KAUNAS UNIVERSITY OF TECHNOLOGY
FACULTY OF MATHEMATICS AND NATURAL SCIENCES

Donatas Opulskis

TREATMENT PLAN VERIFICATION BASED ON IN VIVO DOSE MEASUREMENTS DURING EXTERNAL BEAM RADIOTHERAPY

Master's Final Degree Project

Supervisor
prof. dr. Diana Adlienė

KAUNAS, 2018

KAUNAS UNIVERSITY OF TECHNOLOGY
FACULTY OF MATHEMATICS AND NATURAL SCIENCES

TREATMENT PLAN VERIFICATION BASED ON IN VIVO DOSE MEASUREMENTS DURING EXTERNAL BEAM RADIOTHERAPY

Master's Final Degree Project

Medical Physics (621B92002)

Supervisor
prof. dr. Diana Adlienė

Consultant
Phd student Evelina Jaselskė

Reviewer
dr. Marius Kaminskas

Project made by
Donatas Opulskis

KAUNAS, 2018

KAUNAS UNIVERSITY OF TECHNOLOGY

FACULTY OF MATHEMATICS AND NATURAL SCIENCES

(Faculty)

Donatas Opulskis

(Student's name, surname)

Medical Physics, 621B92002

(Title and code of study programme)

'Treatment plan verification based on *in vivo* dose measurements during external beam radiotherapy'

DECLARATION OF ACADEMIC INTEGRITY

____ _____ 220 ____

Kaunas

I confirm that the final project of mine, **Donatas Opulskis**, on the topic 'Treatment plan verification based on *in vivo* dose measurements during external beam radiotherapy' is written completely by myself; all the provided data and research results are correct and have been obtained honestly. None of the parts of this thesis have been plagiarised from any printed, Internet-based or otherwise recorded sources. All direct and indirect quotations from external resources are indicated in the list of references. No monetary funds (unless required by law) have been paid to anyone for any contribution to this project.

I fully and completely understand that any discovery of any manifestations/case/facts of dishonesty inevitably results in me incurring a penalty according to the procedure(s) effective at Kaunas University of Technology.

(name and surname filled in by hand) *(signature)*

Donatas, Opulskis. ‘Treatment plan verification based on *in vivo* dose measurements during external beam radiotherapy’. *Master's* Final Degree Project / supervisor prof. dr. Diana Adlienė; Faculty of Mathematics and Natural Sciences, Kaunas University of Technology.

Study field and area (study field group): BIOMEDICAL SCIENCES, Medicine and Health

Keywords: *in vivo dosimetry, external beam radiotherapy, semiconductor diodes, radiochromic films, maximum dose, gynaecologic cancer.*

Kaunas, 2018. 66 pages.

SUMMARY

Gynaecologic malignancies are one of the important cause of mortality and morbidity among women around the world. According to Foundation of women cancer in 2015 it was estimated that over 98 000 women would be diagnosed with a gynaecologic cancer and over 30 000 will die from it. Gynaecological cancer is described as uncontrolled growth and spread of abnormal cells originating in the female reproductive organs and there are five main sources from where cancer could spread including the cervix, ovaries, uterus, fallopian tubes, vagina and vulva and all of them as a group are referred as gynaecologic cancers. Techniques which are used for the treatment depend on various factors such as treatment method, cancer type, shape, location and others.

In this Master thesis treatment method using two treatment fields (main and segment) was applied for the treatment of gynaecologic cancer patients. It was aimed to deliver the planned dose to the target (tumour) and to spare ovaries from high doses since ovaries are characterized as being very sensitive to radiation. The main task implementing this method was assessment of dose delivery accuracy performing in vivo and in vitro investigations using radiochromic films and semiconductor diodes.

In vitro measurements revealed that the correct positioning of a segment field has a great influence on treatment accuracy since it is related to the maximum dose which is delivered to the gynaecologic cancer patients. Based on *in vitro* measurements decision was made to check consistency of *in vivo* dose delivery according to prepared dose treatment plans for real patients. Dosimetry for 7 gynaecologic cancer patients have been performed taking into account dose delivery using two overlapping fields. The results of *in vivo* measurements have shown, that the relative dose errors varied within the tolerance limits indicating that patient treatment was performed correctly.

Opulskis, Donatas. *In vivo* dozimetriniais matavimais grįsto dozių planų verifikavimas išorinėje spindulinėje terapijoje. *Magistro* baigiamasis projektas / vadovas prof. dr. Diana Adlienė; Kauno technologijos universitetas, Matematikos ir gamtos mokslų fakultetas.

Studijų kryptis ir sritis (studijų krypčių grupė): BIOMEDICINOS MOKSLAI, Medicina ir sveikata

Reikšminiai žodžiai: *in vivo dozimetrija, išorinė spindulinė terapija, puslaidininkiniai diodai, radiochrominiai filmai, maksimali dozė, ginekologinis vėžys*.

Kaunas, 2018. 66 puslapiai.

SANTRAUKA

Ginekologinis vėžys yra viena iš svarbiausių moterų mirtingumo ir sergamumo priežasčių visame pasaulyje. Pagal Foundation of Women cancer 2015 m. buvo nustatyta, jog daugiau nei 98 000 moterų bus diagnozuotos ginekologinis vėžys, o daugiau nei 30 000 moterų mirs dėl šios vėžio formos. Ginekologinis vėžys yra apibūdinamas kaip nekontroliuojamas vėžinių ląstelių augimas moters reprodukcinėje sistemoje, o pagrindiniai jo atsiradimo šaltiniai aptinkami gimdoje, gimdos kaklelyje, kiaušidėse, makštyje ir kiaušintakiuose. Gydimo metodikos kurios yra naudojamos šio tipo vėžiui gydyti priklauso nuo įvairių faktorių tokiu kaip vėžio tipas, forma, vieta ir kt.

Šiame magistro baigiamajame darbe buvo pritaikyta dviejų laukų (pagrindinio ir segmentinio) spindulinės terapijos gydimo metodika, kuri buvo skirta ginekologiniu vėžiu sergantiems pacientams. Buvo siekiama apšvitinti planuojamą naviką ir tuo pačių apsaugoti kiaušides nuo didelių dozių, kadangi jos yra charakterizuojamos kaip labai jautrios jonizuojančiajai spinduliuotei. Pagrindinis šio darbo uždavinys, naudojant šią gydimo metodiką, buvo įvertinti dozės tikslumą atliekant *in vivo* ir *in vitro* matavimus naudojant puslaidininkinius diodus ir radiochrominius filmus.

Atlikti *in vitro* matavimai parodė, jog teisinga segmentinio lauko padėtis turi didelės įtakos spindulinio gydymo tikslumui, kadangi jis susijęs su maksimalia doze, kuri yra naudojama ginekologiniu vėžiu sergančių pacientų gydime. Remiantis *in vitro* matavimais, buvo nuspręsta patikrinti *in vivo* naudojamos dozės patikimumą pagal gydimo planus suplanuotas dozes tikriems pacientams. Buvo atlikti dozimetriniai matavimai su 7 ginekologiniu vėžiu sergančiais pacientais kurių metu buvo vertinama dozės priklausomybė nuo dviejų laukų persidengimo. buvo atlikta atsižvelgiant į dozės pristatymą naudojant du sutampančius laukus. *In vivo* matavimų rezultatai parodė, kad santykinės dozės paklaidos kito tolerancijos ribose, o tai rodo, kad pacientų spindulinis gydimas buvo atliktas tinkamai.

TABLE OF CONTENT

LIST OF FIGURES

LIST OF TABLES

ABBREVIATIONS

US – Ultrasound

CT – Computer tomography

MRI – Magnetic resonance imaging

PET – Positron emission tomography

EBRT – External beam radiation therapy

SRT – Superficial radiotherapy

2D – Two dimensional

3D – Three dimensional

3D CRT – Three-dimensional conformal radiotherapy

PTV – Planning tumour volume

IGRT – Image guided radiation therapy

IMRT – Intensity modulated radiation therapy

VMAT – Volumetric arc therapy

MU – Monitor units

IMPT – Intensity modulated proton therapy

CTV – Clinical tumour volume

NCDs – Non-communicable deceases

OAR – Organs at risk

GTV – Gross tumour volume

ITV – Internal target volume

MLC – Multileaf collimator

DVH – Dose volume histogram

SSD – Source surface distance

MOSFETs – Metal-oxide semiconductor field effect transistors

PSDs – Plastic scintillation detectors

EPIDs – Electronic portal imaging devices

TLDs – Thermoluminescence dosimeters

OSLDs – Optically stimulated luminescent dosimeters

RPLDs – Radiophotoluminescent dosimeters

1. INTRODUCTION

In vivo dosimetry involves the measurement of radiation doses to cancer patients during their radiation treatment in order to ensure that the treatment which is used is carried out according to treatment plan which is organized by the responsible oncologist. For many years, *in vivo* dosimetry was one of the most common practise to make sure that doses do not exceed the tolerance levels. The main purpose of *in vivo* dosimetry however is quality assurance of the radiotherapy process. It is one of the key parts of quality management of a radiotherapy department. In vivo dosimetry is part of the overall verification chain which is used during the dose preparation and delivery. The global results of measurements of patient doses provide the data which is crucial for assessment of the accuracy and precision in dose planning and delivery for a specific treatment location, or by a given radiotherapy machinery. *In vivo* dosimetry can also be used for the estimation of uncertainties in radiation treatment at a given institution. It also has another side which is, used for the detection of systematic errors and the prevention of unintended exposures of patients undergoing specific radiotherapy. This can minimize or eliminate the possibility of mistreatment consequences of doses to many treatments or many patients so that they would not have suffered because of these errors. In this context, *in vivo* dosimetry takes a crucial part of a radiation safety system of a radiotherapy department and should be used for all patients undergoing radiation treatments. Despite everything *in vivo* dosimetry is recommended for routine verification of the dose delivery for all groups of patients undergoing radiotherapy. In this master thesis *in vivo* dosimetry was used for the evaluation of the treatment methods used for gynaecologic cancer patients in external beam radiotherapy. For this purpose, objective was set up and task were formulated in order to achieve it.

Objective: to adapt *in vivo* dosimetry registration methods and use them for gynaecologic cancer patients dose plan verification.

Tasks:

1. To select dosimetry registration methods and perform calibration procedure for the selected dosimetry equipment.
2. To perform *in vitro* measurements with selected dosimetry methods.
3. To perform comparison between chosen dosimetry methods.
4. To evaluate *in vivo* doses delivered to the gynaecologic cancer patients using two overlapping irradiation fields.

2. LITERATURE REVIEW

2.1. GYNEACOLOGIC CANCER

Gynaecologic malignancies are one of the important cause of mortality and morbidity among women around the world. According to Foundation of Women cancer in 2015 it was estimated that over 98 000 women would be diagnosed with a gynaecologic cancer and over 30 000 will die from it [1]. It should be mentioned that gynaecological cancer is described as uncontrolled growth and spread of abnormal cells originating in the female reproductive organs and there are five main sources from where cancer could spread including the cervix, ovaries, uterus, fallopian tubes, vagina and vulva and all of them as a group are referred as gynaecologic cancers (Figure 1). They take nearly 20% of uterine cancer which leads to be the most common cancer in the developed countries and cervical cancer being the most common in the developing world, however the highest mortality is seen from ovarian malignancies [2]. Early diagnosis of cervical cancer, accurate staging, new advanced radiation therapy techniques and other methods has led to improvement in disease outcome and survival from it, however it still remains one of the most frequent causes of death in women [3, 4]. The management of these gynaecological malignancies have unresolved issues and the biggest one is the recommendations on the use of imaging modalities [5]. Each of those gynaecologic cancers are unique, with different signs, symptoms, and risk factors (things that may increase your chance of getting cancer). All women are at risk for gynaecologic cancers, and this risk increases with age. This risk can be reduced for some of these cancers. When gynaecologic cancers are found early, treatment works best.

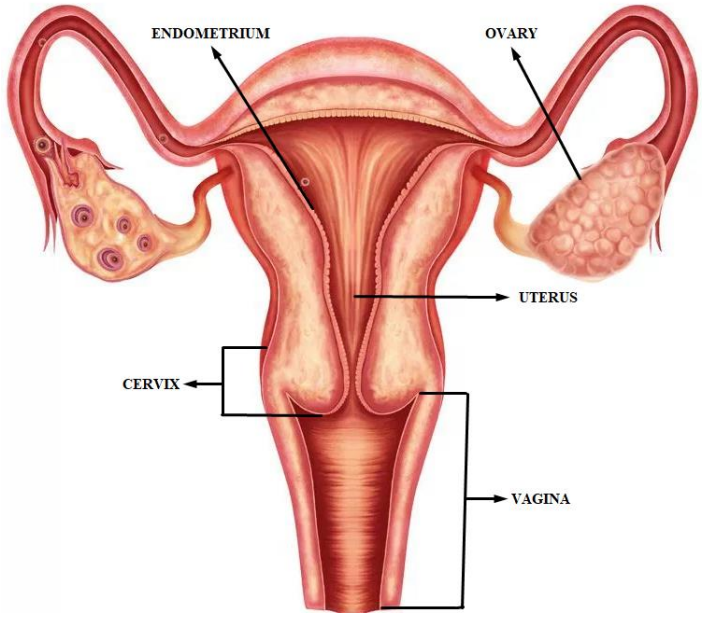

Fig.1. Schematically representation of women's reproductive system and main gynaecologic cancer sources [adapted from 6].

2.2. TREATMENT

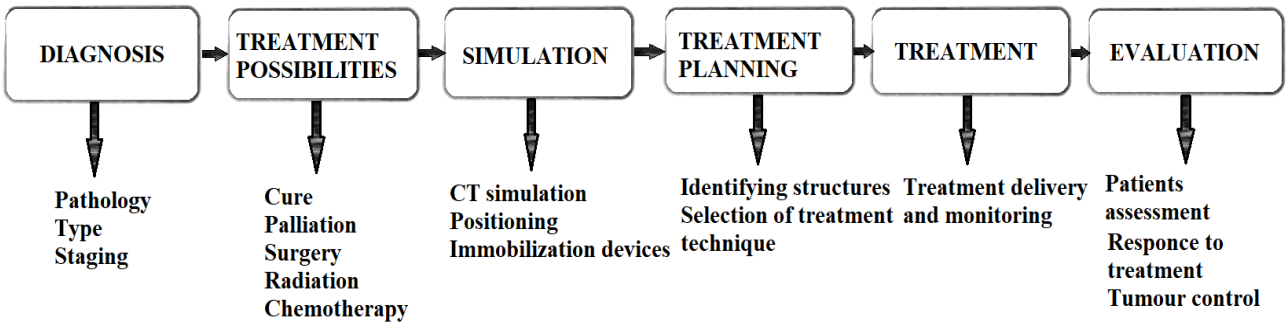

Fig.2. Radiation therapy treatment sequence.

Radiation treatment is a chain of actions and procedures which are needed to be taken in order to maintain same treatment quality and standards for all the patients (represented in Figure 2). It should be mentioned that not all patients need to participate in all these steps.

The first stage which needs to be taken into account is patients diagnosis. It's one of the most important stages because it determines whether the patients need to take part in the further stages of radiation therapy or not. Diagnosis itself shows if the patients has any pathologies (cancer) if so the type and staging could be evaluated to determine if the patients' needs to take part in further stages of treatment with external or internal radiation. Stage two is required in order to decide what kind of treatment should be taken for the patients considering all the possible outcomes. Before starting planning, phase examination is performed (revision of medical history and test results) from which the precise area is marked where the radiation beams will be aimed this process is known as simulation. Patient is asked to lie still on a table while the radiation therapist uses imaging scans (CT, MRI) to define treatment field. These fields are very precise so positioning and immobilization devices are used in order to maintain the same exact position of a patient throughout the whole treatment process. Based on the simulations and other information which is gathered radiation oncologist will decide how much radiation is needed, in what kind of way it will be given and how many treatments are required. At the planning stage identification of planning tumour volume and critical structures are made using different imaging modalities such as CT, MRI, PET etc. and from where the selection of treatment method is determined. During the treatment stage the main procedure is the treatment delivery itself and monitoring is made (dosimetry) to maintain required standards. After the treatment one more phase is following which is evaluation and it contains of patient's assessment, treated place response to a treatment and control of a tumour itself. In this master thesis gynaecologic cancer patients were evaluated who underwent from first to 5th stage.

2.3.TREATMENT TECHNIQUES

Radiation therapy can be delivered in two ways either externally or internally. External radiation delivers high-energy rays which can be photons, electrons protons or neutrons directly to the cancer from a machine outside the body. Internal radiation which is also known as brachytherapy, is the implantation of a specific amount of radioactive material (seeds) in or near the tumour depending on its type, localisation, size and shape. Radiation can also be delivered in a liquid form as an isotope into a vein which from there reaches the cancer.

In this Master thesis, External Beam Radiation Therapy (EBRT) will be described as a method for gynaecologic cancer treatment. However, depending on the usage of X-ray as a tool for diagnostics or therapy there are energy intervals in which X-ray can be used:

- Superficial x-rays (35-60 kV) –penetration can be up to 5 mm, such radiation is mostly used for skin treatment;
- diagnostic x-rays (20 -150 kV)- used in radiodiagnostic procedures for X-ray machinery and CT;
- orthovoltage x-rays (200-500 kV) – penetration dept varies from 4-6 cm, used for treatment of skin, superficial structures, ribs;
- supervoltage x-rays (0,5 -1 MV);
- Megavoltage x-rays (1-25 MV) – are used to treat tumours that are located deep in patient's body. Megavoltage x-rays are preferred for therapy, because of their attenuation for lower energy photons and the penetration of these generated photons are much further comparing with lower energy ones, thus resulting lower does to outer structures such as skin. Also, megavoltage x-rays have much higher relative biological effectiveness [7]. This energy range is also used in our research for the treatment of gynaecologic cancer patients.

The radiation beam depending on its purpose can be deliver using different type of equipment:

- Superficial radiotherapy (SRT) machines – produces low energy (20-150 kV) x-rays, that are used for treatment of skin conditions;
- orthovoltage x-ray tubes – produces orthovoltage x-rays (200-500 kV) and are mostly used for treatment of skin cancer such as necrosis;
- Linear accelerators or "LINACs" - produce megavoltage x-rays as bremsstrahlung spectrum by rapidly decelerating electrons in a target material (usually tungsten). After when intensity and shape of beam can be modified with a help of linac collimators.

- Cobalt units – radiation beam is produces with the help of radioisotope cobalt-60, which produces stable dual energy beams of 1.17 and 1.33 MeV. Nowadays cobalt-60 is mostly replaced by linear accelerators because of their ability to produce much higher energies, yet it is still used in specific applications, such as gamma knife [8].

