	120
Scan time	17.1 s

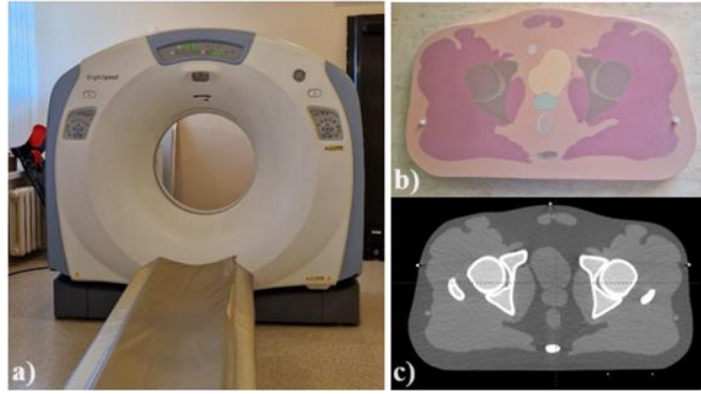


Fig. 22. a) computed tomography, b) cross-sectional view of the slab of anthropomorphic phantom CIRS model 801-P-A, and c) the scan of its inner structures visualised with computed tomography imaging modality

The medical images were used to identify the target (planning tumour volume – PTV) and organs at risk (OARs) for simulation the treatment of prostate cancer. To achieve optimal dose and irradiation dose distribution to the target with the least amount of radiation toxicity to nearby normal tissues, contouring of mentioned structures performs a vital role in radiation treatment planning [120]. Usually, CT images are used for delineation (planning tumour volume (PTV) and organs at risk (OARs)), which are identified and examined by the radiation oncologist. In this study, the main OARs used for the final result evaluation were the bladder, rectum, and left and right femur heads (Fig. 23).

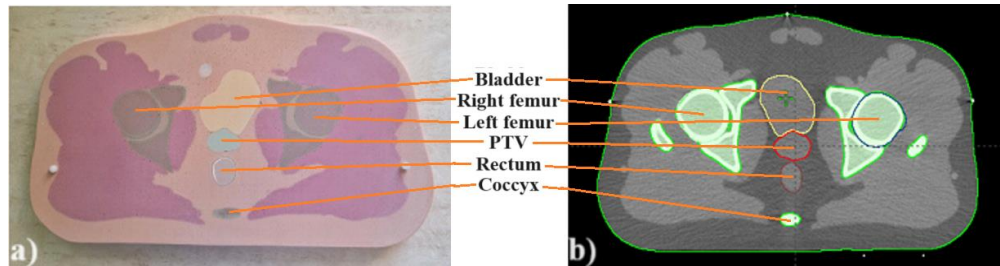


Fig. 23. Anthropomorphic phantom CIRS model 801-P-A a) cross-sectional view and b) on CT images delineated its inner structures (bladder, rectum, and left and right femur heads)

2.2.1. Treatment planning

The dose was delivered with an O-ring linear accelerator (LINAC) called Halcyon (Varian Medical Systems, Palo Alto, CA, USA). It has a single 6 MV flattening filter-free (FFF) beam with a fast gantry rotation speed of 4 rotations per minute (RPM), and a high dosage rate (up to 8 Gy/min). The dual-layer multi-leaf collimator (MLC) blocks greatly reduced the inter-leaf gaps, and the leakage dose [121].

The three-dimensional (3D) treatment planning system *Eclipse* (Varian Medical Systems) [122] was utilized for the dose distribution calculation. Four different treatment plans using intensity-modulated radiotherapy (IMRT), and volumetric arc therapy (VMAT) techniques were planned for each technique using different dose calculation algorithms AcurosXB or AAA [123]. Therefore, simulating the prostate cancer irradiation procedure (60 Gy with 20 fractions in total) on the anthropomorphic phantom CIRS model 801-P-A four treatment plans: 2 VMAT (calculated with two different dose calculation algorithms: AAA and Acuros XB) with 2 full arcs (179°-181°) and 2 IMRT (AAA and Acuros XB) with 8 fields geometry (0°, 45°, 90°, 135°, 180°, 225°, 270°, 315°) were

planned (Fig. 24 a) and b)), optimized regarding the clinical constraints and QUANTEC recommendations (Table 5) [124, 125].

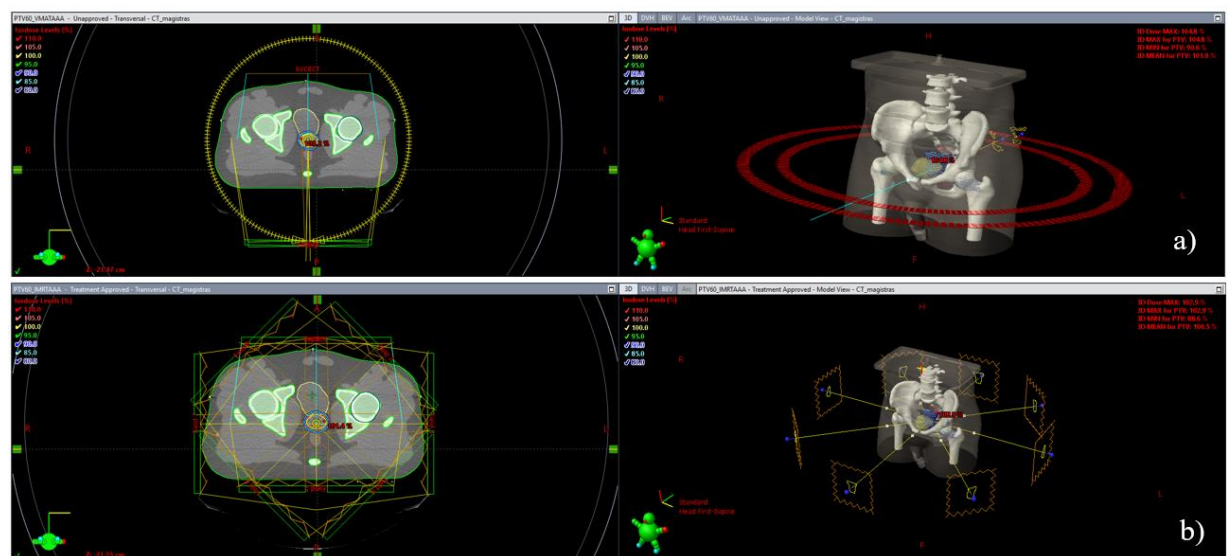


Fig. 24. Geometry of the treatment plans planned with a) volumetric arch therapy (AAA), and b) intensity-modulated radiotherapy (AAA) techniques

Table 6. QUANTEC recommendations [124, 125]