The radiation beam which is generated by a linear accelerator, or linac in our thesis is demonstrated in Fig.3. During external beam radiation therapy, a beam or multiple beams of radiation is directed through the patient's skin to the cancer and the surrounding area where the beam destroys the tumour and any nearby cancer cells. To minimize any side effects which can occur during the treatment, five days a week, Monday to Friday, for several weeks are typically given for the patient. This allows enough radiation to get into your body to kill the cancer while healthy cells have time to recover from given exposure. Using treatment planning systems (computer and software), treatment team controls the size and shape of the beam, as well as how it is entering your body, to effectively treat your tumour while sparing the surrounding normal tissue. There are several special types of external beam radiation therapy methods which are used for gynaecologic cancer.

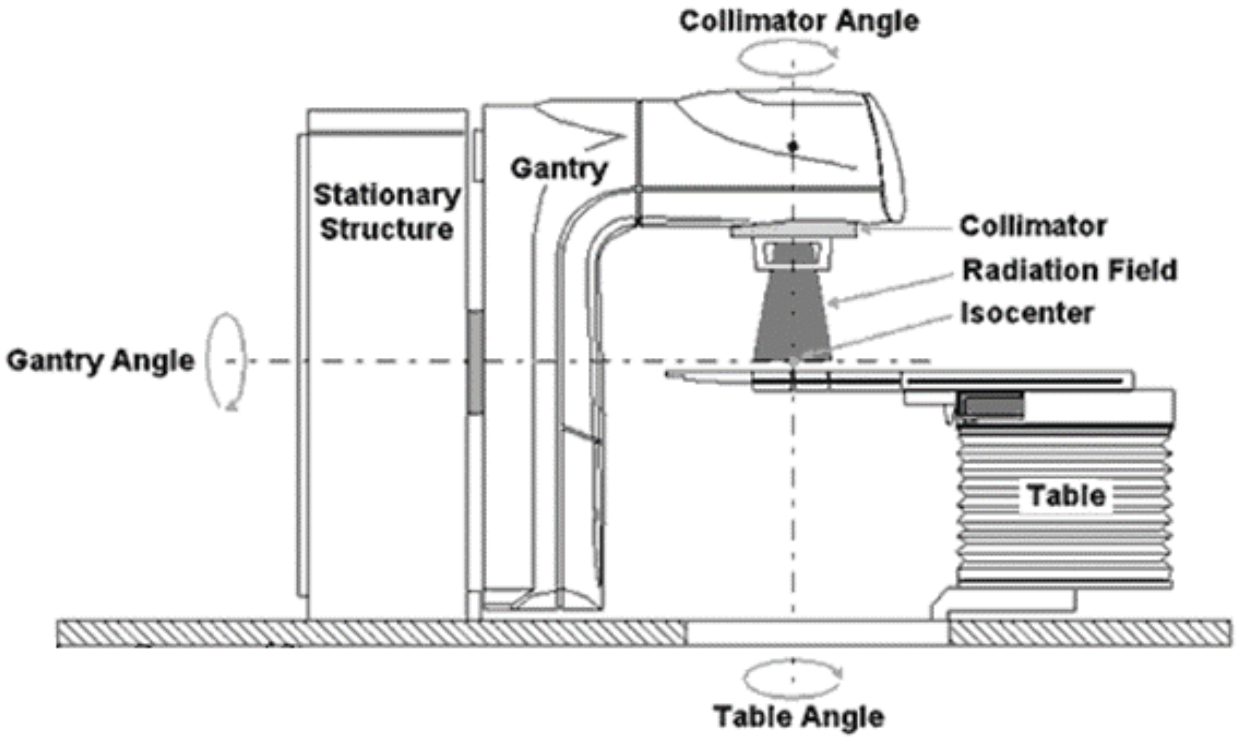

Fig.3. Linear accelerator scheme [9].

2.3.1. THREE-DIMENSIONAL CONFORMAL RADIATION THERAPY (3D CRT)

All Tumours are unique with their different shapes and sizes. Also, every patient's body is different. Three-dimensional conformal radiation therapy, or 3D CRT, uses computers and special imaging modalities such as CT, MRI or PET scans to determine the type, size, shape and location of the tumour as well as surrounding organs. Treatment team can then precisely tailor the radiation beams to the size and shape of a tumour with special shielding. Because the radiation beams are carefully targeted, nearby surrounding normal tissues receive less radiation and can heal better [10]. According to Ahmad N. and his colleges 3D CRT treatment method shows that it is more effective that 2D conventional radiotherapy which was used before. 3D CRT has much better results in decreasing dose to normal tissue without any impact on dose distribution, homogeneity and dose coverage to PTV [11].

2.3.2. INTENSITY MODULATED RADIATION THERAPY (IMRT)

Intensity modulated radiation therapy, or IMRT, is a specialized form of 3D CRT that allows radiation to cover the tumour and spare normal tissue better by specifically shaping photon beam. With IMRT, the radiation beam can be broken up into many smaller beams and the intensity each of them can be applied individually. Using IMRT technique, it is possible for more precise limitation of radiation amount which is received by surrounding healthy tissue near the tumour. In most cases, this may also safely allow a higher dose of radiation to be delivered straight to the tumour [10]. A. Seguro Fernandez in his work tried to show the benefits of IMRT over 3D CRT for organs which are at risk (spinal cord, lung, heart etc.) and the advantageous of IMRT for planning target volume (PTV). The results led to the conclusion that IMRT technique is recommended for better protection of organs at risk but the coverage of PTV has no improvement [12]. D.E. Heron also compared 3D CRT and IMRT techniques in treating gynaecological malignancies. Author submitted that IMRT has several advantageous over 3D CRT such as: significant reduction in treatment volume for bladder, rectum and small bowel. This reduction can further be translated into overall reduction of late treatment-related toxicity [13].

2.3.3. IMAGE GUIDED RADIATION THERAPY (IGRT)

Image guided radiation therapy, or IGRT, is used by treatment team for even more accurate delivery of radiation to the cancer. IGRT technique involves conformal radiation treatment which is guided by imaging, such as CT, ultrasound or X-rays. This imaging procedure is taken in the treatment room just before the patient is given the radiation treatment on a daily basis. Because of the tumours

motion due to differences in organ filling or movements of internal structures while breathing can occur during or between treatments, IGRT is used which allows for better targeting of cancer cells. The patient will first undergo a CT scan as part of the planning process then the information from the CT scan is transmitted to a computer in the treatment room to allow the treatment team to compare the earlier image with the images taken just before treatment. During image guided radiation therapy images are compared in order to see if the treatment needs to be adjusted. IGRT allows the team to better target the cancer while spearing healthy surrounding tissues [10].

2.3.4. VOLUMETRIC ARC THERAPHY (VMAT)

Volumetric Arc Therapy or (VMAT) is an advanced form of IMRT technology that allows to deliver a precisely planned 3D dose distribution with a 360-degree rotation of the gantry in a single or multi-arc treatment. Unlike IMRT where the machine has to rotate several times around the patient or to make repeated stops and start to treat the cancer cells from several different angles VMAT treatment technique allows to deliver the dose to the entire tumour in a single 360-degree rotation. This can typically be achieved in less than two minutes. One of the key factors which distinguishes volumetric arc therapy from other techniques such as: IMRT or intense modulated arc therapy (IMAT) is that it delivers dose to the whole tumour volume, rather than slice by slice and the treatment planning algorithm ensures that surrounding tissues are left healthy [14]. Haiyun Liu in his recent work investigated radiotherapy plans for patients with left breast cancer using 3D-CRT, IMRT and VMAT techniques. Author concluded that all three treatment modalities can achieve same clinical dosimetry demands and emphasized that VMAT technique can achieve less monitor units (MU) for the patient and the shortest treatment time [15].

2.4. 3D CRT FOR PELVIS

3D CRT is one of the most popular treatment method which is used for patients with malignancies located at the pelvis region. One of the earliest trials which was performed at Royal Marsden NHS Trust and Institute of Cancer Research 266 cancer patients who were required to be treated with EBRT to pelvis were investigated in order to compare conventional and conformal treatment methods by evaluating the symptoms after the treatment. Most of these patients were diagnosed with bladder and prostate cancer. Results which were received from this trial showed that the proportions of patients who experienced symptoms with conformal treatment were consistently lower compared with those who were treated conventionally, 9% in perception of mild symptoms and 7% for severe symptoms [16].

Mundt et al. publicised the paper where outcomes for whole pelvic radiotherapy were analysed using conformal intensity modulated radiotherapy (IMRT). Before the investigation 40 gynaecological patients underwent the contrast enhanced CT scan. CTV for these patients consisted from upper vagina, parametria, uterus and lymph nodes regions. PTV for treatment planning was created by adding additional 1cm to clinical target volume. Using the planning software plans were generated for all these patients. In order to compare the results acute toxicities in 35 previous treated patients with conventional method were analysed. Evaluation was performed by using acute toxicity scale from 0 to 4: 0-no toxicity; 1-weak, no medications were required; 2- average, medications were required; and 3-severe, treatment breaks or hospitalization was needed. Results showed that using intense modulated technique no patients developed 3 grade toxicity and 2 grade acute toxicity was less seen than in conventional group. This study concluded that 3D CRT resulted excellent PTV coverage and ability to spare normal tissues. Apart from that the whole treatment using conformal method was well tolerated for patients and it associated with less acute consequences that conventional one [17].

2.5. 3D CRT, IMRT AND OTHER EBRT TECHNIQUES OVER BRACHYTHERAPY

According to author most studies of IMRT with patients who have cervical cancer have focused on IMRT as a replacement for locoregional treatment, IMRT and other conformal treatment methods have also been offered as a replacement for brachytherapy; e.g. as a consistent boost after external pelvic irradiation [18]. In a work were 44 patients with cervical cancer could not receive brachytherapy for various reasons outcome data was described and published from Christie Hospital, Manchester, United Kingdom. A total radiation dose which was deliver to those patients vary from 54–70 Gy and it was delivered by using EBRT plus 3D conformal radiation boost in most of those cases. Results showed that repetitive disease was seen in 48% of those patients and the median time to recurrence was 2.3 years. It also showed that the 5-year overall survival rate was 49.3%. These results led to the conclusion that they are inferior to ones obtained from using image guided brachytherapy but are comparable to standard brachytherapy showing that IMRT is not an acceptable alternative to brachytherapy when BT is possible [19-23].

Another work from Princess Margaret Hospital, Toronto, analysed dosimetric and toxicity data which was gathered form 12 patients. 8 of them with cervical cancer cases, 2 endometrial and 2 vaginal. All of them were previously treated with external EBRT and conformal radiotherapy (CRT) boost. IMRT treatments plans were customized for each of the patient and then compared with the ones using CRT in terms of dose conformality and critical normal tissue avoidance. Results showed

that 2 of 12 patients who had large PTVs developed rectal bleeding. It also showed that dose conformity was much better comparing with CRT and that dose to volume distribution was relatively improved. The volume of rectum that received the highest dose was reduced by 22% and bladder volume was reduced by 19% using IMRT comparing with CRT. It was achieved by the expense of an increase in the volume of organs which received lower (<33%) dose [24].

There is other paper where EBRT using photons (IMRT) and protons (IMPT) was compared with image guided brachytherapy. In this work gross tumour volume, clinical tumour volume, bladder, rectum and sigmoid were evaluated. Brachytherapy planning was optimized with respect to organ dose limits. Additional margins (3 mm and 5 mm) were added to CTV in order to describe PTV for external beam radiation treatment. Fractionated doses for target structures and normal tissue volumes were compared. All received results led author to the conclusion that using IMRT or IMPT for cervix cancer boost treatments results are inferior comparing with the ones received from brachytherapy [25]. In addition, there are works who say that planning EBRT using IMRT for patient's cervical cancer, cervix regression and internal organ motion should be taken into account as they contribute to the cervical target [26-28]. A research which was did at MD Anderson Cancer Centre scientists tried to quantify these organ movements. They observed that mean maximum changes at the centre of the cervix tumour were 2.1 cm in superior-inferior, 1.6 cm in anterior-posterior and 0.82 cm in right-left dimensions. This work also contributes to the work which was mentioned before that organ motion should be taken into account when EBRT planning is performed [29].

In conclusion it should be mentioned that EBRT is a useful tool that is particularly beneficial in the treatment of patients with cervical cancer. The extent of this treatment technique is quite limited, but it clearly shows that it is helpful in the treatment of some of the cancer diseases where brachytherapy is not an option for the patient and especially in less experienced hands. However, this EBRT technique should be used wisely considering that the cervix can undergo some dramatic and unpredictable changes in its location, size, and shape during the course of treatment.

2.6. CORRELATION BETWEEN EBRT AND NON-COMMUNICABLE DISEASES (NCDS)

Despite highly sophisticated delivery systems for the treatment malignancies, complications can occur. It is known that treatment related cancer is a side effect of radiotherapy [30]. The possibility of developing second cancer depends on two things, irradiation of the entire volume and on the volume where the highest dose is located. And with all the respect to sarcomas which are induced by

radiation the main concern is the dose which is delivered directly in the path of the beam [31]. Kaido et al. concluded that relative risk of developing secondary cancer is inferior for the patients with smaller treatment volumes [32]. Most of the studies showed that secondary cancers are most common to be found close to the location where primary cancer irradiation field was used [33]. With that to be sad is it obvious that using EBRT as a treatment method for malignancies there is possibility to get secondary cancer. Non-communicable diseases are described as chronic diseases which are tending to last for a long period of time and are the result of a combination of genetic, physiological, environmental and behaviours factors and cancer itself is called one of non-communicable diseases [34,35]. By this information it can be concluded that there is some relationship between EBRT and NCDs and by using external beam radiation therapy (EBRT) NCDs could be provoked.

3. TREATMENT PLANNING

Treatment planning is described as all the decisions and actions which are required to take for a patient during radiotherapy treatment. The difficulty of this process depends on the treatment intent and technique which are required, but the design of most modern treatments has many common elements. The target site, where the tumour volume is located, will determine the patient's treatment position and immobilizations needed to apply. Imaging modalities give information about the patient in the chosen position which then allows the target volume to be defined. Imaging will also provide physical for the dosimetry calculations. The dosimetry calculations vary in different software's which are provided by different vendors from the determination of dose at a single point within the patient to a full 3D dose calculation which are summarized by dose volume histograms for target volumes and organs at risk (OAR) e.g. Figure 4. Treatment planning will also be influenced by other factors such as patients position during the external beam treatment, immobilization facilities used during the treatment, organs motion etc.

Fig.4. An example of possible dose volume histograms (DVH) for gynaecologic cancer patient.

3.1. VOLUME DEFINITIONS USED IN TREATMENT PLANNING

Volume definition is a necessity for meaningful 3D treatment planning and for accurate dose prescription. According to ICRU Reports No. 50 and 62 these volume definitions can define and describe several target and critical structures that contribute in the radiation treatment planning process. It can also provide a valuable information in order to compare it with different treatment outcomes. The following volumes are defined as principal volumes related to 3D treatment planning: gross tumour volume (GTV), clinical target volume (CTV), internal target volume (ITV) and planning target volume (PTV). Figure 5 shows how the different volumes are related and located [36].

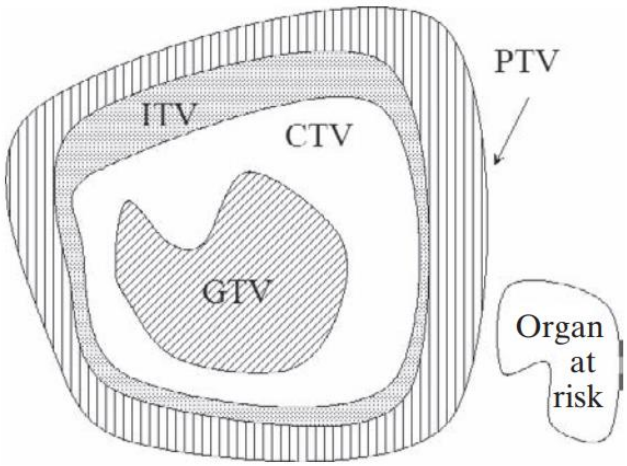

Fig.5. Graphical presentation of volumes related to 3D treatment planning [36].

- Gross tumour volume (GTV) - The GTV is based on information which is obtained from of imaging modalities such as computed tomography, magnetic resonance imaging, ultrasound and others, diagnostic modalities: pathology and histological reports and clinical examination performed by doctors.
- Clinical tumour volume (CTV) - The CTV is the tissue volume that is surrounded by GTV and/or sub-clinical microscopic malignant disease, which must be treated. This volume thus has to be treated properly in order to achieve the best results of therapy, cure or palliation. The CTV is usually stated as a fixed or variable value around the GTV (e.g. CTV = GTV + 1 cm), but there are some cases where CTV is the same as the GTV (e.g. prostate boost to the gland only).
- Internal target volume (ITV) - The ITV consists of the CTV plus an internal margin. The internal margin is designed to consider the variations in the size and position of

the CTV based on the patient's reference frame which is usually defined by the bony anatomy;

- Planning target volume (PTV) - The PTV includes the internal target margin and an additional margin for set-up uncertainties, machine tolerances etc. The PTV is used in the treatment machine as a reference frame and is often described as the CTV plus a fixed or variable value (e.g. PTV = CTV + 1 cm).
- Organ at risk (OAR) - The organ at risk is an organ which is near the PTV and whose sensitivity to radiation is such that the dose received from a treatment may be significant compared with its tolerance level of it and which requires changes in treatment planning by rearranging the beam (shape, angle, etc.) or dose to PTV [36].

3.2.IMAGING TECHNIQUES USED TO DEFINE TUMOUR VOLUME

As it was mentioned before imaging capabilities play crucial part in gynaecological malignancies management. There are several techniques which allows radiation therapists to provide valuable clinical information regarding the presence and extent of gynaecological malignancies and reduce the consequences of it and from there to determine whether the patients have gynaecologic cancer and if so the stage and type of it is diagnosed [37]. These techniques have significant advances which led to increasing precision for radiation therapy treatment planning. They can provide more accurate and effective radiation dose delivery for both external beam and brachytherapy. All modalities which will be mention below have their own advantages and should be taken into consideration in order to successfully diagnose and treat patients with gynaecological malignancies.