Organs at risk	Dose (Gy) or dose/volume parameters
Rectum	$V_{50} < 50\%$
	$V_{65} < 25\%$
	$V_{70} < 20\%$
Bladder	$V_{55} < 50\%$
	$V_{65} < 50\%$
	$V_{70} < 35\%$
Penile bulb	$D_{60-70\%} < 70\text{ Gy}$
	$D_{95\%} < 50\text{ Gy}$
Femoral heads	$V_{50} < 5\%$
Small intestine	$D_{max} \leq 52\text{ Gy}$
	$V(\geq 50\text{ Gy}) < 5\%$
Colon	$D_{max} \leq 55\text{ Gy}$
	$V_{50} < 10\%$
Pelvic bone	$V(\geq 30\text{ Gy}) < 30\%$, $D_{mean} < 20\text{ Gy}$

Having evidence-based guidelines for dose-volume risks and consensus constraints is critical to ensuring that tumour control is optimized while minimizing toxicity safely and effectively. Clinical trials involving radiotherapy depend on understanding of how normal organs respond to different doses in order to determine appropriate dose constraints for treatment protocols [126]. These constraints are based on clinical data, radiation biology, and tolerance of the organs [127, 128]. Each organ has different dose constraints and varies accordingly with dose and volume. For example, for the bladder case, the volume of the target receiving 55 Gy dose should be less than 50 %. In the simplicity, no more than half of the target area should receive the specified dose in order to minimize the risk of side effects and reduce the side effect probability of the treatment. Probability of the side effects, such as radiation-induced toxicity, is also taken into consideration when the treatment plan is

created. Due to this reason, dose volume histograms (DVHs) are used (Fig. 25). DVHs show dependence on the radiation dose delivered to any volume.

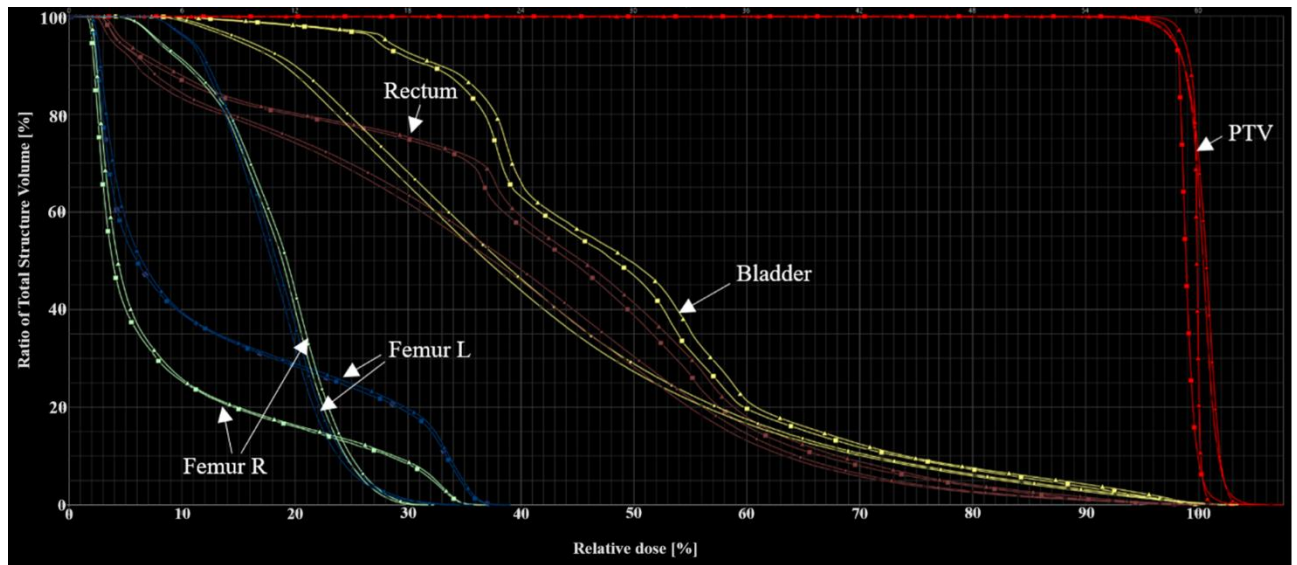


Fig. 25. Dose Volume Histograms (DVHs) of the planned plans planning tumour volume (red) and organs at risk (bladder (yellow), rectum (brown), left (green) and right (blue) femur) representing different planning techniques and algorithms

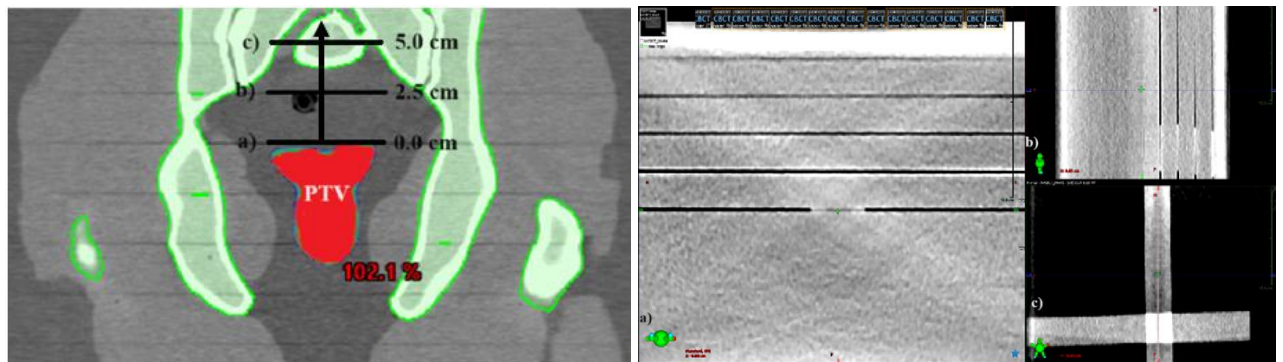


Fig. 26. The schematic representation of the radiochromic films placement for out-of-field doses evaluation: a) field edge (edge of the planning tumour volume), b) 2.5 cm from the field edge, c) 5.0 cm from the field edge

The fundamental analysis of out-of-field doses is shown in Figure 26, showing the radiochromic films positioned at various distances in a phantom. Since each phantom slab thickness is 2.5 cm the measurements were done every 2.5 cm from field edge up to 7.5 cm.

2.3. 2D radiochromic films dosimetry

Additionally, to the treatment planning system calculated dose distribution, radiochromic films RTQA2 were used for irradiation doses experimental measurements, and analysis.

It is known that radiochromic films RTQA2 are developed specifically for the linear accelerators' various quality assurance (QA) tests, for example, tests for radiation field alignment, and 2D irradiation dose distribution. The dose registration response differs from 0.02 Gy to 8.00 Gy, while the energy range varies from 100 keV to MeV [126, 129, 130]. Since radiochromic films are polymer-type, it is recommended to wait for the stabilization of the polymerization process after irradiation

was performed. The manufacturer usually recommends scanning the irradiated films for at least after 48 hours [131, 132].

The flatbed scanner *HP Officejet Pro 8600 Plus* was used to scan irradiated films with 600 dots per inch resolution. The film is covered in transparent yellow polyester on the front/upper side and opaque white polyester material on the reverse due to this it is recommended for the analysis of the films to use a red channel [132].

Before the irradiation dose measurements, radiochromic films need to be calibrated. Fourteen pieces of radiochromic films with dimensions of $(1.5 \times 1.5) \text{ cm}^2$ were irradiated with the different amounts of dose in Gy (0.0 Gy, 0.1 Gy, 0.3 Gy, 0.5 Gy, 0.7 Gy, 1.0 Gy, 1.2 Gy, 1.5 Gy, 1.7 Gy, 2.0 Gy, 2.2 Gy, 2.5 Gy, 3.0 Gy, and 3.5 Gy). The main parameters of irradiation: 1) 6 MeV flattening filter-free (FFF) energy beams, 2) source-surface distance (SSD) was equal to 100 cm, 3) on the radiochromic film were placed poly methyl methacrylate (PMMA) slab (thickness equal to 1.5 cm) to create a build-up region for the 6 MeV FFF energy beam (Fig. 27).

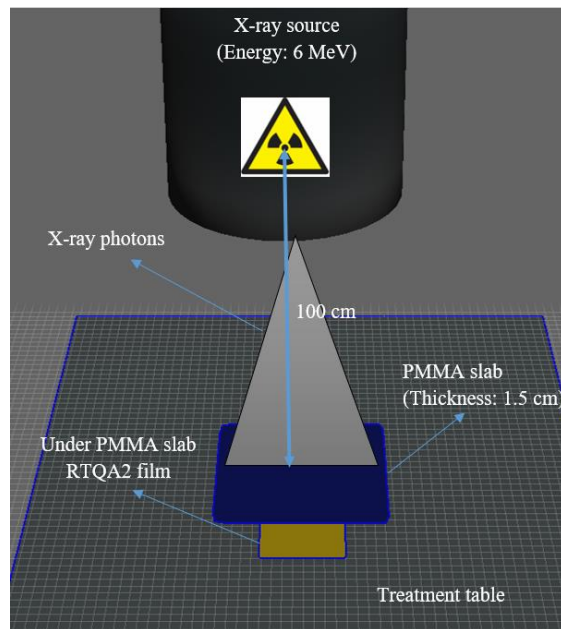


Fig. 27. Radiochromic film irradiation procedure

Radiochromic films RTQA2 were scanned and analysed 48 hours after the irradiation procedure. The higher the prescribed dose the more intense the polymerization process and the darker the film appears (Fig. 28). This polymerization process in the sensitive element is reflected in a variation at the visible level and the colour of the film is related to the dose measurements.



Fig. 28. Radiochromic RTQA2 scanned films (before and after irradiation: 0.0 Gy, 0.1 Gy, 0.3 Gy, 0.5 Gy, 0.7 Gy, 1.0 Gy, 1.2 Gy, 1.5 Gy, 1.7 Gy, 2.0 Gy, 2.2 Gy, 2.5 Gy, 3.0 Gy, 3.5 Gy)

Software *ImageJ* is a freely accessible open-source program tool that enables users to visualize, analyze, measure, and confirm scientific image data. It can determine area and pixel value statistics

based on custom selections made by the user [134, 135]. For that reason, it was used for film processing, data registration, and analysis of the obtained results (Fig. 29).

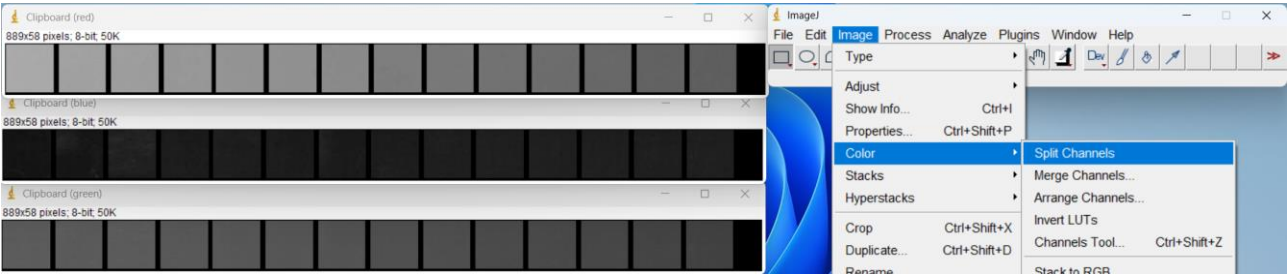


Fig. 29. Software *ImageJ* with an active function of split channels

For analysis of the films the manufacturer provides a recommendation to use a red channel (Fig. 30). According to the authors [132], an approach that uses the red channel in a dose interval from 0 Gy to 4 Gy has better precision <1.5%.

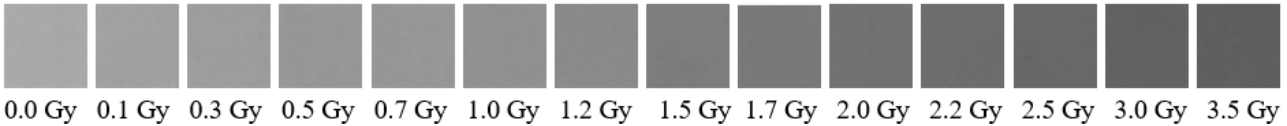


Fig. 30. Red channel of the radiochromic films *RTQA2*

Every irradiation section of the film had a measurement area of the identical dimension selected for evaluation of the results (Fig. 31).

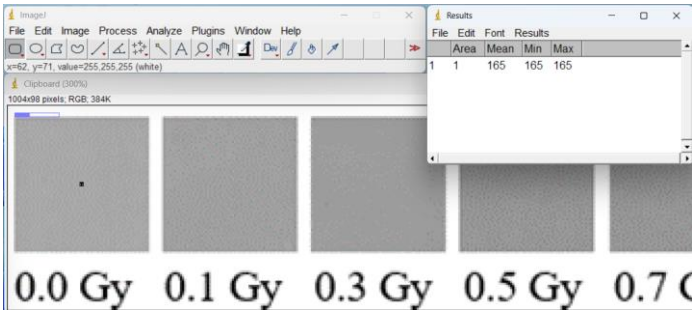


Fig. 31. Red channel measurements

The obtained calibration curve (Fig. 32) was utilized to convert mean pixel values of unknown doses into corresponding absorbed doses, thus enhancing the precision of dosimetry measurements. The relationship between the mean pixel value and the absorbed dose was effectively illustrated through the calibration curve based on the determined outcomes.