3.2.1. ULTRASOUND (US)

According to one of the works ultrasonography, especially with a transvaginal approach, is the initial imaging modality in patients with gynaecologic malignancies where endometrial cancer is suspected. Endometrial cancer most often appears as thickened endometrium wall that is more than 5 mm in a postmenopausal woman or 15 mm in a premenopausal woman [38]. In other works, it was concluded that transvaginal ultrasonography should be used in the initial evaluation of women with postmenopausal bleeding [39-41]. There are several other ultrasound techniques such as Color Doppler US and Spectral Doppler with allows to detect endometrium malignancies [42-45]. The accuracy of US for evaluation the depth of surgical invasion is around 73% - 93%, but US is better for grade 2-3 tumours and should not be used as the single criteria for the decision to perform extensive surgery [46–48]. Ultrasound can be used in detecting other types of gynaecologic cancers as well. Leeber S. Cohen in his work concluded that using three-dimensional power Doppler imaging

was better in defining the morphological and vascular characteristics of ovarian lesions. All malignancies were correctly identified by both 2D and 3D imaging. However, the 3D power Doppler was better comparing with 2D technique [49]. L.Valentin mentioned that using pattern recognition of the gray-scale US imaging correct diagnosis can be made in almost half of adnexal tumours which were scheduled for surgery [50]. Apart from all the US advantages there is additional one which should be emphasised ant it is the cost and harm risk from radiation comparing with a computer tomography (CT) [51].

3.2.2. COMPUTER TOMOGRAPHY (CT)

Joseph P. Connor in his work came up with a conclusion that Routine preoperative CT scanning rarely changes treatment and is a poor predictor of nodal disease. Furthermore, CT scanning of any patients with endometrial cancer should be discouraged unless evaluation of a symptoms is needed [52]. Apart from that, there are works that says using conventional CT for diagnosis 84% to 88% staging accuracy for endometrial cancer can be reached [53,54]. According to Oguz Akin CT is most commonly used in the assessment of more advanced gynaecologic cancer cases. CT is often used in preoperative staging and treatment planning for cervical cancer. But there are several advantages which CT has according to author. In the evaluation of cervical cancer, oral and intravenous contrast is needed. The advantages of CT are rapid acquisition time, lack of motion artefacts, and the ability to image organs during the peak of vascular enhancement, which allows to segregate between blood vessels and lymph nodes. Advances in CT technology, such as multidetector scanners, are improving tumour evaluation by CT. Multidetector CT uses thinner section collimation and higher table speed per rotation, which allows better spatial and contrast resolution than single-detector helical CT. Reconstruction of axial data in the coronal and sagittal planes is helpful in depicting local spread of disease. The accuracy using contrast-enhanced CT technique in the detection of parametrial invasion was 76% to 80% according to [55]. In advanced disease with hydronephrosis and pelvic sidewall invasion, the accuracy of CT increased [56]. There are some cases where CT results are similar to magnetic resonance (MR) imaging, for example detecting lymph node involvement in gynaecologic malignancies, CT has similar accuracy comparing with MR imaging (83%– 85% for CT, 88%–89% for MR imaging) [57]. So, it shows that CT can be a valuable tool in detecting some types of gynaecologic cancer cases as well.

3.2.3. MAGNETIC RESONANCE IMAGING (MRI)

Magnetic resonance (MR) imaging is one of the durable imaging modality for the imaging of gynaecologic malignancies and is generally regarded as preeminent to CT in the staging of female

pelvic malignancies. If it is available, MR should replace CT in the staging evaluation of patients with a known or suspected gynaecologic tumour. Several reports have shown that MR imaging has been more accurate than CT and US, more over it is the most advantageous technique for the evaluation of endometrial cancer [58,59]. MRI is more accurate comparing with sonography and CT for evaluation of tumour enlargement into cervix and myometrium and staging accuracy of MR imaging ranges from 83- 92% [60, 61]. There are some works which says that MR has almost the same accuracy as CT in detecting nodal metastasis. 83 - 90% for CT and 86 - 90% for MRI [62,63]. MR imaging is superior in the evaluation of gynaecologic tumour size (one of the prognostic factors in cervical cancer) and provides measurements which are similar comparing with surgical measurements in most cases [64,65]. Because of its excellent soft-tissue resolution, MR imaging has a better edge in the depiction of vaginal involvement, rectal and bladder invasion. The reported accuracy of MR imaging for vaginal invasion was between 86% to 93% [66,67]. Overall MRI plays a crucial part in the diagnosis, staging and treatment planning for patients with gynaecologic malignancies.

3.2.4. POSITRON EMISSION TOMOGRAPHY (PET) WITH CT

Positron emission tomography (PET) in combination with CT has emerged in recent years as a powerful tool in the evaluation of more advanced, widely metastatic gynaecologic malignancies. One of the key factors which distinguishes PET/CT combination from other imaging modalities is the ability to show not only the structural images, but also shown the cell functional changes in patient's body. Hyuck Jae Choi in his work came to the conclusion that PET/CT was more sensitive than MRI in detecting lymph node metastases for patients with uterine cervical carcinoma [68]. PET/CT combination also shows better results in treatment planning using three-dimensional conformal radiation therapy because it reduces the risk of anatomical misses which reduces the dose of ionizing radiation to surrounding organs and tissues by taking into account the ability to show metabolic and biological features of tumour [69]. PET/CT technique is also a valiable tool in detecting cancerous structures which were unnoticed by using CT imaging. Moreover, it may help planning the management of treatment especially in the selection of radiation field. However further studies are needed in order to recommend PET/CT technique as an alternative to pre-treatment surgical staging [70]. Eun Ji Nam in his work stated that PET/CT is superior to pelvis US, abdomino-pelvic CT, and pelvic MRI imaging for diagnosis of malignant ovarian cancer and is useful tool in showing metastatic ovarian cancer and co-existing malignant tumours. Therefore, he suggested that PET/CT could be used during pre-operative evaluation of patients who are suspected with ovarian cancer [71]. To

conclude this technique, we can say that PET/CT imaging has promising results over US, CT and MRI, but it also need further research for more detailed information about the impact on treatment planning and staging for patients who are diagnosed with gynaecologic cancer.

To summarize this chapter, it should be mentioned that the imaging techniques and modalities have evolved significantly over the past several years in the purpose of noninvasively characterisation of gynaecologic malignancies. Diagnostic imaging will continue to be one of the key components in detection, evaluation and treatment procedures for these malignancies. Ultrasound and CT continue to be the assistant component in diagnosis of cancer structures, but MR will undoubtedly remain the best standard in the localization assessment of pelvic malignancies. However, combination between PET and CT will continue to evolve as an obligatory tool in diagnosing gynaecologic cancer and particularly in those cases where metastatic diseases can be found.

3.3. PATIENT POSITION, IMMOBILIZATION DEVICIES AND ORGAN MOTION INFLUENCE ON PLANNING

During the external beam radiation treatment patient position should be chosen intently and must not change between the planning and treatment stages. It is valid that the position for the patient is optimal for dosimetry and that the patient remains relaxed and comfortable during the treatment procedure. According to Claudio Fiorino immobilization of the patient in the treatment position has been shown to significantly reduce setup errors and improvement in accuracy and reproducibility of the patients positioning [72]. Such errors can then lead in a failure to deliver the planned dose to the tumour volume resulting in a possible under dose to the target or overdose to nearby OAR. Different immobilization systems are used during EBRT depending upon the treatment site where the cancer is located. Immobilization may be as minimal as in the use of a knee rest and ankle stocks for pelvic radiotherapy where these immobilization supports play only the ancillary role. It should be considered that each immobilization system is evaluated in terms of the accuracy and reproducibility of patient positioning. In terms of gynaecologic cancer patients there are two immobilizations devices which are used during the treatment: knee and head rests.

Immobilization systems are decent in helping to set up the patient reproducibly, but they are not able to prevent the internal motion of the target volume and surrounding organs. These internal physiological motions are difficult to control and if not handled correctly will also lead to inadequate treatment delivery. If techniques are not approachable to manage internal organ motion it is obligatory to evaluate tumours volume for each of the possible motion position and increase the target volume accordingly. There are several works with a different imaging approach to a tumour motion using X-

ray, CT or MRI techniques. All those investigations led to a conclusion that these approaches were limited by poor soft tissue definition. CT imaging provide more soft tissue information about uterus and cervix, but it is difficult discrimination between other components of the clinical tumour volume (CTV). MRI can provide softest tissue detail and has been used properly to explore motion of the cervix and uterus during radiotherapy treatment procedure [73-75].

3.4. DOSE PLANNING SYSTEMS

Treatment planning systems are one of the key components of radiation therapy systems and they are great tool to improved patient outcomes. Once all the data is gathered and the tumours are identified, the systems develop a complex plan for each of the patients on how the therapy system will deliver radiation. The software is also capable of computing the expected dose distribution in the patient's tissue. These systems can also navigate beam placement which is based on avoiding critical structures that are more sensitive to radiation to reduce damage from the therapy. This may include complex algorithms for multi-leaf collimator (MLC) where each leaf is sequencing to shape the beam around critical structures during dose delivery to PTV. Planning systems can also be modified to compensate for the reduction of tumour size over the course of treatments. Different types of planning systems are provided by different vendors who distinguishes them from others by various features some of them will be discussed in this master thesis as well [76].

Table.1. Different planning systems and their capabilities [76].

Company name	**Elekta**	**Philips Healthcare**	**Varian Medical Systems, Inc.**
Product name	XiO	Pinnacle_	Eclipse Treatment Planning System
3-D conformal	+	+	+
4-D conformal	-	+	+
IMRT	Conjug. grad. descent optimiz; DVH prescription; step and shoot, dMLC, manual segmentation; QA outputs	One-Step IMRT with Direct Machine Parameter Optimization; SmartArc for variable and constant dose rate VMAT planning; automated IMRT and VMAT planning with auto-planning	Supports step and shoot, sliding window, and RapidArc (VMAT) technology for either flattened or unflattened beams; ability to interatct in real time with optimization
Brachytherapy	US guided pre-plan templates, auto seed detect; low dose rate, TG43, 3-D dose display/analysis	2-D, symmetric dose lookup; geometric and TG43; combined dose evaluation	MRI, CT and film based, all isotopes supported, advanced dose calculation correction for patient and applicator inhomogeneities, interactive optimization
Conformal arc	+	+	+
Volumetric modulated arc	-	+	+
Photon algorithms	FFT convolution, multi-grid superposition	Collapsed cone convolution superposition	Acuros XB, AAA (Anisotropic analytical algorithm)
Electron algorithms	Pencil Beam and Electron Monte Carlo	Hogstrom pencil beam	Monte Carlo
Proton algorithms	Broad beam, pencil beam and scanned beam	Customized pencil beam	Acuros PT, ocular

4. IN VIVO DOSIMETRY

In vivo dosimetry involves the assessment of external irradiation doses to cancer patients with the aim to ensure high precision and accuracy in dose planning and delivery during radiotherapy procedure. *In vivo* dosimetry can also be used for the estimation of uncertainties that may occur during radiotherapy treatment and for prevention against systematic errors and undesirable exposure. Implementation of *in vivo* dosimetry during irradiation can assist in detecting of doses that exceed the limits or are insufficient to treat the cancer according to the prepared dose plan. However, the availability of the various *in vivo* dosimetry systems remains is limited. This is partially related to the needs for the new installations of dose recording and dose verification systems and the general belief in the usefulness of these systems in detecting patient set-up errors, as well as beam energy, treatment accessory and geometry errors. Despite of this, implementation of *in vivo* dosimetry systems is ongoing and is seen as a crucial part of a radiation safety system in radiotherapy department.

According to Ben Mijnheer *in vivo* dosimeters can be divided into two types: real time and passive detectors which need some amount of finite time in order to do their analysis. Both types need calibration which is made by comparing their response with ionizing chamber at standard radiation conditions (source to surface distance (SSD), field size, beam energy etc.) [77].

- **Real-time dosimeters** are the ones which are capable of measuring the total dose in real time during the treatment procedure and able to measure the dose rate, which may then be used as an additional information is some cases. Real time dosimeters include diodes, metal-oxide semiconductor field effect transistors (MOSFETs), plastic scintillation detectors (PSDs) and electronic portal imaging devices (EPIDs) [77].
- **Passive detectors** can't provide real time and immediate measurements. In order to read those detectors finite time is required which can be from minutes to hours depending on dosimeter. These types of dosimeters include thermoluminescent dosimeters (TLDs), optically stimulated luminescent dosimeters (OSLDs), radiophotoluminescent dosimeters (RPLDs), implantable MOSFET detectors and they are capable of providing point dose measurements while radiographic and radiochromic films can offer two-dimensional dose distribution information [77].

4.1. DIODES FOR DOSIMETRY

It's been almost 40 years since the first introduction of diodes as a dosimetry tool [77]. Nowadays these semiconductor diodes can be applied in to all fields that are related with radiation

medicine such as: nuclear medicine, radiology and radiation therapy and according to Marion Essers they are one of the most common practises in *in vivo* dosimetry for EBRT [78]. These detectors are useful in radiation dosimetry because of their high radiation sensitivity relative to the ionization volume. Therefore, the measuring volume can be very small, leading to good spatial resolution. Semiconductor diodes offer many advantages for clinical dosimetry:

- Higher relative sensitivity;
- Quick response – (1 – 10 μs);
- Good mechanical stability;
- No external bias needed;
- Small size;
- Smaller energy dependence of mass collision stopping power ratios (between silicon and water compared to air and water).

However, diodes can be influenced from several factors:

- Dependence on temperature, dose rate, energy dependence;
- Require an electrical connection during irradiation [79].

4.1.1. WORKING MECHANISM

The density of silicon and the low average energy (1.1eV) required to form a carrier pair in silicon results in a radiation current density which is about 18,000 times that of air, allowing a small volume (approximately 10^{-2} to 10^{-1} mm^3) of silicon diode to produce an easily measured current. As a result, diodes have a high sensitivity (charge collected per unit dose to the diode). Their small volumes and real-time readout make diodes attractive for in vivo dosimetry. Most semiconductor diodes are made from silicon that is either n-type where acceptor impurities are doped into a region of n-type silicone (impurities can be pentavalent elements, e.g. phosphorus) or p-type which is formed by doping donor impurities into a p-type substrate (impurities of trivalent material, e.g. boron). To form a dosimeter, a p–n junction must be created. Therefore, the majority carriers in n-type silicon are electrons, and holes are the minority carriers p-type. Both of semiconductors n-type and p-type are commercially available in the market. According to author p-type diodes can resist radiation much better comparing with n-type detectors because holes can be more easily trapped that electrons [80]. Other advantage which p-type detectors have over n-type is the dependence of diode sensitivity on dose rate and temperature which is greater for n- type than p-type detectors [81,82]. In either of these detectors, a spatially varying doping creates a region where p and n-type silicon are in direct contact.

The majority carriers from each side diffuse to the opposite side (electrons on the n side diffuse to the p side, leaving positively charged donor ions, while holes on the p side diffuse to the n side leaving negatively charged acceptor ions). These oppositely charged ions establish an electric field which is also known as built-in potential which then prevents further diffusion of the majority carriers. This spatially charged region is the p-n junction, also known as "depletion region". For diodes used for *in vivo* dosimetry, the typical width of the depletion region is less than several microns. Although the typical built-in potential is less than 1 volt, the electric field across the p-n junction is very high (greater than 103 V/cm). The high electric field across the p-n junction makes charge collection possible for the diode without external bias. Without external bias, the output signal of the diode can be measured in short circuit mode (current) or open circuit mode (voltage). A simple electrometer can be used in each case [83].

Figure 6 shows the schematic representation where the incident ionizing radiation generates electron-hole pairs throughout the diode. The minority carriers (electrons on the p side and holes on the n side) diffuse toward the p-n junction. Those carriers within approximately one diffusion length from the junction edge are able to reach it before they recombine. They are then swept across the junction by the built-in potential and measured by the electrometer. The total current consists of the radiation-induced photocurrent (radiation current) and the electrical leakage current due to the offset voltage from the electrometer [83].

Direct recombination is highly unlikely to be happened in silicon. The dominant mode in a silicon diode is indirect recombination. This is a function of material defects, which facilitate recombination, and also of the density of radiation-generated electrons and holes. Indirect recombination determines the lifetime of radiation-generated carriers and thus the fraction of carriers that diffuse to the p-n junction and are collected. Thus, the carrier lifetime controls the diode sensitivity (the charge collected per unit dose to the diode). Exposure to large (>kGy) doses from a high-energy beam (>2 MeV) produces radiation-damage which shorten the minority carrier's lifetime and reduce the diode's sensitivity. The magnitude of these sensitivity changes depends upon the material characteristics of the diode (n- or p-type, doping levels), and pre-damage of the material [83].

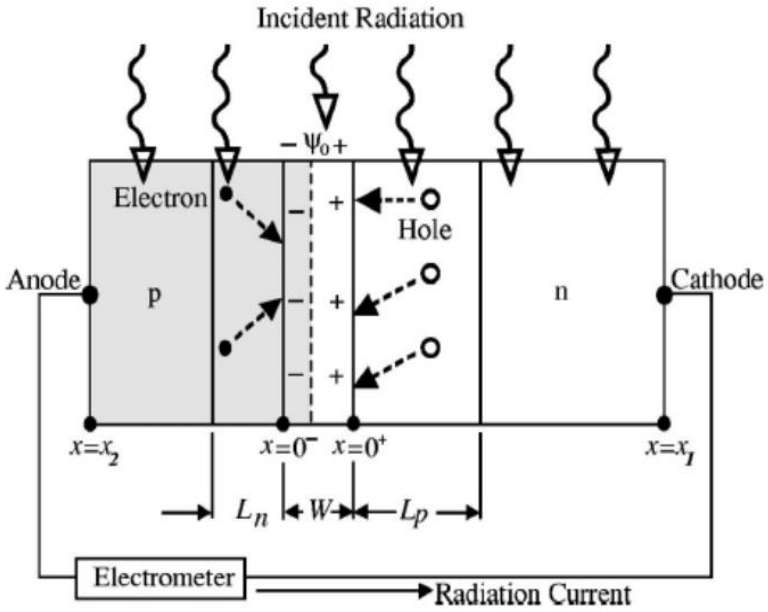

Fig.6. Schematics of a Si p-n junction diode as a radiation detector. The excess minority carriers (electron — • and hole — o) generated by radiation within one diffusion length, Lp on the n side and Ln on the p side, can diffuse to the p-n junction (width W). They are then swept across the junction by the built-in potential ψ_0 and are collected by the electrometer [84].

4.1.2. TEMPERATURE EFFECTS

The internal resistance of a diode decreases when the diode temperature is increasing. This property can be used to measure the temperature of the diode before each measurement, and it's also installed into some commercial systems. The sensitivity usually increases with temperature (Figure 7) [85].