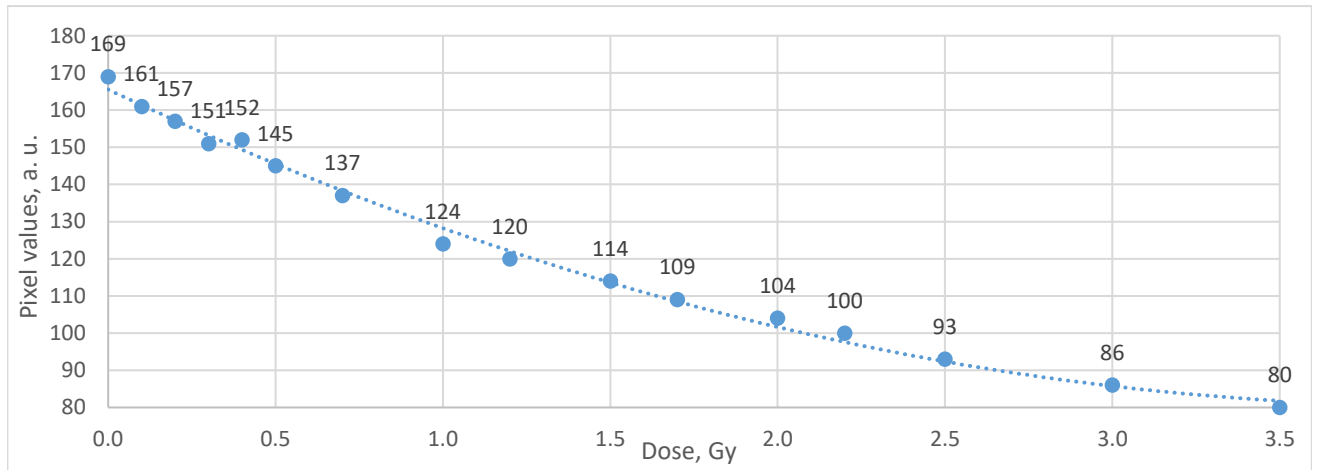


Fig. 32. Calibration curve of the radiochromic films *RTQA2*

The radiochromic films were located between two slabs in the axial and sagittal views. Meanwhile, in the coronal plane, the films are distributed through all the phantom slabs (Fig. 33). The arrows indicate the measurement directions and locations of radiochromic films. Accordingly, with the arrow, the treatment planning systems' dose distribution was measured and compared with the data gathered from the experimental measurements with radiochromic film.

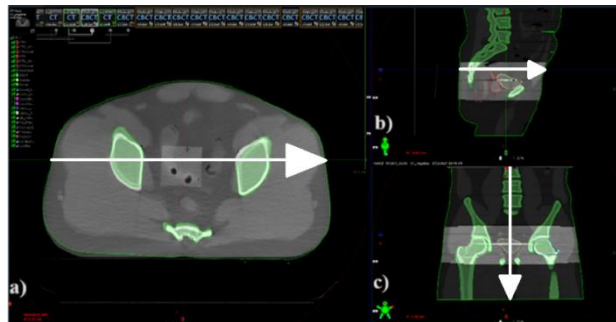


Fig. 33. Views of the treatment planes a) axial; b) sagittal; c) coronal with the direction of the measurements

3. Results

The procedure of this research was separated into 1) analysis of the treatment plans planned using two different techniques (intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT)) with two different dose calculation algorithms (AAA and Acuros XB), and 2) all the planned plans were analysed using 2D radiochromic films *RTQA2* dosimetry. Therefore, regarding experimental results of 2D radiochromic films *RTQA2* dosimetry were prepared as the principal recommendations of the dose constraints used for the prostate cancer patient treatment.

3.1. Analysis of the planned treatment plans

Dose distribution for certain profiles was evaluated for two inverse treatment planning techniques (IMRT and VMAT) (Fig. 34). It could be visually seen the different dose distribution per whole scanned phantom volume for different treatment planning techniques. It is known that for the IMRT plans it is common to deliver the radiation dose through multiple beams each having a different degree of freedom. Meanwhile, VMAT delivers radiation dose using arcs and the gantry rotates continuously until provides conformal dose distribution [30].

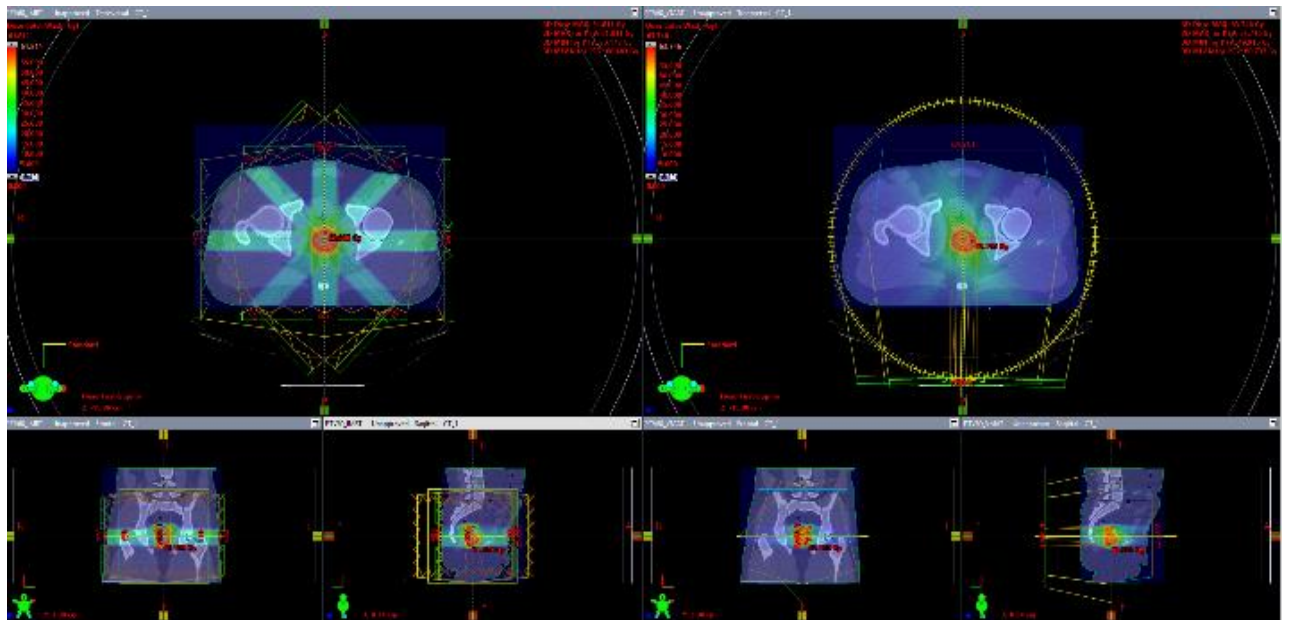


Fig. 34. Evaluation of inverse treatment planning techniques

Each planned IMRT and VMAT plan had a different dose calculation algorithm (AAA or Acuros XB), which showed quite similar results for the target (planning tumour volume – PTV) of all the planned plans (within 0.6 % mean dose difference in between) (Fig. 35).