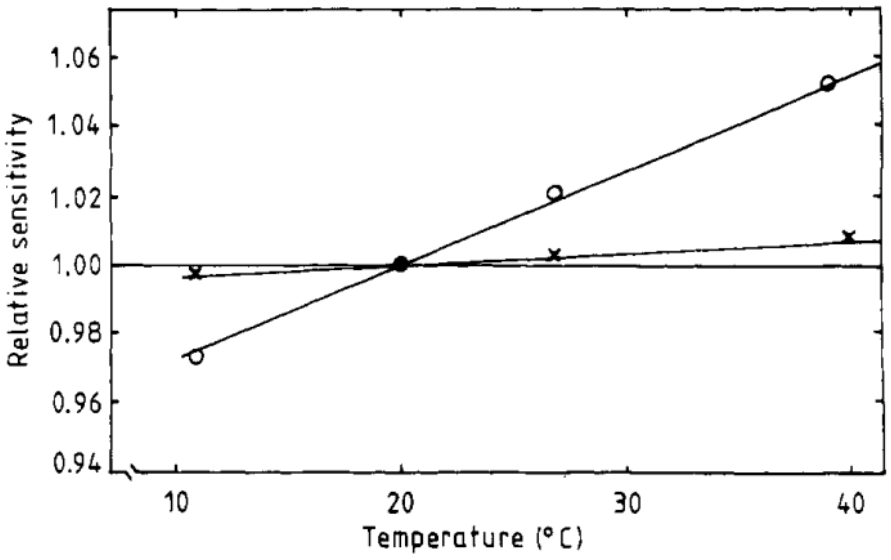

Fig.7. Mean values of the relative sensitivity as a function of the temperature for unirradiated detectors (x) and when pre-irradiated with 20 MeV electrons to 6 kGy (o) [86].

This occurs because of carrier mobility and the number of traps in the dosimeter crystal lattice. The variation of sensitivity with temperature depends on the dose which is received by the diode. The sensitivity can increase with temperature by less than 0.1% per °C when the diode is not irradiated, but after a dose of 6 kGy with 20 MeV electrons, this relationship may increase to 0.4% per °C [78, 79]. The sensitivity and temperature dependence of an unirradiated diode varies quite rapidly with the dose which was received and for this reason vendors preirradiate diodes before selling them in order to produce a more stable product. When a diode is placed on a patient, its temperature will rise by approximately 10°C from room temperature in 2 to 3 minutes and then diode reaches a steady state. If the sensitivity variation is found to be significant, the diodes should be left to reach body temperature for at least 3 minutes before the measurement is begun and the correction should be made for the difference in temperature between calibration and measurement conditions. Diodes can be calibrated at body temperature using a water phantom containing warm water or a thin layer of expanded polystyrene insulator can be placed between the diode and the patient so that the diode remains at room temperature [85].

4.1.3. BACKGROUND SIGNAL

Even if the diode is in unbiased mode of operation it will generate a dark current because of thermally generated charge carriers. This can only occur when low doses and dose rates are measured and if the electrometer is not zeroed. The background signal strongly depends on temperature so because of that some diodes generate increasingly high currents as the temperature rises and it can be seen even at low doses. The background signal can change by 4 mGy/min between room temperature and body temperature. This effect appears to be greater for n-type diodes than for p-type diodes. So, because of that the current can be zeroed before any measurements, several minutes are necessary to obtain a satisfactory background measurement and any changes in temperature can cause a change in diode response [85].

4.1.4. RADIATION DAMAGE

Radiation damage can occur when silicon atoms are displaced from their lattice sites. This creates new recombination centres which capture charge carriers leading to the reduction in sensitivity and to an increase in dose rate dependence. P-type diodes are generally less affected by radiation damage than n-type diodes, which show a sharp drop in sensitivity with radiation doses. The amount of damage for a given dose is dependent on radiation type. For example, 20 MeV electrons are 20 times more damaging than 8 MeV photons [88]. When n-type diodes are damaged by radiation, diode response becomes non-linear with dose rate. Therefore, the more expensive p-type diodes are

recommended for general use as they show a linear response with dose rate even after very high dose irradiation, and have a smaller sensitivity drop with accumulated doses [85].

4.1.5. ENERGY AND ANGULAR DEPENDENCE

Silicon is far from being tissue equivalent, especially for low energy radiation. The charge in diodes designed for *in vivo* dosimetry often depends on beam energy. Although the mass absorption coefficient and the stopping power of the silicon die contributes to the energy dependence for photon and electron beams respectively. Most of this energy dependence is due to the materials around the die, such as the build-up cap. Because of that it is common to have combinations of Al, Cu, Sn, Au, Ag, Pb, W, Ta, and Fe surrounding the die. Because electrons which are scattered from these high Z materials near the die contribute to the ionization they play a crucial part in the construction procedure of diode models [89]. For photon beam *in vivo* dosimetry, vendors provide different detectors with different dynamic energy ranges. A diode which is designed for optimal use at 6 to 12 MeV energy range might have a higher response per MU to 18 MV photons due to dose from electrons which are not stopped by the build-up cap of a diode. These electrons might also cause a 6 to 12 MeV energy range detector to a greater source surface distance (SSD) and field-size dependence if diode is used in an 18 MeV energy beam. On the other hand, the attenuation of a detector which is designed for 15 to 25 MeV photons reduces its effective sensitivity in a 6 MeV beam. The difference could be greater if a higher Z build-up material such as tungsten is used for the 15 to 25 MeV detector [89]. For electron *in vivo* dosimetry, a diode model with minimal build-up can cover the entire clinical energy range. The energy dependence of the diode response per MU results mostly from the energy dependence of the electron depth dose curve [90]. For example, the directional dependence for the domed diodes is not a important factor until the radiation beam is angled > 30° from an axis which is perpendicular to the diode baseplate. The angular dependence of the diode is related to the shape and construction. In most of the cases the diodes are placed on the surface which is perpendicular to the radiation beam axis and correction factors can be ignored. In one of the work cylindrical diode response was evaluated and results showed that diodes have cylindrically symmetrical response, but the response reduces by approximately 15% towards the tip of the diode [91].

4.2.RADIOCHROMIC FILMS FOR DOSIMETRY

Radiochromic films are solid state dosimeters and they are new type of films which are used in radiotherapy dosimetry. This type of films has near tissue equivalent composition (9.0% hydrogen, 60.6% carbon, 11.2% nitrogen and 19.2% oxygen) and therefore have a near linear energy dependence over the range of clinical energies where radiographic films rely on radiation interaction

with silver particles. They can be made in various forms such as gels, liquids, films or pellets and they do not need neither developer nor fixer for the image. Radiochromic films work in a way that their structural properties change when films are exposed to radiation. They contain a special dye which change colours due to polymerization process. Material which is responsible for coloration is known as crystalline polyacetylene and in particular it is diacetylene which during the thermal changes or radiation exposure undergo polymerization process which turns film into blue or red depending on their composition. After the irradiation absorbed light and the transmission of light through the film can be measured with a densitometer. One of the most common practise of Radiochromic films are the measurements of 2D dose distribution. Since this type of film is grainless it has high resolution and can be used in high dose regions comparing with radiographic films they are increasingly being used in radiotheraphy dosimetry. Other advantages over radiographic films are that they don't need darkroom facilities, film cassettes and film processing equipment, dose rate independence, insensitivity to environment conditions (apart from humidity which should be avoided). Radiochromic film energy dependence relies on specific compositions of the films where different variations of layers are made in order to mark them out from others Figure 8.

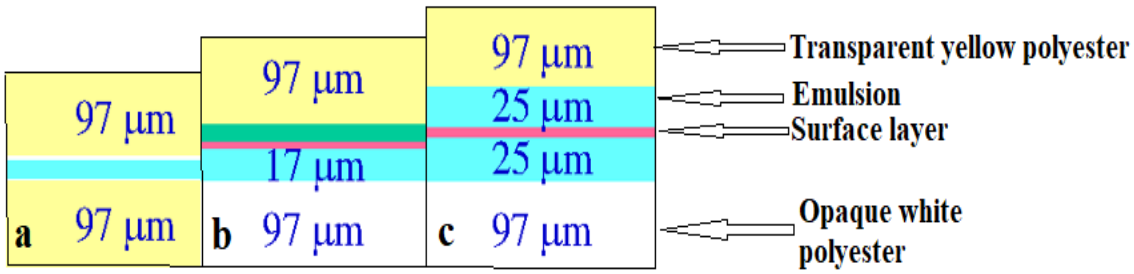

Fig.8. Different Radiochromic (GAFCHROMIC) films with different layer variations (**a** – XR-T, **b** – RTQA, **c** – XR-QA) [93].

All these layer variations (Figure.8.) allow to reach different dose ranges. For example, XR-T and RTQA films are able to operate at 0.01Gy to 5Gy and XR-QA film can operate in 0.001 – 0.2Gy range [92,93].

5. EQUIPMENT AND METHODOLOGY

5.1. TREATMENT EQUIPMENT

Treatment itself was performed using 15MeV photon energy beam which was generated by using Varian "Clinac 2100C/D" linear accelerator. Linear accelerator is illustrated in Figure 9. Some of the parameters of this linear accelerator are presented in Table 2.

Table.2. Varian "Clinac 2100C/D" linear accelerator parameters [95].

Power Source	**Photon Energy Configurations**	**Electron Energies**	**Multi-Leaf Collimator (MLC)**	**Treatment Delivery**
Klystron	• 6 and 10 MeV • 15 MeV • 18 MeV	Yes	• 52 MLC (Field size 26x40cm, leaf widths 10mm) • 80 MLC (Field size 40x40cm); • 120 MLC (Field size 40x40cm, Central 20cm of field - 5mm leaf width, Outer 20cm of field - 10mm leaf width)	3D, IMRT, SRS (optional)

Fig.9. Linear accelerator "Clinac 2100C/D" which was used during the treatment.

5.2. DOSIMETRY EQUIPMENT

All *in vivo* and *in vitro* dosimetry measurements which were did at this master thesis and will be explained below, were performed using diode detectors and radiochromic films.

P-type diodes (type T60010HP red, PTW) were used for dose measurement (Figure 10).

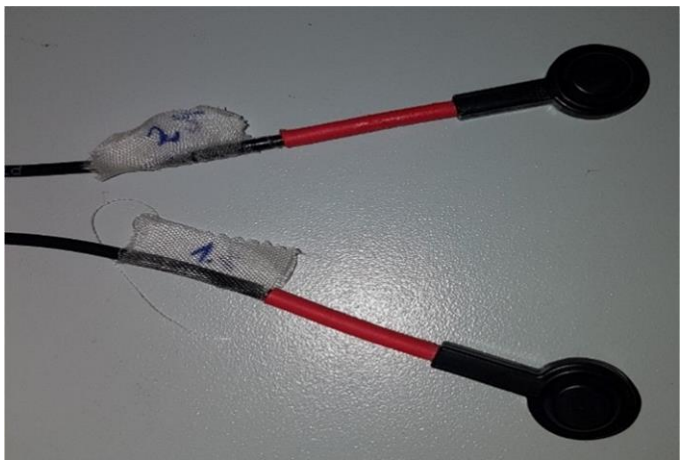

Fig.10. PTW diode detectors.

Diodes of this type are suitable for the use in a 13-25 MeV photon energy range (Fig. 10). The field sizes these detectors are able to read are from (1 x 1) cm^2 to (40 x 40) cm^2 for electrons and in a range of (1 x 1) cm^2 - (10 x 10) cm^2 for photons. Each diode is encapsulated by a cylindrical build-up cap made from W with a total buildup of 3.0 g/cm^2. The dose stability of the diode was $\leq$ 1 % / kGy (15MeV) and the sensitivity variation with a temperature was $\leq$ 0.4 %/K [96]. All diodes were read out with a PTW VIVODOS electrometer (Figure 11). This electrometer consists of twelve high-precision independent channels and is operated in the short circuit mode. It secures measurements accuracy of $\leq \pm$ 0.5 % and the long-term stability of the electrometer is $\leq \pm$ 0.5 % per year. The signal of the diode-electrometer system is linear with the delivered dose within 1% over its whole range. Uncertainties due to the non-linearity of the diode-electrometer system were ignored [97].

Fig.11. PTW VIVODOS electrometer.

Films which were used for dose evaluation were GAPCHROMIC RTQA^2. According to manufacturer these films have such features:

- Dynamic range 0.02 Gy - 8 Gy;
- Large measurement area;
- Self develops in real time;
- Near tissue-equivalent;
- High spatial resolution;
- Can be handled in room light;
- Water resistant (can work in water phantoms);
- Can operate in temperatures up to 70° C;
- Indoor lighting resistance [98].

The composition of GAFCHROMIC RTQA^2 films according to vendor are represented in Fig.12.

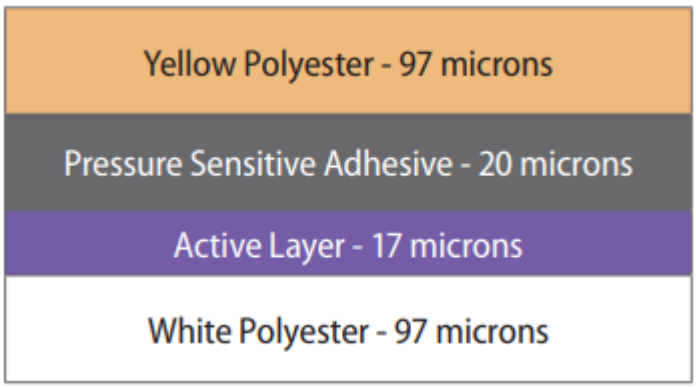

Fig.12. Composition of GAFCHROMIC RTQA^2 films [98].

Before all measurements calibration for these dosimeters were performed and each of this procedure will be discussed in the following section.

5.3. DIODE CALIBRATION

The reproducibility and stability of PTW detectors were checked before calibrating them. The first step in calibrating a diode for clinical use is to measure a calibration factor for each diode. The calibration is made with a combination of diode and electrometer and changing either of them requires a new calibration. The entrance dose to a patient is determined with the *in vivo* semiconductor probes. The entrance dose $D_{entrance}$ is the dose in the depth d_{max} (Figure 13).

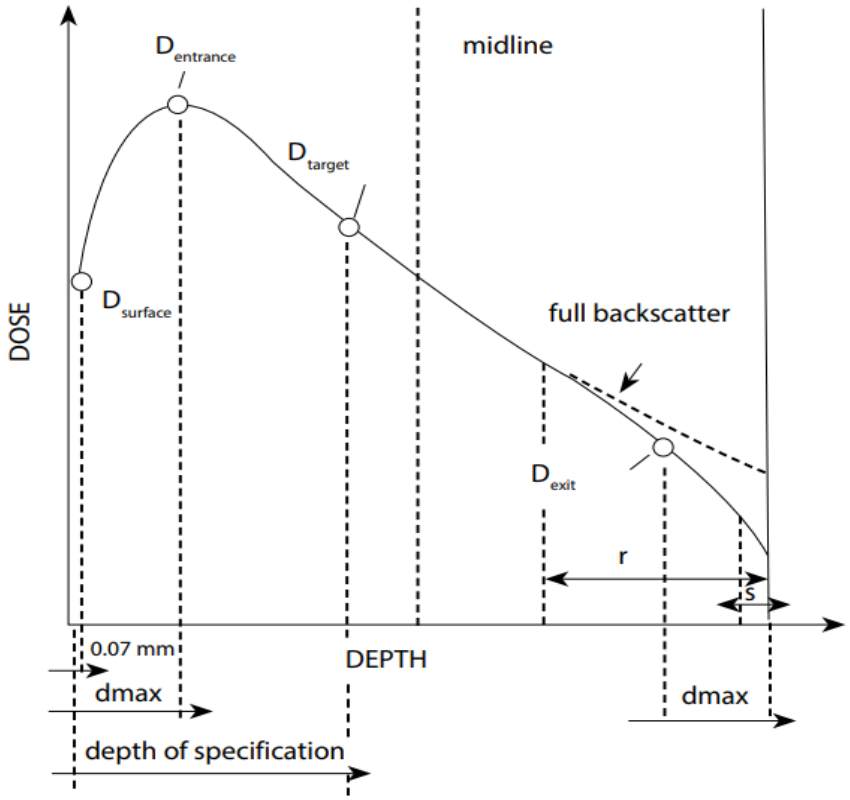

Fig.13. Percentage depth dose curve for diode calibration [99].

The dose in depth d_{max} is calculated with the help of calibration factors and measured values from the surface of phantom. The calibration factor is defined as the coefficient which links the dose in a phantom in depth d_{max} and the signal of the diode which is measured at the surface of the phantom. Calibration factor should be measured under standard conditions (SSD = 100cm, field size 10 cm x 10 cm, room temperature) and the deviations from these conditions should be considered by correction factors. The measurement directly at the patient's surface contains a large insecurity because of the very steep rise of the depth dose curve therefore semiconductor probes for photons are

made with build-up material to bring the radiation sensitive region of the detector always into the distance d_{max} [100].

To determine entrance dose the *in vivo* semiconductor probe is positioned at the phantom for determination of the calibration factor (Figure 14). According to the definition of the entrance dose the reference depth corresponds to the depth of the dose rate maximum [100].

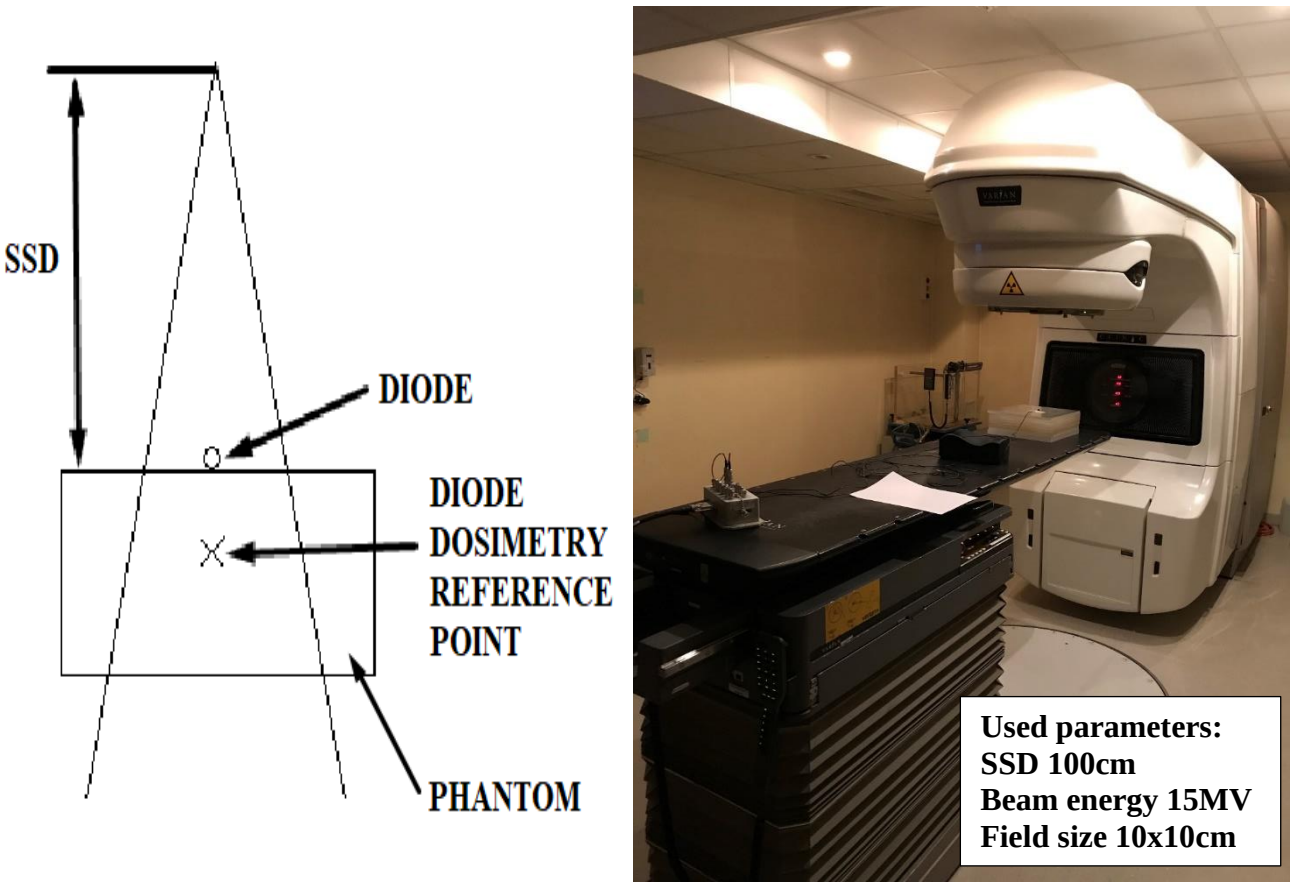

Fig.14. Schematic and actual setup for measuring entrance dose calibration factor.

5.4. FILM CALIBRATION

In order to perform accurate dosimetry with Radiochromic films dose response of the film to the radiation source is necessary to be characterized. A variation of known doses, preferably which includes the dose region of interest, should be delivered to the film and the changes of optical density (OD) of the film should be measured. In ideal case the relationship between the dose and OD should be linear but there are cases where it is not. Because of that various methods are used in order to determine the relationship between dose rate and OD such as polynomial fits or empirical models. To evaluate the amount of dose which was delivered to the Radiochromic film the change in the films absorbance is measured. To quantify this, changes in the OD of the film is measured. The optical density (OD) is defined as:

$$OD = log_{10}(I_0/I) \quad (1)$$

where I_0 as the initial intensity and I as the transmitted (or reflected) intensity. This formula in general could be written as a function of dose (2):

$$dose\ response = f(Dose) \quad (2)$$

Which means that calibration curve shows the relationship between the dose rate and the response. In this master thesis case calibration was made with radiation fields which were used during gynaecologic cancer patient's treatment and films were placed at the centre of isocentre where absorbed dose rate was known [92,93].

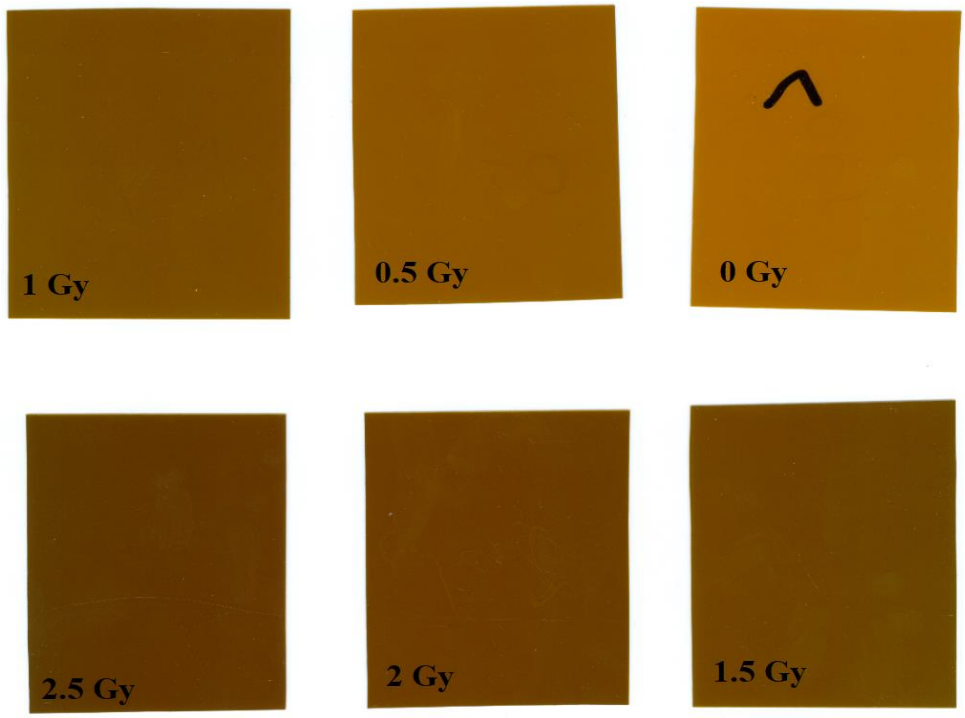

Fig.15. GAFCHROMIC RTQA^2 films for calibration at different dose rates.

5.5. *IN VIVO* MEASUREMENTS

In our *in vivo* experiment semiconductor probes were used in order to evaluate the actual maximum dose distribution in main and segment fields which were created in order to protect ovaries and deliver necessary radiation to gynaecologic cancer patients during their treatment procedure. Semiconductor probes were placed above and below the isocentre which was located on the junction area of two irradiation fields. One of the two fields was smaller (segment field) and had different field weight value indicating contribution of the beam to the whole dose delivered to the target during one fraction of treatment. This method with two fields of different size (main and segment) was chosen with the intention to protect ovaries against waste irradiation as it was mentioned before. The size of

each field was chosen according to the patient individual anatomic structures, tumour size and location. Semiconductor probes were sticked in the area of belly button of the gynaecologic cancer patients. Location of dosimeters was indicated in the dose treatment plans for zero main (000) and segment (000s) fields (linear accelerator gantry above the patient) that were produced using treatment planning system. Both treatment fields are in conjunction thus creating the possibility to overlap each other.

5.6. *IN VITRO* MEASUREMENTS

In vitro maximum dose evaluation measurements were performed using PTW diodes and GAPCHROMIC RTQA2 films on polymethylmethacrylate (PMMA) phantom. For the evaluation using diodes, semiconductor probes were placed on PMMA phantom at which one of the gynaecologic cancer patient's treatment field was formed (Main field collimator coordinates: X1= 10cm, X2 = 10cm, Y1= 16cm, Y2 = 19cm. Segment field collimator coordinates: X1= 7cm, X2 = 8cm, Y1= 0cm, Y2 = 19cm). In order to measure the maximum dose profile across the treatment field and field movement impact on maximum dose scanning axis and parameters used in measurements are demonstrated in Figure 16.

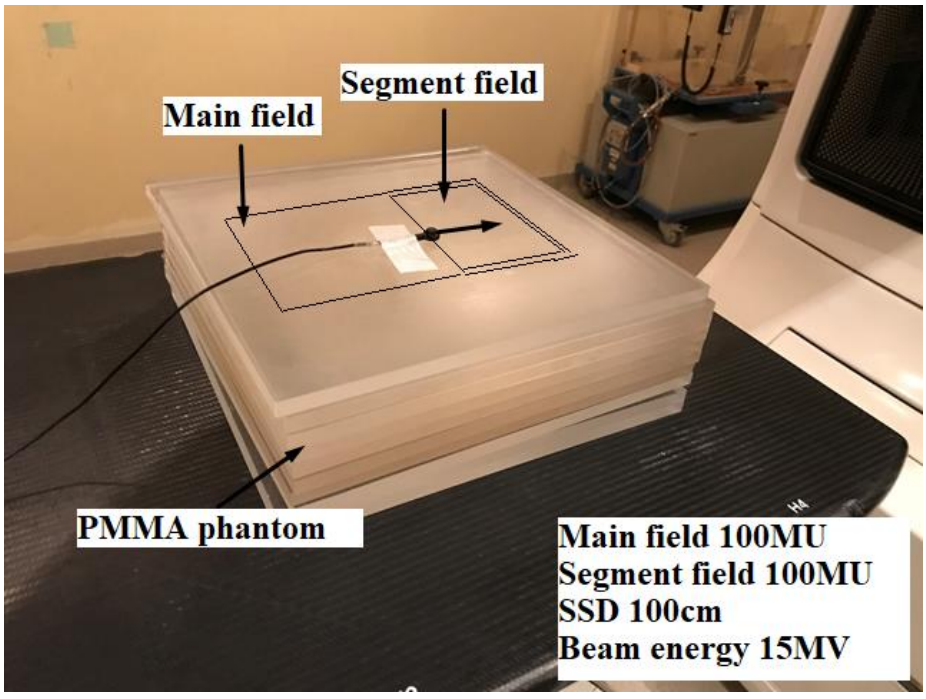

Fig.16. Diode based diose measurements scheme.

The measurements were performed in three stages. At first stage diode was placed on the isocentre axis where the junction of those two fields (main and segment) locating (Figure 17, a)). Results taken from this method were then used as an evaluation point for further measurements. At

the second stage measurements were performed moving segment field further to the left from isocentre axis (decreasing the segment field overlap region on treatment procedure) by 1 mm step. It was accomplished by moving collimator Y1 axis (Figure 17, b)). This was done with an intention to see how segment field reduction can impact the maximum dose values throughout the phantom. And at the last stage measurements were performed when segment field was moved further to the right from the isocentre axis (increasing the segment field impact on treatment procedure) by 1 mm step in order to see how maximum dose changes due to increased segment field region (Figure 17, c)).

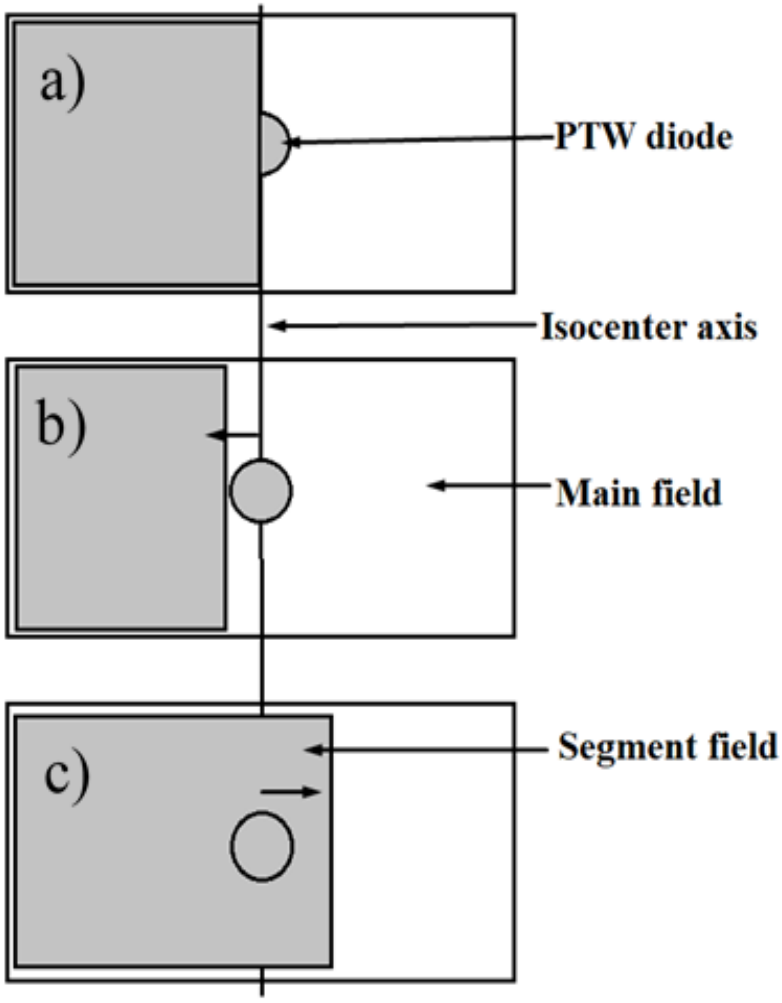

Fig.17. Diode based setup for dose profile measurements.

Using GAFCHROMIC RTQA^2 films same maximum dose evaluation was performed with fields used for gynaecologic cancer patient's which were achieved by using linear accelerator collimators. Before film measurements modelling was performed in order to know at which depth maximum dose is locating in the PMMA phantom in order to put films at the right location. "Eclipse" treatment planning system was used for that purpose and information is demonstrated at the Fig. 18.

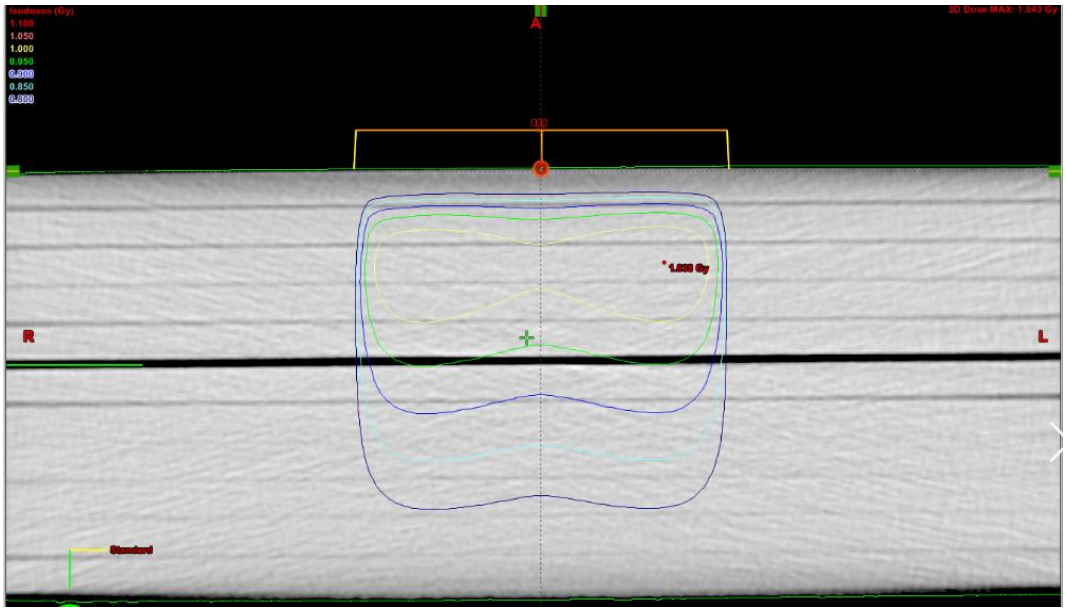

Fig.18. Evaluation of a Maximum dose location in the PMMA phantom using "Eclipse" treatment planning system.

When this location was found films were placed on the PMMA phantom. Before the measurements two field junction area was marked using light field in order to place films correctly. Films were placed on the phantom and irradiated at the same conditions as semiconductor diodes.

6. RESULTS AND DISCUSSIONS

6.1. PTW DIODE CALIBRATION RESULTS

In order to make sure that calibration was performed correctly, and entrance dose was measured precisely "Eclipse" treatment planning system analysis was used to evaluate the isodose distribution and dose profile at the PMMA phantom using standard calibration conditions (SSD = 100 cm, field size = 10 x 10 cm). From the figure 19 we can see that maximum dose at the d_{max} according to treatment planning system was 1.008 Gy.

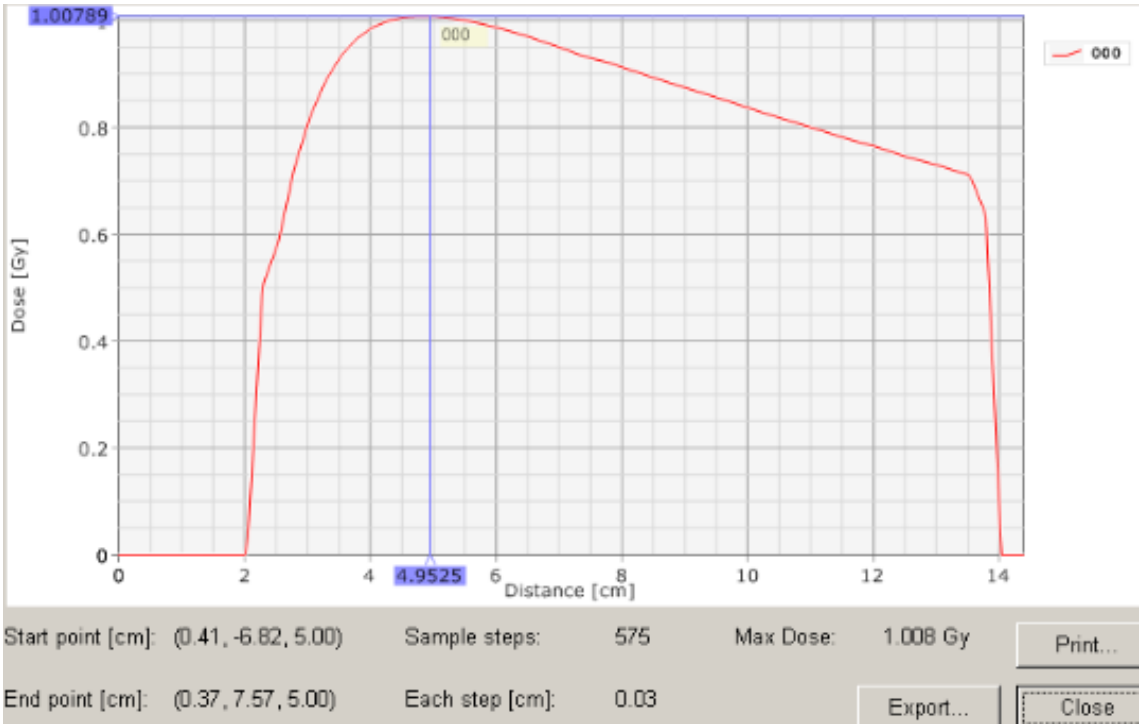

Fig.19. Dose profile across the depth of PMMA phantom using standard calibration conditions.

During the calibration procedure entrance dose calibration factors were measured for two diode dosimeters. Results are presented in Table 4.