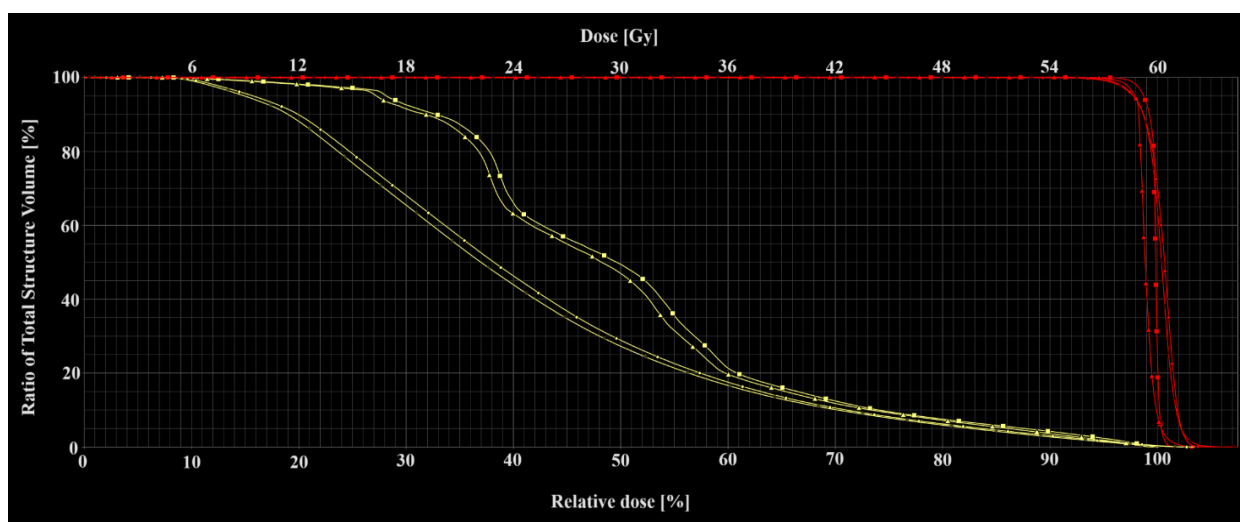


Fig. 35. Dose Volume Histograms (DVHs) of the four planned plans: planning tumour volume (red) and organ at risk (bladder (yellow)), representing different planning techniques IMRT Acuros XB (triangles), IMRT AAA (squares), VMAT Acuros XB (empty points), VMAT AAA (dots)

All other evaluated structures in DVH are represented in Appendix 1. The highest percentage difference and the mean dose was observed for the critical organs: bladder – 24.0 %, right femur – 51.4 %, rectum – 17.2 %, and left femur – 28.5 % between IMRT and VMAT treatment plans, since between algorithms (AAA and Acuros XB) the difference was not so significant and differed up to 4.6 % (Table 6).

Table 7. Mean dose percentage difference for OARs

Organs at risk	Treatment planning technique				
	Difference of the mean dose, %				
	IMRT (AAA vs. Acuros XB)	VMAT (AAA vs. Acuros XB)	IMRT (AAA) vs VMAT (AAA)	IMRT (Acuros) vs VMAT (Acuros XB)	IMRT (AAA) vs VMAT (Acuros XB)
Rectum	2.6 % (0.7 Gy)	3.0 % (0.7 Gy)	13.8 % (3.1 Gy)	14.2 % (3.1 Gy)	17.2 % (3.8 Gy)
Bladder	2.2 % (0.7 Gy)	2.7% (0.7 Gy)	20.7 % (5.2 Gy)	21.3 % (5.2 Gy)	24.0 % (5.9 Gy)
Right femur	4.6 % (0.2 Gy)	2.2 % (0.2 Gy)	50.3 % (5.6 Gy)	51.4 % (5.6 Gy)	26.3 % (2.8 Gy)
Left femur	3.1 % (0.2 Gy)	2.8 % (0.3 Gy)	28.3 % (3.1 Gy)	28.5 % (3.1 Gy)	49.2 % (5.3 Gy)

Furthermore, in addition to assessing the percentage difference values different treatment planning techniques and dose calculation algorithms used revealed that the highest mean dose was registered for bladder – 5.9 Gy, right femur – 5.6 Gy, rectum – 3.8 Gy, and left femur – 5.3 Gy in comparison of IMRT and VMAT treatment plans, since for the same treatment planning technique between different dose calculation algorithms (AAA and Acuros XB) the difference were not so significant and differed up to 0.7 Gy. It is noteworthy that the treatment plans were well-crafted and maintained compliance with the prescribed dose limits for organs at risk.

Therefore, analysis of out-of-field doses (the main evaluation criteria is organs at risk – OARs) as it was expected showed the largest differences between plans planned with IMRT and VMAT (Fig. 36 a) and b)), while the distinction among AAA and Acuros XB was not so significant (Fig. 36 c) and d)).