Table.3. Results from diode calibration procedure.

Diode Nr.	Diode	Energy Range	Calibration factor	Result [Gy/C]
1	Red-1 15MV	13-25 MeV	Entrance	-6.825×10^{7}
2	Red-2 15MV	13-25 MeV	Entrance	-7.169×10^{7}

After the diode calibration, testing was done in order to assure that diodes produce accurate results. Wherefore 15MeV energy beam with 50 MU and 10×10 cm field sized was formed. From the

results we can see that calibration was done correctly and deviation was 0,02% which means that diode measured results were correct and did not exceed tolerance level (Figure 20).

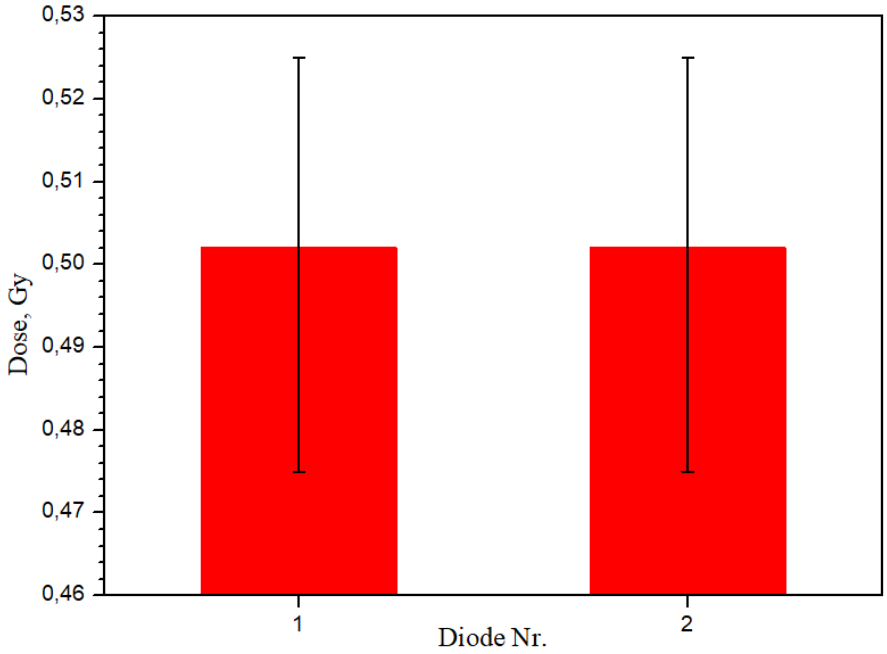

Fig.20. Diode test results.

6.2. GAFCHROMIC RTQA^2 FILM CALIBRATION RESULTS

After the GAPCHROMIC RTQA^2 film irradiation with known dose rates (0 Gy, 0.5 Gy, 1.0 Gy, 1.5 Gy, 2 Gy and 2.5 Gy) calibration curve was rendered (Figure 21) using linear fit function. The curve shows the relationship between dose rate and relative response which was calculated as a pixel density at the specific area of interest (in the middle of the calibration film).

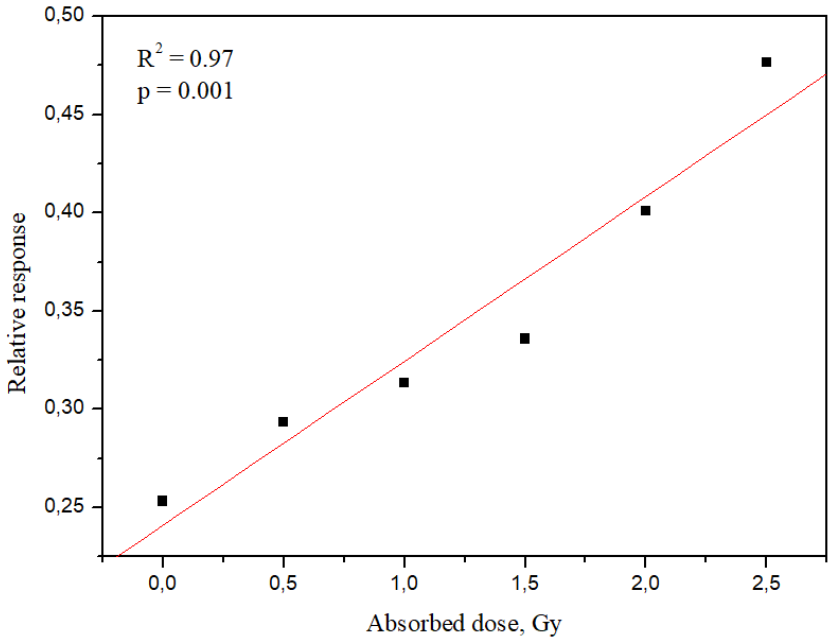

Fig.21. GAFCHROMIC RTQA^2 film calibration curve.

By characterizing response of film to known dose rates, the measured relative response of the unknown dose can be used to calculate the actual dose which was delivered to the film during the irradiation procedure.

6.3. *IN VITRO* MEASUREMENT USING DIODES

The results which were received using semiconductor diodes when segment field was moved to the left and right from the isocentre axis in order to change the impact region are represented in the table 4.

Table.4. Results received from diode based *in vitro* measurements where segment field movement impact was analysed.

Moving Step, mm	D_{Left}, Gy	$D_{Isocentre}$, Gy	D_{right}, Gy	D_{Left} deviation from isocentre	D_{right} deviation from isocentre
1 mm	1.2735 Gy	1.5005 Gy	1.756 Gy	15.1 %	17 %
2 mm	1.156 Gy		1.926 Gy	22.9 %	28.3 %
3 mm	1.1085 Gy		2.016 Gy	26.1 %	34.4 %
4 mm	1.0925 Gy		2.0465 Gy	27.2 %	36.4 %
5 mm	1.088 Gy		2.053 Gy	27.5 %	36.8 %
6 mm	1.086 Gy		2.054 Gy	27.6 %	36.9 %

From these results we can see that:

- When segment field is moving to the left from the isocentre axis (impact region is decreasing) by 1 mm, maximum dose decreases by 15.1 %, when the step is 2 mm maximum dose decreases by 22.9 %. Further segment field movement to the left shows that maximum dose decreases until it reaches the maximum dose value which is equal to the main fields maximum dose value only.
- When segment field is moved right from the isocenter axis (impact region is increasing) by 1 mm maximum dose increases by 17 %, when the step is 2 mm maximum dose increases by 28.3 %. Further segment field movement to the right shows that maximum dose increases until it reaches the maximum dose value which is equal to the sum of main and segment fields maximum dose value.

Received result were compared with the “Eclipse” treatment planning system. Figure 22 shows the maximum dose distribution throughout the length of a treatment fields. The curves show the distributions of main field (red curve) and segment fields (green curve) which were used for the gynaecologic cancer patients and sum curve which is presented in blue. From the results we can see that at the isocentre sum of main and segment fields maximum dose decreases and reaches the value equal only to the main field maximum dose value.

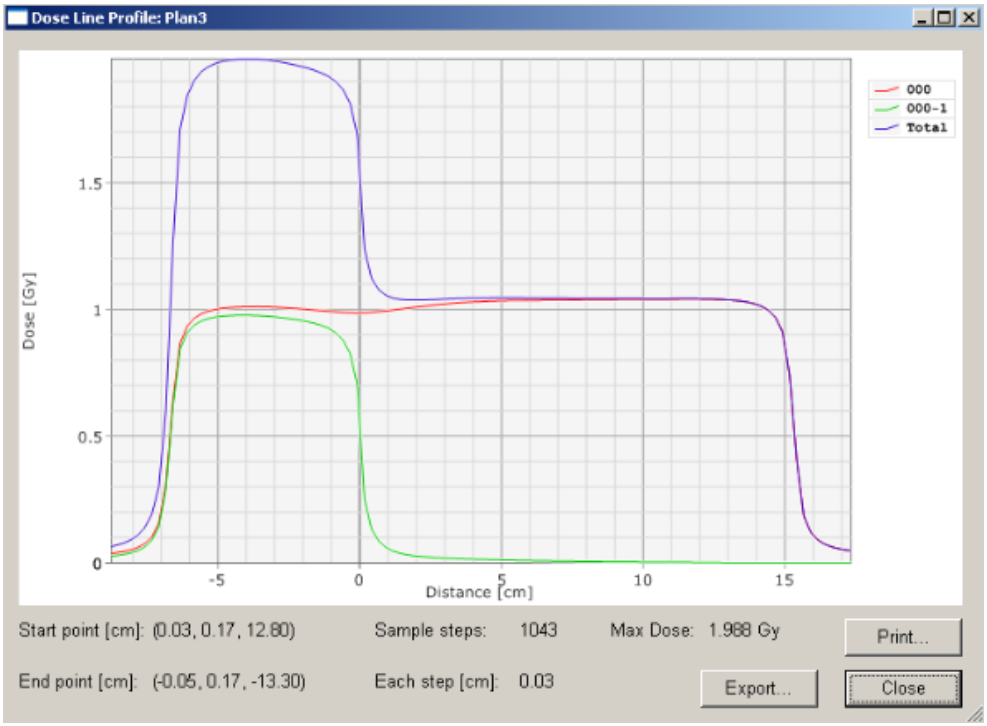

Fig.22. Dose profile distributions throughout the length of a treatment fields (main (red), segment (green) fields and sum (blue) curves).

6.4.COMPARISON BETWEEN DIODE AND FILM BASED MEASUREMENTS

Evaluation between diode and film-based measurements were made in order to find out and see which dosimetry equipment gives more precise results on the conditions which were used for gynaecologic cancer patients.

For the GAPCHROMIC RTQA^2 film analysis 4 radiochromic films were placed in the PMMA phantom where maximum dose was locating and were irradiated at the following conditions:

- Main field 100 MU;
- Segment field 100MU;
- Beam energy 15MeV.

Results gained from film irradiation are demonstrated in the figure 23. After the irradiation procedure radiochromic films were analysed using “ImageJ” program package. This program allowed us to obtain the maximum dose spectra across the film length. Results were averaged and from there specific area of interest was chosen in order to compare results with diode-based measurements (Figure 24).

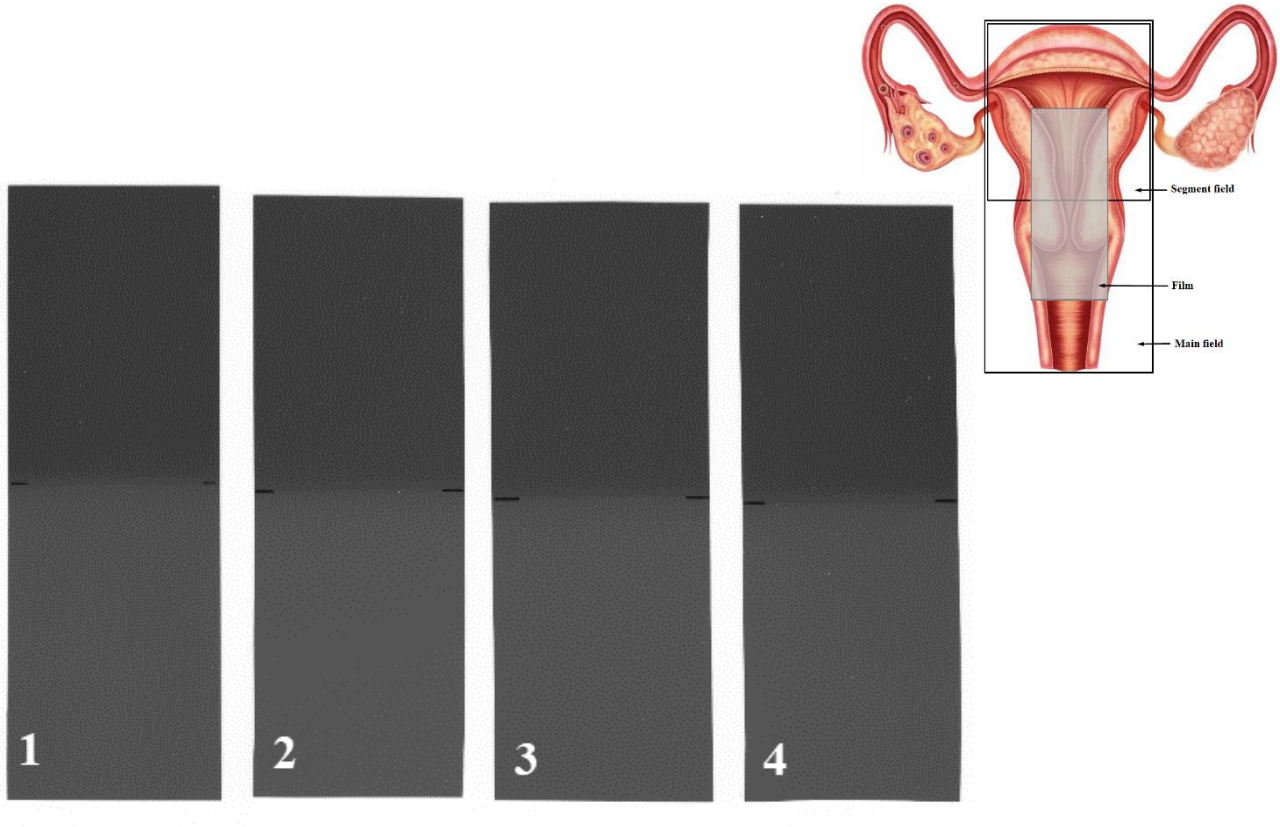

Fig.23. GAFCHROMIC RTQA^2 film irradiation results and schematical representation of film placement [adapted from 6].

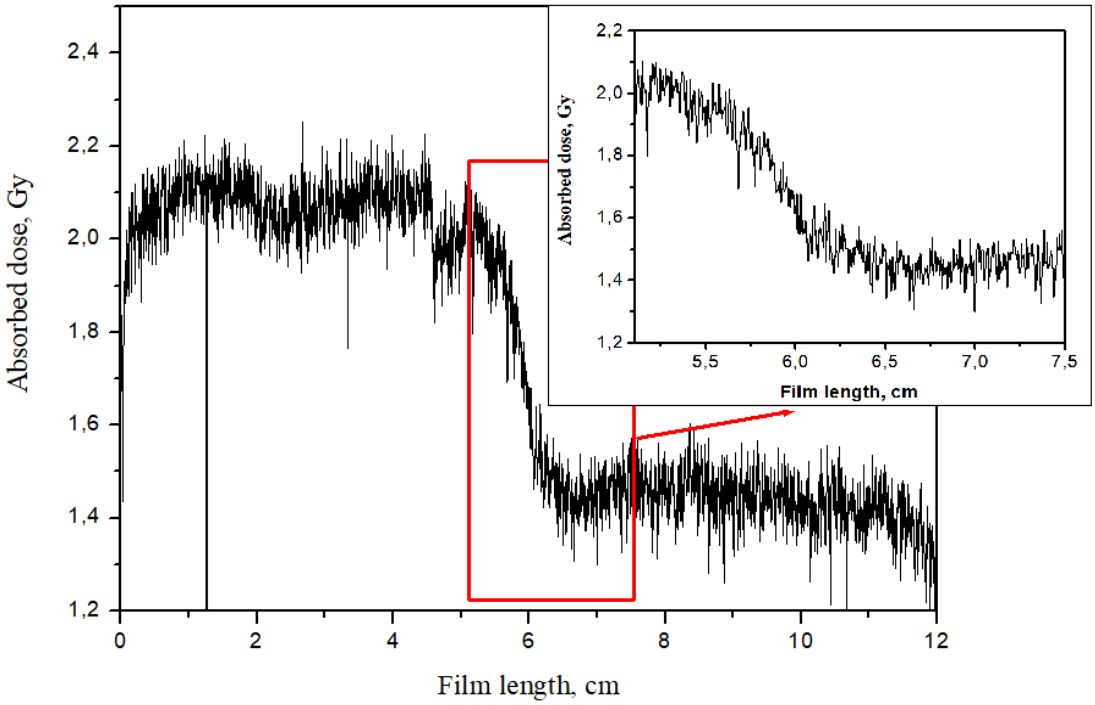

Fig.24. Averaged maximum dose profile distribution across the films length and specific area of interest.

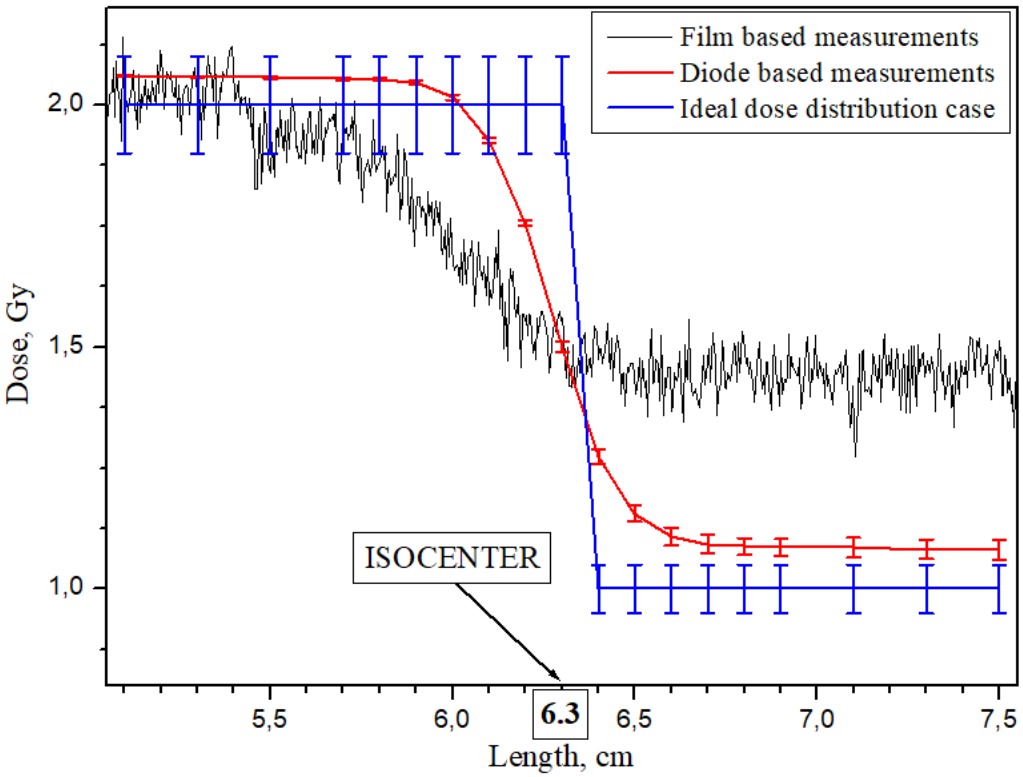

Fig.25. Results from diode and film-based measurements and ideal case of dose distribution for comparison.