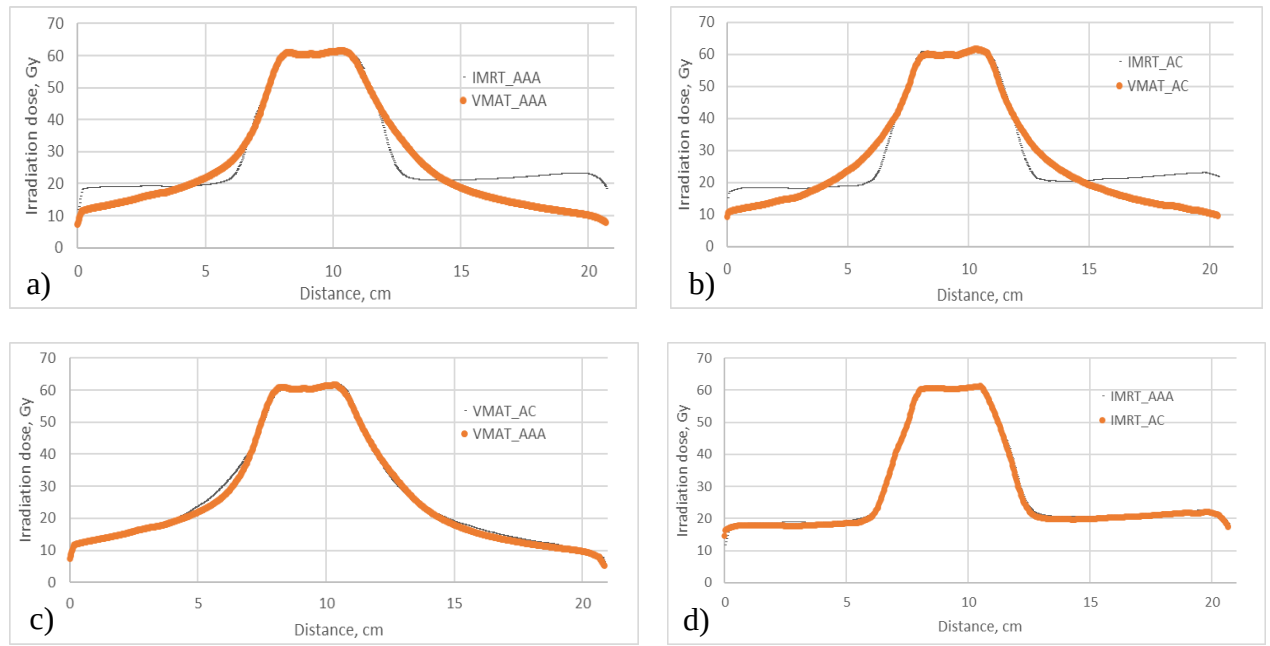


Fig. 36. a) and b) differences between plans planned with IMRT and VMAT, c) and d) the difference between AAA and Acuros XB

Therefore, even the significant difference of the calculated doses for the organs at risk using the same treatment planning technique, but different dose calculation algorithm was not observed, due to experimental measurements it is known that at about 3.5 cm from the field edge, the treatment planning system (TPS) miscalculates the dose up to 30.0 % [69]. Accordingly, to these data, some additional experimental measurements of the out-of-field irradiation doses is recommended to be done [62, 73].

3.2. Analysis of the 2D dosimetry experimental results

As it is known TPS has a good estimation for in-field (target region – PTV) dose distribution but out-of-field doses are underestimated, especially for IMRT and VMAT plans [64, 66, 69, 131]. It in turn may influence the higher dose of the OARs, which can lead to adverse effects. According to the results of these studies additionally, 2D radiochromic films dosimetry for this research was done (Fig. 37).

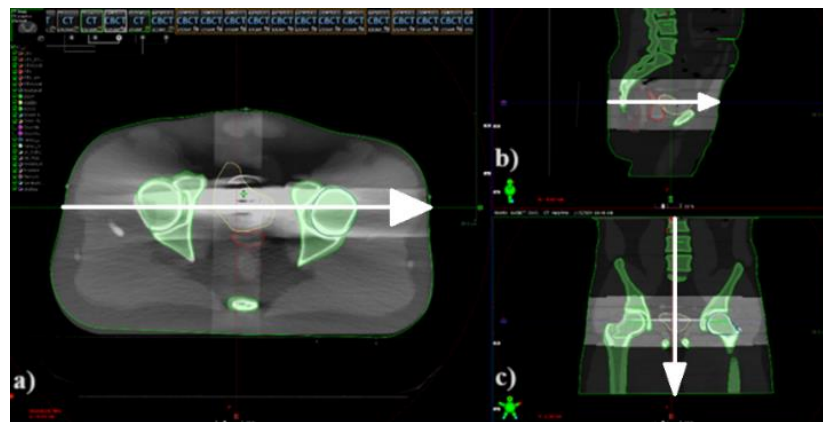


Fig. 37. Different views of 2D dosimetry insertions a) coronal, b) sagittal, c) axial planes

The obtained results showed that irradiation doses calculated with TPS and measured with radiochromic films *RTQA2* differed up to 26 %. The highest disagreement was observed using dose

calculation algorithm AAA (independently on treatment planning technique (IMRT or VMAT)), since the lowest one using Acuros XB (Table 7).

Table 8. Differences of irradiation doses for the mostly influenced OARs in comparison between IMRT and VMAT plans calculated with the different calculation algorithms (AAA and Acuros XB)

Technique	Calculation algorithm	Organs at risk (OARs)	Distance from the treatment field edge, cm	Dose (TPS), Gy	Dose (2D radiochromic films), Gy	TPS versus 2D dosimetry measurements, %
IMRT	AAA	Bladder	2.5	27.6	30.9	12.0
			5.0	20.7	25.6	23.7
			7.5	20.8	26.9	30.0
		Mean dose (whole organ), Gy		29.5	-	-
	Acuros XB	Rectum	2.5	27.3	30.6	12.1
			5.0	19.5	23.6	21.0
			Mean dose (whole organ), Gy		23.9	-
		Bladder	2.5	29.2	31.2	6.8
			5.0	20.2	22.4	10.9
			7.5	20.4	22.1	8.3
VMAT	AAA	Bladder	2.5	37.0	41.5	12.2
			5.0	23.7	26.0	9.7
			7.5	15.4	19.0	23.4
		Mean dose (whole organ), Gy		32.1	-	-
	Acuros XB	Rectum	2.5	30.2	32.7	8.3
			5.0	21.3	25.1	17.8
			Mean dose, Gy		23.6	-
		Bladder	2.5	32.3	35.4	9.6
			5.0	23.8	26.2	10.1
			7.5	17.1	22.1	29.2
		Mean dose, Gy		31.7	-	-
	Acuros XB	Rectum	2.5	33.9	35.7	5.3
			5.0	23.4	26.3	12.4
		Mean dose, Gy		23.5	-	-

It was observed that for most of the analysed cases, undercalculations of the treatment planning systems were increased with the distance from the planning tumour edge (Fig. 38). The most significant difference for the bladder was registered (for IMRT treatment planning technique and AAA) and were equal to 30.0 % (6.2 Gy). Bladder-sparing results have shown that the IMRT technique using the Acuros XB algorithm has the highest level of agreement between calculated and measured doses, with a discrepancy of 6.9% (2 Gy). The most significant discrepancies of the dose calculations for rectum were found for the IMRT technique using the AAA algorithm, with a difference of 21.0% (4.1 Gy) at a distance of 5.0 cm from the PTV edge. However, regardless of the distance from the PTV edge (2.5 cm or 5.0 cm), the VMAT Acuros XB demonstrated the best agreement between TPS-calculated and 2D dosimetry doses. At 2.5 cm from the edge, the dose difference was 1.8 Gy, and at 5.0 cm from the edge, it was 2.9 Gy.

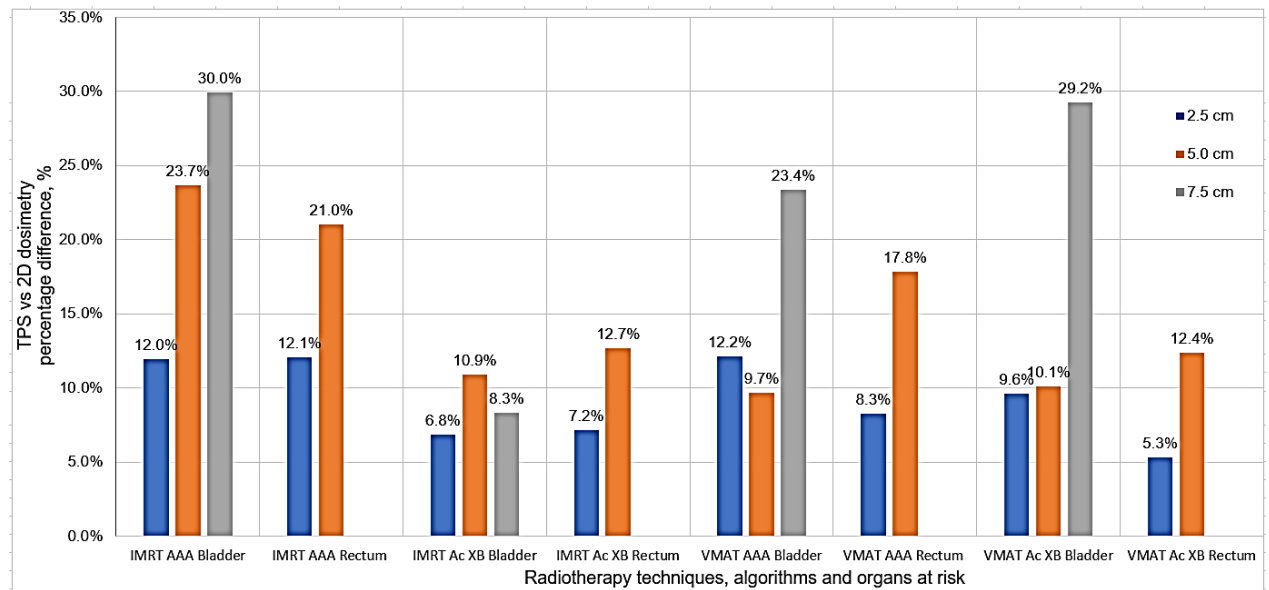


Fig. 38. The discrepancy between TPS-calculated and 2D dosimetry measurements of absorbed dose as a function of distance from the PTV edge

Moreover, the selection of the treatment modality and the dose calculation algorithm accuracy are crucial factors that greatly influence the precision of the calculated dose delivered to critical organs, e.g. bladder (Fig. 39) or rectum (Fig. 40).

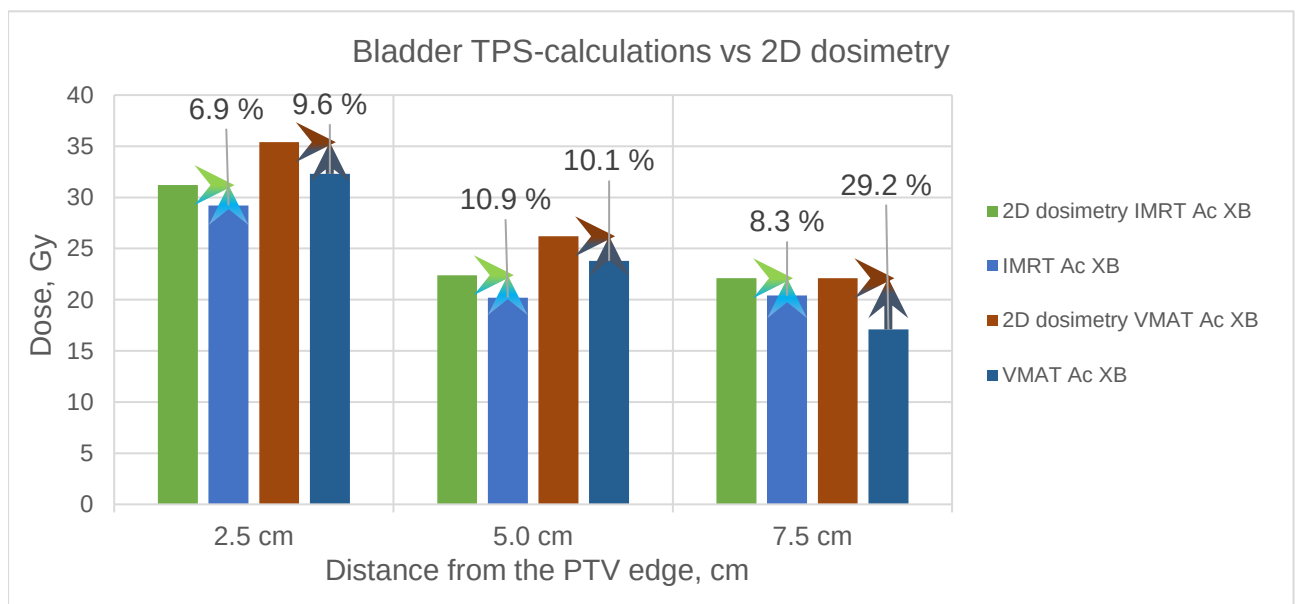


Fig. 39. The discrepancy between TPS-calculated and 2D dosimetry measurements of absorbed dose to the bladder depending on the distance from PTV edge

Overall, it is commonly observed that treatment planning techniques and their algorithms tend to overestimate the absorbed dose (Table 7 and fig. 39). However, it is important to note that each comparison may yield different results. The radiotherapy treatment technique IMRT planned with the AAA algorithm represented the highest dose underestimation in the bladder and it was familiar for a greater distance from the PTV edge (5.0 cm and 7.5 cm). The differences between the TPS calculations and 2D measurement doses range from 12 % to 30.0 %. On the other hand, for the IMRT technique planned with the Acuros XB algorithm, the differences between the calculated and

measured doses were generally lower, ranging from 6.8 % to 10.9 %. This indicates that the Acuros XB algorithm may be more accurate in predicting the delivered dose to the bladder than the AAA algorithm for IMRT treatment plans. For the VMAT technique with the AAA algorithm, the differences between the TPS-calculated and 2D dosimetry-measured doses differed from 9.7 % to 23.4 %. Similar to the IMRT technique used with the AAA algorithm, this indicates a potential underestimation of the delivered dose to the bladder for VMAT treatments planned with the AAA algorithm. Lastly, for using the treatment planning technique VMAT planned with Acuros XB, the differences between the TPS-calculated and 2D-measured doses were generally lower, and differed from 9.6 % to 29.2 %. The better agreement was represented in 5 cm from the treatment edge (VMAT AAA (9.7 %) vs VMAT Acuros XB (10.1 %)). This suggests that the Acuros XB algorithm could be more accurate in predicting the delivered dose to the bladder compared to the AAA algorithm for VMAT treatments as well.