Figure 25 shows the results obtained using film and diodes-based measurements and blue curve shows the ideal maximum dose distribution across the treatment field. From the results we can

see that diode-based measurements were more accurate in showing the dose distribution throughout the treatment field length comparing with the film-based ones. Result analysis showed that some of the diode-based measurements felt into the limits of ideal dose distribution case and relative errors varied from 0.8% to 3.7%. These results were obtained at the region where both main and segment fields where used (from 5.1 cm to 6.1 cm). At the junction area diode relative errors were much higher and varied from 12% to 27% (6.2 cm to 6.4 cm). And errors which were calculated at the area where only main field was used (from 6.5 cm to 7.5 cm) varied from 8.1% to 15.6% and they did not fall into the tolerance limits which is 5% (blue curve). These results shown that diode-based measurements were more accurate at the area where both fields (main and segment) were used. From the results which were gather using GAPCHROMIC RTQA^2 films we can see that relative errors exceed the tolerance limits almost throughout the whole area of impact length. There is only small area at the beginning of the curve where they enter the tolerance limits.

According to the results the relative errors, which were calculated from diode-based measurements and film-based measurements, were significant lower on diode-based measurements and the region where uncertainties did not exceed the tolerance limit were much greater comparing with the film-based ones.

6.5. *IN VIVO* RESULTS

For the *in vivo* measurements seven gynaecologic cancer patients were investigated (after their consent was given). Before the treatment individual treatment plans for each of the patient were made according to gynaecologic cancer location and individual anatomic properties. All imaging data which was gathered during planning stage was transferred to 3D conformal computer treatment planning system “Eclipse”. This planning systems is a product of Varian Medical System company. All plans were performed using AAA (Anisotropic Analytical Algorithm) algorithm for dose volume evaluation and PBC (Pencil Beam Convolution) algorithm for compensator. Those two algorithms allow to deliver treatment with a static multileaf collimator (MLC). The idea behind this treatment procedure was the intention to protect gynaecologic cancer patient’s ovaries from unnecessary irradiation during treatment procedure. This is one of the most common methods used for relatively young gynaecologic cancer patients who are and still have plans to give birth in near future. Because ovaries are very sensitive to radiation (maximum 3D dose = 1.5 Gy [94]) two different treatment fields were formed. Main field which was formed using box method (4 fields formed by gantry rotation from 0° to 270° with a 90° step) included lower part of women’s reproductive system and segment field which was formed by gantry rotation 0° and 180° and included upper part of women’s

reproductive system. Both of these fields (segment and main) had different field weight value which indicates the contribution of the beam to the whole dose delivered to the target during one fraction. Figure 26 illustrates the placement of those two fields.

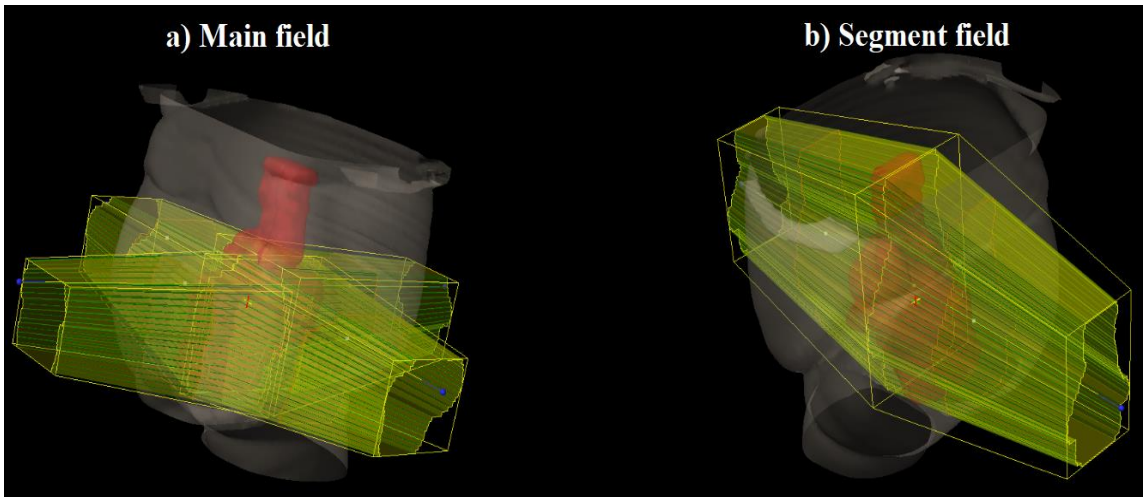

Fig.26. Schematic presentation of fields placement for gynaecologic cancer patient using "Eclipse" treatment planning system, **a)** shows the technique to form main field, **b)** shows the technique to form segment field.

"Eclipse" treatment planning system also gave information about field positioning, 3D view of PTV, 3D dose values for PTV (max and min) etc. (Figure 27).

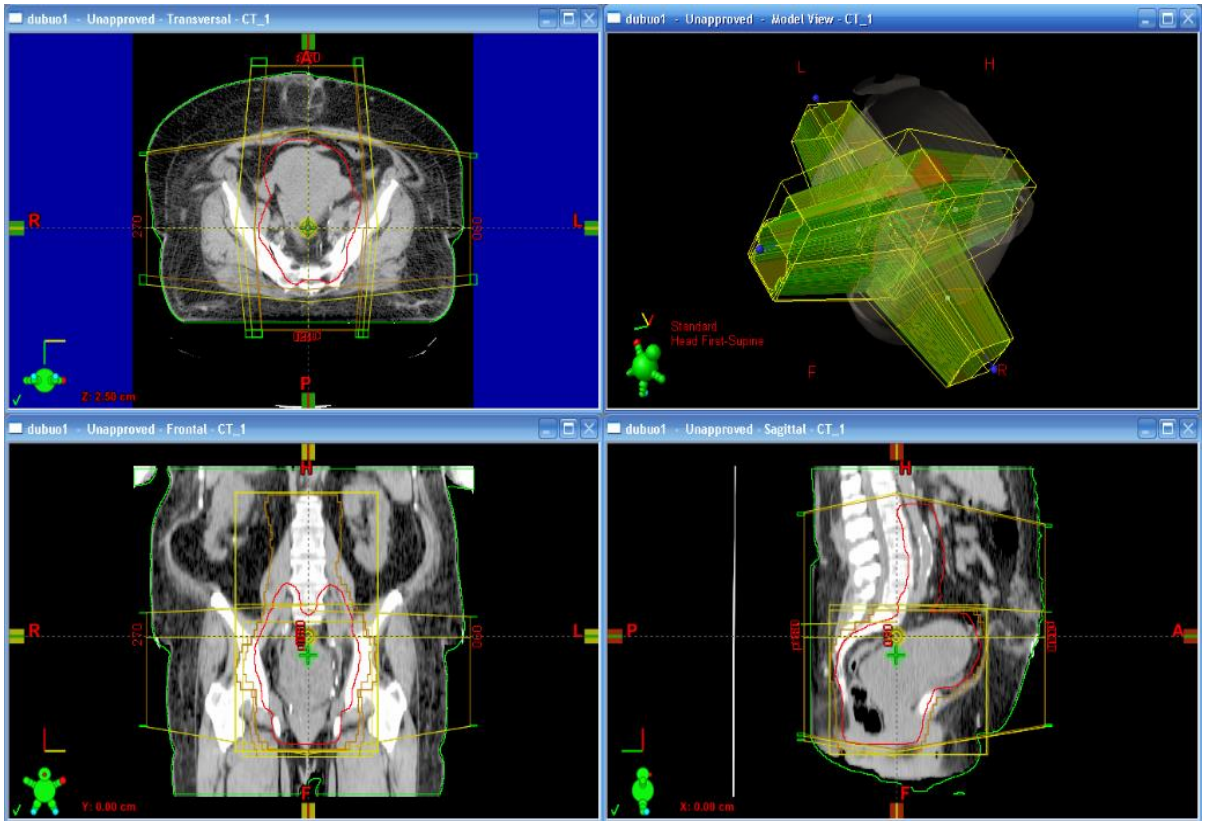

Fig.27. Eclipse treatment planning system capabilities.

In vivo experiment maximum dose measurements were performed for 7 gynaecologic cancer patients. Semiconductor probes were placed in two different points at once for each patient. The points were chosen above and below the isocentre which was located on the junction area of two irradiation fields according to the established individual treatment plan. Two treatment field were measured: one diode was placed in segment field which was created towards the head and another one - in the main beam field which was created towards the patient's legs. Both beam field had different field weight values which indicated the contribution of the beam to the whole dose delivered to the target during one fraction. This method with two fields of different size (main and segment) was chosen with the intention to protect ovaries from unnecessary irradiation. The size of each field was chosen according to the patient individual anatomic structures, tumour size and location. Semiconductor probes were sticked in the area of belly button of the gynaecologic cancer patients. Dosimeter locations were chosen as follows: one semiconductor probe was placed 3 cm above the isocentre towards the patient head and the second one 3cm below the isocentre towards the patient's legs. The results of experimentally and theoretically evaluated doses are provided in the Table 3. Location of dosimeters was indicated in the dose treatment plans for zero main (000) and segment (000) fields that were produced using treatment planning system (Eclipse). Both treatment fields are in conjunction thus creating the possibility to overlap each other. The results of experimental dose measurements were compared with theoretically calculated doses obtained by using of treatment planning system ("Eclipse") in order to estimate an accuracy of the treatment procedure which gynaecologic cancer patients underwent for their treatment.

Table.5. Results from in vivo measurements for gynaecologic cancer patients.

Patients Nr.	Dose in main field			Dose in segment field		
	$D_{calculated}$	$D_{measured}$	Relative dose error	$D_{calculated}$	$D_{measured}$	Relative dose error
1	1.452	1.453	0.07%	0.912	0.948	3.80%
2	1.480	1.469	0.75%	0.650	0.648	0.31%
3	1.348	1.333	1.13%	0.665	0.647	2.78%
4	1.432	1.470	2.59%	0.689	0.710	2.96%
5	1.432	1.481	3.31%	0.689	0.705	2.27%
6	1.432	1.475	2.92%	0.689	0.695	0.86%
7	1.395	1.372	1.68%	0.352	0.343	2.62%

Graphical representation of results is demonstrated in the Fig. 28 and Fig. 29 where main and segment field doses are presented in the histogram forms and uncertainties are demonstrated above for each of the patient. It can be seen that relative uncertainties values varied between 0.07% and 3.80% however these values do not exceed 5% tolerance limit.

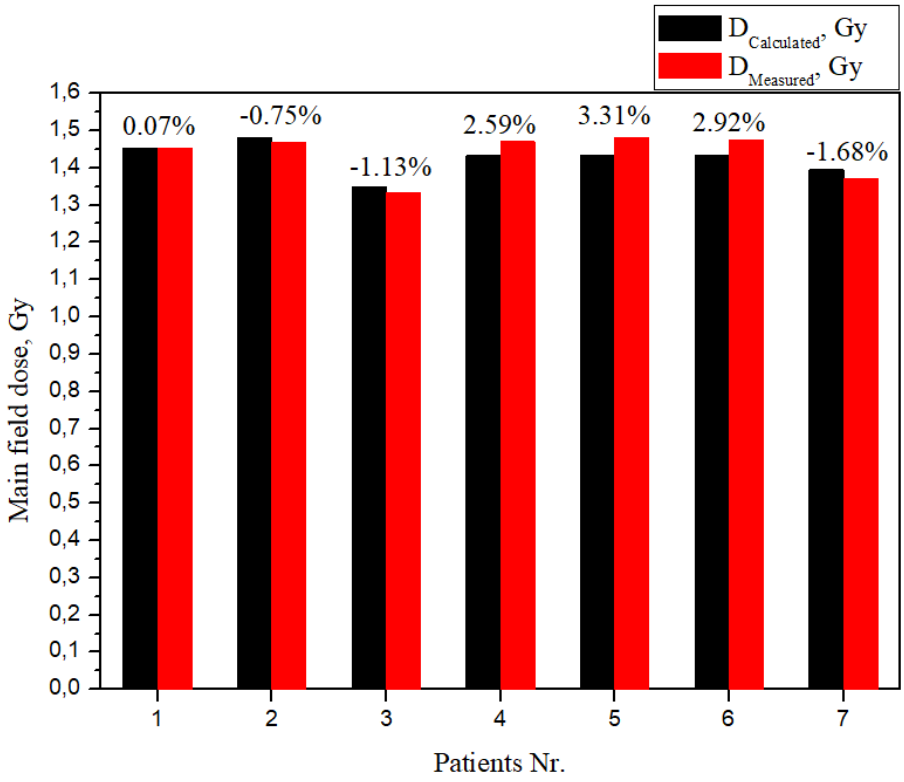

Fig.28. Doses to patients at the point of interest in the main field with indicated relative errors: red - measured dose, black- calculated using treatment planning system dose.

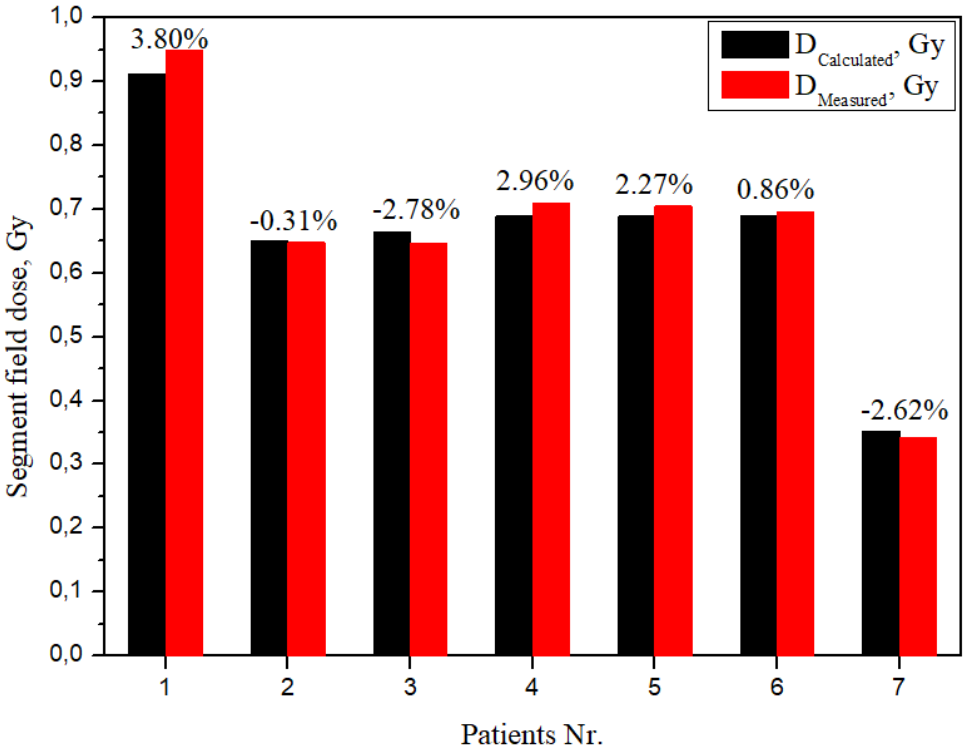

Fig.29. Doses to patients at the point of interest in the segment field with indicated relative errors: red - measured dose, black- calculated using treatment planning system dose.

These errors may be related to the diodes calibration procedure, which was performed using PMMA phantom. PMMA phantom which imitates anatomical region, has a homogeneous structure with a density of 1.18 g/cm^3, however human anatomic structure contains different organs and tissues characterized by different densities (e.g. blood - 1.0428 g/cm^3, fat - 0.9094 g/cm^3 and muscle - 1.0599 g/cm^3). Another reason why errors may occur is random errors impact. These errors are caused by unknown and unpredictable changes. For example, movement of patient during the treatment procedure can influence dose distribution within patient's body; variations of physical factors and environmental conditions (temperature, humidity etc.) may lead to the instrument related measurement errors. Also, systematic errors must be evaluated. Need to note that, obtained relative errors may indicate that the overlap of the irradiation fields was not adjusted properly.

7. CONCLUSIONS

1. Calibration for PTW semiconductor diodes and GAFCHROMIC RTQA^2 films has been performed prior to start in vitro dose measurements. Entrance dose calibration factors - 6.825×10^7 Gy/C and -7.169×10^7 Gy/C, for the first and second diode respectively, were evaluated. Linear optical response to irradiation dose was estimated for GafChromic films.
2. Performing in vitro dose measurements for the case when two overlapping fields are being used for the treatment it was found, that the shift of the segment field from the isocentre line towards reduction of overlapping area may cause dose reduction from by 15.1 % - 27.6 %. The shift of segment field in opposite direction (increase of the overlapped area) may cause maximum dose increase by 17 % to 36.9 %.
3. The diodes were more sensitive to irradiation dose and provided better maximum dose distribution results across the treatment field length as compared to GafChromic films. Also estimated relative errors for diodes were lower and varied from 0.8% to 27%. Furthermore, the regions where these errors did not exceed tolerance limits were broader as compared with film-based measurements.
4. *In vivo* dose measurements for 7 gynaecologic cancer patients have been performed using semiconductor diodes. Diodes were located at the points of interests seeking to evaluate possible field overlapping during the treatment. It was found, that the relative measurement errors varied between 0.07 % and 3.8 % for different patients but did not exceed 5% limit.

8. LITERATURE

[1] About Gynaecologic Cancer. From Foundation for Women's Cancer [interactive]. 2018, [checked 2018-04-01]. Access throughout internet http://www.foundationforwomenscancer.org/about-gynecologic-cancers/

[2] SIEGEL, R.L. and Miller K.D. Jemal A. Cancer statistics. CA Cancer J Clin. 2015;65(1):5-29.

[3] SZKLARUK, F. et al. MR Imaging of common and uncommon pelvic masses. RadioGraphics 2003; 23:403-24.

[4] MAHAJAN, M. et al. MR imaging of carcinoma cervix. Indian J Radiol Imaging 2013; 23:247-52.

[5] COLE, L. and Stoler MH. Issues and inconsistencies in the revised gynaecologic staging systems. Seminar for Diagnostic Pathology. 2012 Aug;29(3):167-73.

[6] Uterus Size. From MD Health [interactive]. 2018, [checked 2018-04-01]. Access throughout internet http://www.md-health.com/Uterus-Size.html

[7] CHERRY, P. and Duxbury A. *Practical Radiotherapy. Physics and Equipment*. London: Oxford University Press, 1998. ISBN 1-900-151-06-5.

[8] PODGORSAK, E.B. Radiation Oncology Physics: *A Handbook for Teachers and Students*. Vienna: International Atomic Energy Agency, 2005. ISBN 92–0–107304–6.

[9] Linear Accelerator (Linac). From Biomedical Engineering [interactive]. 2009, [checked 2018-05-08]. Access throughout internet: http://bmeng.blogspot.lt/2009/07/linear-accelerator-linac.html

[10] 3D Conformal Radiation Therapy. From Hillman cancer center [interactive]. 2018, [checked 2018-04-17]. Access throughout internet: http://hillman.upmc.com/cancer-care/radiation-oncology/treatment/external-beam/3d-conformal

[11] AHMAD, N. et al. Conventional (2D) Versus Conformal (3D) Techniques in Radiotherapy for Malignant Pediatric Tumors: Dosimetric Perspectives. J Egypt Natl Canc Inst. 2009; 21(4):309-314.

[12] SEGURO, A. F. et al. COMPARATIVE BETWEEN IMRT AND 3D-CRT FOR UPPER GI MALIGNANCIES. Physica Medica 2016; 32: 284–339.

[13] HERON, D.E. et al. Conventional 3D conformal versus intensity-modulated radiotherapy for the adjuvant treatment of gynecologic malignancies: a comparative dosimetric study of dose–volume histograms. Gynecologic Oncology 2003; 91: 39–45.

[14] VMAT / RAPIDARC Volumetric Arc Therapy. From Varian [interactive]. 2018, [checked 2018-04-17]. Access throughout internet: https://www.varian.com/oncology/treatment-techniques/external-beam-radiation/vmat

[15] HAIYUN, L. et al. Evaluation of 3D-CRT, IMRT and VMAT radiotherapy plans for left breast cancer based on clinical dosimetric study. *Computerized Medical Imaging and Graphics 2016; 54:1-5.*

[16] TAIT, D.M. et al. Acute toxicity in pelvic radiotherapy; a randomised trial of conformal versus conventional treatment. Radiother Oncol. 1997;42(2):121–136.

[17] MUNDT, A.J. et al. Initial clinical experience with intensity-modulated whole-pelvis radiation therapy in women with gynaecologic malignancies. Gynecol Oncol. 2001;82(3):456–463.

[18] ALINA, S. et al. Morbidity Related to the Use of 3D-Based External Beam Radiation and Image-Guided Brachytherapy. Gynecologic Radiation Therapy. 2011; 283-297.

[19] BARRACLOUGH, L.H. et al. External beam boost for cancer of the cervix uteri when intracavitary therapy cannot be performed. Int J Radiat Oncol Biol Phys. 2008;71(3):772–8.

[20] POTTER, R. et al. Clinical impact of MRI assisted dose volume adaptation and dose escalation in brachytherapy of locally advanced cervix cancer. Radiother Oncol. 2007;83(2):148–55.

[21] CHARGARI, C. et al. Physics contributions and clinical outcome with 3D-MRI-based pulsed-doserate intracavitary brachytherapy in cervical cancer patients. Int J Radiat Oncol Biol Phys. 2008; 74:133–9.

[22] PEREZ, C.A. et al. Tumor size, irradiation dose, and long-term outcome of carcinoma of uterine
cervix. Int J Radiat Oncol Biol Phys. 1998;41(2):307–17.

[23] EIFEL, P.J. et al. Time course and outcome of central recurrence after radiation therapy for carcinoma of the cervix. Int J Gynecol Cancer. 2006;16(3):1106–11.

[24] CHAN, P. et al. Dosimetric comparison of intensity-modulated, conformal, and four-feld pelvic
radiotherapy boost plans for gynecologic cancer: a retrospective planning study. Radiat Oncol. 2006;1:13.

[25] GEORG, D. et al. Image-guided radiotherapy for cervix cancer: high-tech external beam therapy
versus high-tech brachytherapy. Int J Radiat Oncol Biol Phys. 2008;71(4):1272–8.

[26] LIM, K. et al. Cervical cancer regression measured using weekly magnetic resonance imaging during fractionated radiotherapy: radiobiologic modeling and correlation with tumor hypoxia.
Int J Radiat Oncol Biol Phys. 2008;70(1):126–33.

[27] LEE, C.M. and Shrieve D.C. Gaffney DK. Rapid involution and mobility of carcinoma of the cervix. Int J Radiat Oncol Biol Phys. 2004;58(2):625–30.

[28] VAN DE BUNT, L. et al. Motion and deformation of the target volumes during IMRT for cervical cancer: what margins do we need? Radiother Oncol. 2008;88(2):233–40.

[29] BEADLE, B.M. et al. Cervix regression and motion during the course of external beam chemoradiation for cervical cancer. Int J Radiat Oncol Biol Phys. 2009;73(1):235–41.

[30] VAN LEEUWEN, F. E. *et al.* Role of radiotherapy and chemotherapy in the risk of second malignant neoplasms after cancer in childhood *Br. J. Cancer 2005;* 56:792–796.

[31] GEORGE, X. et al. A review of dosimetry studies on external-beam radiation treatment with respect to second cancer induction. PHYSICS IN MEDICINE AND BIOLOGY. 2008: 53:193-241.

[32] KAIDO, T. et al. Radiosurgery-induced brain tumour. Case report J. Neurosurg. 2005; 95:710 –713.

[33] FOSS, A. A. et al. Long-term risk of second malignancy after treatment of Hodgkin's disease: the influence of treatment, age and follow-up time Ann. Oncol. 2002; 13: 1786–1791.

[34] Noncommunicable diseases. From World Health Organization [interactive]. 2018, [checked 2018-05-01]. Access throughout internet: http://www.who.int/en/news-room/fact sheets/detail/noncommunicable-diseases

[35] WAGNER, K.H. et al. A global view on the development of non-communicable diseases. Preventive Medicine. 2012; 54:38–41.

[36] PODGORSAK, E.B. Radiation Oncology Physics: *A Handbook for Teachers and Students*. Vienna: International Atomic Energy Agency, 2005. ISBN 92–0–107304–6.

[37] JEANNE, C. et al. Gynaecologic cancer treatment and the impact of cancer-related infertility. Gynaecologic oncology. 2005, 97(1): 90–95.

[38] OGUZ, A. et al. Imaging of Uterine Cancer. Radiologic Clinics of North America, 45 (2007) 167–182.

[39] GOLDSTEIN, R.B. et al. Evaluation of the woman with postmenopausal bleeding: Society of Radiologists in Ultrasound-Sponsored Consensus Conference statement. J Ultrasound Med 2001; 20:1025–1036.

[40] GOLDSTEIN, S.R. et al. Ultrasonographically-based triage for perimenopausal patients with abnormal uterine bleeding. Am J Obstet Gynecol 1997; 177:102–108.

[41] MEDVERD, J.R. and Dubinsky T.J. Cost analysis model: US versus endometrial biopsy in evaluation of peri-and postmenopausal abnormal vaginal bleeding. Radiology 2002; 222:619–627.

[42] SAWICKI, V. et al. Color Doppler assessment of blood flow in endometrial cancer. Eur J Gynaecol Oncol 2005; 26:279–284.

[43] ALCAZAR, J.L. et al. Reproducibility of endometrial vascular patterns in endometrial disease as assessed by transvaginal power Doppler sonography in women with postmenopausal bleeding. J Ultrasound Med 2006;25: 159–163.

[44] TIMMERMAN, D. et al. The pedicle artery sign based on sonography with color Doppler imaging can replace second stage tests in women with abnormal vaginal bleeding. Ultrasound Obstet Gynecol 2003;22: 166–177.

[45] BOURNE, T.H. et al. Detection of endometrial cancer by transvaginal ultrasonography with color flow imaging and blood flow analysis: a preliminary report. Gynecol Oncol 1991; 40:253–159.

[46] TEEFEY, S.A. et al. Local staging of endometrial carcinoma: comparison of transvaginal and intraoperative sonography and gross visual inspection. AJR Am J Roentgenol 1996; 166:547–552.

[47] ARKO, D. and Takac I. High frequency transvaginal ultrasonography in preoperative assessment
of myometrial invasion in endometrial cancer. J Ultrasound Med 2000; 29:639–643.

[48] FISHMAN, A. et al. The value of transvaginal sonography in the preoperative assessment of myometrial invasion in high and low grade endometrial cancer and in comparison, to frozen section in grade I disease. Eur J Gynaecol Oncol 2000; 21:128–130.

[49] LEEBER, S. C. et al. Three-Dimensional Power Doppler Ultrasound Improves the Diagnostic Accuracy for Ovarian Cancer Prediction. Gynecologic Oncology 2001, 82, 40–48.

[50] VALENTIN, *L.* Pattern recognition of pelvic masses by gray-scale ultrasound imaging: the contribution of Doppler ultrasound. *Ultrasound Obstet Gynecol* 1999; 14:338–347.

[51] ALINA, S. et al. Morbidity Related to the Use of 3D-Based External Beam Radiation and Image-Guided Brachytherapy. Gynecologic Radiation Therapy. 2011; 283-297.

[52] JOSEPH, P. C. et al. Computed Tomography in Endometrial Carcinoma. *Obstetrics and Gynecology.* 2000; 95:692– 696.

[53] BALFE, D.M. et al. Computed tomography in malignant endometrial neoplasms. J Comput Assist Tomogr 1983;7: 677–681.

[54] WALSH, J.W. and Goplerud D.R. Computed tomography of primary, persistent, and recurrent endometrial malignancy. AJR Am J Roentgenol 1982;139: 1149–1154.

[55] JANUS, C.L. et al. Staging of cervical carcinoma: accuracy of magnetic resonance imaging and computed tomography. Clin Imaging 1989; 13:114–116.

[56] WALSH, J.W. and Goplerud D.R. Prospective comparison between clinical and CT staging in primary cervical carcinoma. AJR Am J Roentgenol 1981;137: 997–1003.

[57] KIM, S.H. et al. Preoperative staging of uterine cervical carcinoma: comparison of CT and MRI in 99 patients. J Comput Assist Tomogr 1993; 17:633–640.

[58] VARPULA, M.J. and Klemi P.J. Staging of uterine endometrial carcinoma with ultra-low field (0.02 T) MRI: a comparative study with CT. J Comput Assist Tomogr 1993;17:641–647.

[59] YAMASHITA, Y. et al. Assessment of myometrial invasion by endometrial carcinoma: transvaginal sonography vs contrastenhanced MR imaging. AJR Am J Roentgenol 1993; 161:595–599.

[60] FREEMAN, S.J. et al. The revised FIGO staging system for uterine malignancies: implications for MR imaging. Radiographics. 2012 Oct;32(6):1805-1827.

[61] MANFREDI, R. et al. Local-regional staging of endometrial carcinoma: role of MR imaging in surgical planning. Radiology 2004; 231:372–378.

[62] PELIKAN, H.M.P. et al. Diagnostic accuracy of preoperative tests for lymph node status in endometrial cancer: a systematic review. Cancer Imaging. 2013;13(3):314-322.

[63] CHOI, H.J. et al. Comparison of the accuracy of magnetic resonance imaging and positron emission tomography/computed tomography in the presurgical detection of lymph node metastases in patients with uterine cervical carcinoma: a prospective study. Cancer. 2006 Feb 15;106(4):914-922.

[64] SUBAK, L.L. et al. Cervical carcinoma: computed tomography and magnetic resonance imaging for preoperative staging. Obstet Gynecol 1995; 86:43–50.

[65] HAWNAUR, J.M. et al. Staging, volume estimation, and assessment of nodal status in carcinoma of the cervix: comparison of magnetic imaging with surgical findings. Clin Radiol 1994; 49:443–452.

[66] HRICAK, H. et al. Invasive cervical carcinoma: comparison of MR imaging and surgical findings. Radiology 1998;166: 623–631.

[67] KIM, S.H. et al. Uterine cervical carcinoma: comparison of CT and MR findings. Radiology 1990; 175:45–51.

[68] HYUCK, J. C. et al. Comparison of the Accuracy of Magnetic Resonance Imaging and Positron Emission Tomography/Computed Tomography in the Presurgical Detection of Lymph Node Metastases in Patients with Uterine Cervical Carcinoma. Cancer 2006; 106:914-922.

[69] CIERNIK, I. F. et al. Radiation treatment planning with an integrated positron emission and computer tomography (PET/CT): a feasibility study. Int. J. Radiation Oncology Biol. Phys. 2003; 57:853-863.

[70] YILDIRIM, Y. et al. Integrated PET/CT for the evaluation of para-aortic nodal metastasis in locally advanced cervical cancer patients with negative
conventional CT findings. Gynaecologic Oncology 2008; 108:154–159.

[71] EUN, J. N. et al. Diagnosis and staging of primary ovarian cancer: Correlation between PET/CT, Doppler US, and CT or MRI. Gynecologic Oncology 2010; 116: 389–394.

[72] CLAUDIO, F. et al. Set-up error in supine-positioned patients immobilized with two different modalities during conformal radiotherapy of prostate cancer. Radiotherapy and Oncology. 1998; 49:133-141.

[73] KAATEE, R.S. et al. Detection of organ movement in cervix cancer patients using a fluoroscopic
electronic portal imaging device and radiopaque markers. Int J Radiat Oncol Biol Phys. 2002;54(2):576–583.

[74] BUCHALI, A. et al. Impact of the filing status of the bladder and rectum on their integral dose distribution and the movement of the uterus in the treatment planning of gynaecological cancer. Radiother Oncol. 1999;52(1):29–34.

[75] CHAN, P. et al. Inter- and intrafractional tumour and organ movement in patients with cervical cancer undergoing radiotherapy: a cinematic-MRI point-of-interest study. Int J Radiat Oncol Biol Phys. 2008;70(5):1507–1515.

[76] Treatment Planning Systems. From Imaging Technology News [interactive]. 2017, [checked 2018-05-08]. Access throughout internet: https://www.itnonline.com/article/treatment-planning-systems-overview

[77] BEN, M. et al. In vivo dosimetry in external beam radiotherapy. American Association of Physicists in Medicine. 2013; 40(7).

[78] MARION, E. et al. In Vivo Dosimetry During External Photon Beam Radiotherapy. Int. J. Radiation Oncology Biol. Phys. 1999; 43(2): 245–259.

[79] TIMOTHY, C. Z. Diode dosimetry for Megavoltage Electron and Photon Beams. Department of radiation oncology. University of Pennsylvania. Philadelphia, 2009.

[80] RIKNER, G. and Grusell E. Effects of radiation damage on p-type silicon detectors. *Phys Med Biol* 1983; 28:1261–1267.

[81] GRUSELL, E. and Rikner G. Evaluation of temperature effects in p-type silicon detectors. *Phys Med Biol* 1986; 31:527–534.

[82] RIKNER, G. and Grusell E. Patient dose measurements in photon fields by means of silicon semiconductor detectors. *Med Phys* 1987; 14:870–873.

[83] ELLEN, Y. et al. Diode in Vivo Dosimetry for Patients Receiving External Beam Radiation Therapy . Medical Physics Publishing, 2005, Nr. 87, p. 3-5, ISBN 978-1-888340-50-9

[84] WILKINSON, D. Commissioning of an in vivo dosimetry system for high dose rate gynecologic brachytherapy. Master thesis. University of Wollongong, Department of Engineering physics, 2010.

[85] Development of Procedures for In Vivo Dosimetry in Radiotherapy. From IAEA, International Atomic Energy Agency [interactive]. 2013, [checked 2017-06-01]. Access throughout internet: http://www-pub.iaea.org/books/iaeabooks/8962/Development-of-Procedures-for-In-Vivo Dosimetry-in-Radiotherapy.

[86] GRUSELL, E. and Rikner G. Evaluation of temperature effects in p-type silicon detectors. Physics in Medicine & Biology [interactive] 1985, 31(5), 527-534. Access through: doi.org/10.1088/0031-9155/31/5/005

[87] EUROPEAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY, Practical Guidelines for the Implementation of In vivo Dosimetry with Diodes in external radiotherapy with photon Beams (Entrance Dose), Physics for clinical radiotherapy, 2004, Nr. 5, ESTRO, Brussels.

[88] GRUSELL, E. and Rikner G. General specifications for silicon semiconductors for use in radiation dosimetry, Physics in Medicine & Biology [interactive] 1987, 32(9), 1109–1117. Access through: doi.org/10.1088/0031-9155/32/9/004

[89] ELLEN, Y. et al. Diode in Vivo Dosimetry for Patients Receiving External Beam Radiation Therapy . Medical Physics Publishing, 2005, Nr. 87, p. 13-14, ISBN 978-1-888340-50-9

[90] The Calibration and Use of Plane-Parallel Ionization Chambers for Dosimetry of Electron Beams, AAPM Radiation Therapy Committee Task Group 39, Medical Physics [interactive] 1994, 21(8), ISBN 1-56396-461-9

[91] MAYLES, W.P.M. Treatment verification and In vivo Dosimetry in Radiotherapy Physics in Practice. Oxford University Press, Oxford, 2000, 220–246.

[92] MATHEW, J. W. et al. Radiochromic film dosimetry and its applications in radiotherapy. 4th SSD Summer School: Concepts and Trends in Medical Radiation Dosimetry. 2011; 75-99.

[93] IAEA. Radiochromic films slides. 2018.

[94] GRIMM, J. App Clin Med Phys. 2011

[95] Varian High Energy Linear Accelerator Comparison Chart. From Oncology Systems [interactive]. 2018, [checked 2018-05-10]. Access throughout internet:

https://www.oncologysystems.com/radiation-therapy/linear-accelerators/varian-high-energy-linear-accelerator-comparison-chart.php

[96] PTW. From Application-Specific In Vivo Semiconductor Diodes for VIVODOS® and MULTIDOS® Dosimeters [interactive]. 2017, [checked 2018-05-10]. Access through internet: http://www.ptw.de/2341.html?&cId=296

[97] PTW. From Increasing Patient Safety in Treatment Delivery VIVODOS® 12[interactive]. 2017, [checked 2018-05-10]. Access through internet: http://www.ptw.de/2328.html?&cId=3416

[98] Gafchromic™ RTQA2 film. From Gafchromic [interactive]. 2018, [checked 2018-05-10]. Access through internet: http://www.gafchromic.com/documents/PC 11804_Gafchromic_RTQA2.pdf

[99] NAZMIYE, D. K. In Vivo Dosimetry in External Radiotherapy. Turkish Journal of Oncology, 2017;32(4):173–180.

[100] ESTRO: Practical guidelines for the implementation of in vivo dosimetry with diodes in external radiotherapy with photon beams (entrance dose); Physics for clinical radiotherapy Booklet No. 5.