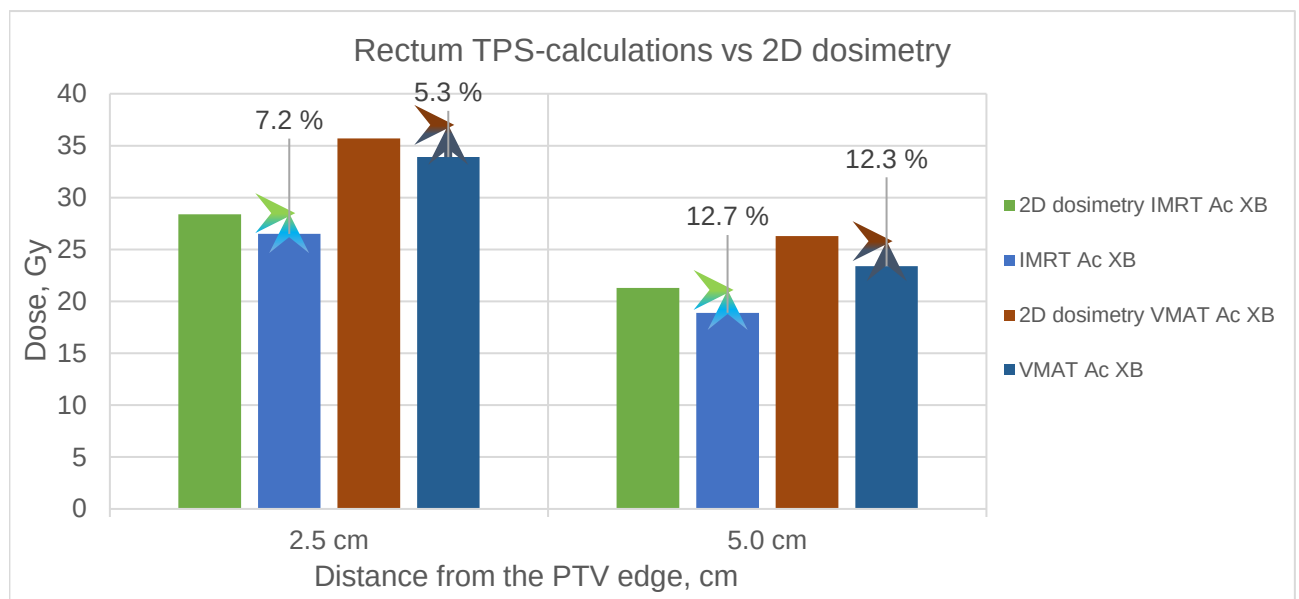


Fig. 40. The discrepancy between TPS-calculated and 2D dosimetry measurements of absorbed dose to the rectum depending on the distance from PTV edge

Moreover, the treatment planning techniques planned with algorithms tends to overestimate the out of field doses, especially underestimations that increase with the distance from PTV edge (Table 7). In the IMRT techniques plan cases, the AAA algorithm overestimated the absorbed dose at 2.5 cm and 5.0 cm distances, with 12 % and 21 % differences, respectively. On the other hand, the Acuros XB algorithm represented lower discrepancies, with differences of 7 % (at 2.5 cm) and 12 % (at 5.0 cm). The use of VMAT plans with algorithms such as AAA or Acuros XB may still result in inaccurate absorbed dose calculations. However, it was observed that the use of VMAT with the Acuros XB algorithm generally yields closer agreement with TPS calculations compared to 2D dosimetry measurements, regardless of the distance from the PTV edge, with differences of 5.3 % and 12.4 % at 2.5 cm and 5.0 cm distances, respectively. Overall, the Acuros XB algorithm provided improved accuracy in predicting out-of-field doses to the rectum compared to the AAA algorithm for both IMRT and VMAT plans. Further investigation may be needed to determine the cause of discrepancies between calculated and measured values and potential ways to improve dose calculation accuracy.

A similar tendency of the results was observed by Howell et al. [70], who showed that the TPS miscalculated out-of-field doses by a mean of 40% over the measurement range. One of the reasons

for these differences is that the dose calculation algorithm AAA does not take into account the leakage from the linear accelerator head [66]. Due to this reason, some further investigations could be recommended to be done evaluating irradiation doses distributed further from the edge of the irradiation field since it is found that differences between Acuros XB and experimental measurements can be up to 91.2 % for VMAT and up to 60.4 % in 3D-CRT at 15 cm from the PTV edge [66].

These discrepancies could be due to various factors such as uncertainties in the TPS algorithms, dosimetry measurement errors, and anatomical variations in the patients. These discrepancies between calculated and measured doses can have clinical implications as they affect the accuracy of treatment delivery and dose distribution [137].

Conclusions

1. Two radiotherapy plans for IMRT and VMAT techniques were planned, and each was calculated using two different dose calculation algorithms (AAA and Acuros XB). The analysis of the same treatment technique but utilizing a different dose calculation algorithm revealed a minor dose difference of up to 4.6%. The highest difference more than 50% was represented in comparison of two different treatment planning techniques (e.g. IMRT AAA vs VMAT AAA).
2. The treatment planning system (TPS) could not correctly calculate the out-of-field doses from the field edge up to 7.5 centimetres. Regardless of the treatment planning strategy (VMAT or IMRT), the dose calculation algorithm AAA showed the largest discrepancy (up to 30%), while Acuros XB showed the lowest (5.3%). The highest observed dose difference between the dose calculated with TPS and 2D dosimetry was 30%.
3. During the treatment planning of prostate cancer, although the treatment planning system did not show any significant difference between the algorithms, for the different treatment planning techniques the differences were significantly high (up to 50 %). However, regarding experimental measurements, it could be observed that regardless of treatment planning techniques and dose calculation algorithms the irradiation dose is underestimated using TPS, which means that using the dose constraints for the organs at risk has to be taken into account, especially if a distance from the field edge increases. Depending on the distance from the field edge, it could be recommended to lower the irradiation dose constraints for the organs at risk up to 30 %.

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Appendices

Appendix 1. Dose Volume Histograms (DVHs) of the four planned plans: planning tumour volume (red) and organs at risk (bladder (yellow), rectum (brown), right (green) and left (blue) femur) representing different planning techniques (IMRT and VMAT) and algorithms (AAA and Acuros XB)

