T.C
YEDITEPE UNIVERSITY
INSTITUTE OF HEALTH SCIENCES
DEPARTMENT OF HEALTH PHYSICS

PATIENT- SPECIFIC INTERNAL DOSIMETRY WITH QUANTITATIVE SPECT/CT IN LUTETIUM-177 PSMA TREATMENT

MASTER THESIS

GÜLÇİN ÇELİK

İstanbul , 2019

T.C
YEDITEPE UNIVERSİTY
INSTITUTE OF HEALTH SCIENCES
DEPARTMENT OF HEALTH PHYSICS

PATIENT- SPECIFIC INTERNAL DOSIMETRY WITH QUANTITATIVE SPECT/CT IN LUTETIUM-177 PSMA TREATMENT

MASTER THESIS

GÜLÇİN ÇELİK

SUPERVISOR
Prof. Dr. Ş. İpek KARAASLAN

CO-ADVISOR
DR. TÜRKAY TOKLU

İstanbul , 2019

THESIS APPROVAL FORM

Institute : Yeditepe University Institute of Health Sciences

Programme : Medical Physics

Title of the Thesis : Patient-Specific Internal Dosimetry With Quantitative SPECT/CT in Lutetium-177 PSMA Treatment

Owner of the Thesis : Gülçin Çelik

Examination Date :05/09/2019

This study have approved as a Master/~~Doctorate~~ Thesis in regard to content and quality by the Jury.

	Title, Name-Surname (Institution)	(Signature)
Chair of the Jury: Supervisor:	Prof. Dr. Şerife İpek KARAASLAN Yeditepe Üniversitesi	
Co-advisor	Dr. Türkay TOKLU Yeditepe Üniversitesi İhtisas Hastanesi	
Member/Examiner:	Doç. Dr. Nalan ALAN SELÇUK Yeditepe Üniversitesi Hastanesi	
Member/Examiner:	Prof. Dr. Mustafa DEMİR İstanbul Üniversitesi-Nükleer Tıp	
Member/Examiner:	Prof. Dr .Nesrin ALTINSOY İstanbul Teknik Üniversitesi-Radyasyon Bilimleri	

APPROVAL

This thesis has been deemed by the jury in accordance with the relevant articles of Yeditepe University Graduate Education and Examinations Regulation and has been approved by Administrative Board of Institute with decision dated ..05/09/2019..... and numbered 10314117

Prof. Dr. Bayram YILMAZ

Director of Institute of Health Sciences

DECLARATION

I hereby declare that this thesis is my own work and that, to the best of my knowledge and belief, it contains no material previously published or written by another person nor material which has been accepted for the award of any other degree except where due acknowledgment has been made in the text.

Date
Signature

Gülçin ÇELİK

ACKNOWLEDGEMENT

Bu tezi çalışmamda ve ikinci kez yüksek lisansımı yapmamda destek olan ve daima bilgi ve tecrübelerini esirgemeyen Yeditepe Üniversitesi Rektör Yardımcısı sayın Prof. Dr.Ş. İpek KARAASLAN' a, eğitimimiz ve tez süresince sabırla bizi yönlendirmeleri, bilgi paylaşımları ve danışmanlığı ile Yeditepe Üniversitesi Öğretim görevlisi sayın Dr. Türkay TOKLU' ya,

Kalbimde daima farklı bir yere sahip olan 13 yıldır birlikte çalışmaktan mutluluk ve onur duyduğum, manevi desteklerini esirgemeyen Yeditepe Üniversitesi Rektörü Prof. Dr. Canan AYKUT BİNGÖL, Nöroloji Anabilim Dalı Başkanı Prof. Dr. Berrin AKTEKİN ve Nöroloji Anabilim Dalı Öğretim görevlisi Doç. Dr. Burcu ÖRMECİ'ye

Yoğun iş tempomuza rağmen manevi desteklerini esirgemeyen Yeditepe Üniversitesi çalışanaları, Nörofizyoloji laboratuvarı teknikerlerine, Uzman tekniker Emine Sarıyıldız ÖLÇÜ' ye ve Yeditepe Üniversitesi Nükleer Tıp Anabilim dalında görev yapan uzman tekniker Sema ÇELİK'e

Son olarak, Yaşamım boyunca emeği çok olan, daima destekleyen, eğitime gönül veren babam Erdal İRİM, annem Yüksel İRİM ve kardeşim Burçin İRİM' e

Sevgili eşim Kasım ÇELİK'e ve hayatımın anlamları ikiz oğullarım Burak ÇELİK ve Mert ÇELİK' e

En içten teşekkürlerimi sunarım.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLE

LIST OF ABBREVIATIONS

E	Energy
R_i	Decay corrected count rate
$T_{acq,i}$	Duration of the i'th acquisition
T_{cal}	Time of the activity calibration
T_{half}	Half life of radionuclide
α	Alpha
β	Beta
γ	Gamma
λ	Lambda
CT	Computed Tomography
PSMA	Prostate Specific Membrane Antigen
NTCP	Normal Tissue Complication Probability
TD 5/5	The probability of 5% complication within five years from treatment
TD 50/5	The probability of 50% complication within five years
Ci	Curie
CT	Computerized Tomography
DTPA	Diethylenetriaminepenta-acetic
FOV	Fielf of View
FWHM	Full width at half maximum
Hex	Hexagon
LEGP	Low Energy Generel Purpose
LSO	Lutetium Orthosilicate
FDC	Fluoro-Deoxy Glucose
SPECT/CT	Single Photon Emission Computerized Tomography
GC	Gamma Camera
TEW	Triple Energy Window
DEW	Dual Energy Window

CDR	Collimator Detector Response
FBP	Filtered Back Projection
HU	Hounsfield Units
RC	Recovery Coefficient
PSF	Point Spread Function
CF	Calibration Factor
MEGP	Medium Energy General Purpose
LAC	Linear Attenuation Coefficient
FT	Fourier Transform
ART	Algebraic Reconstruction Technique
DC	Dose Calibrator
MIRD	Medical Internal Radiation Dosimetry
NM	Nuclear Medicine
RT	Radioactive Tracers
RNT	Radionuclide Therapy
TAT	Targeted Alpha Therapy
PRRT	Peptide Receptor Radionuclide Therapy

ABSTRACT

Çelik, G. Patient- Specific Internal Dosimetry with Quantitative SPECT/CT in Lutetium-177 PSMA Treatment. Yeditepe University, Institute of Health Science, Department of Medical Physics, MSc Thesis, İstanbul.

In present times, treating prostate cancer resistant to castration with modalities of nuclear medicine such as Lutetium-177 (Lu-177) marked PSMA (prostate-specific membrane antigen) has become more prevalent. Lu-177 with PSMA is administered intravenous, spreading radioactivity through the body of the patient. The agent, reaching the cancerous prostate cells and metastasis, shows its effect by the ionizing beta rays. PSMA also affects healthy tissues such as the kidney, salivary glands, and lacrimal glands, meaning that also healthy tissue is affected by the radiation. In order to avoid toxicity within the kidneys, administration of lower kidney doses are recommended. Hence, dosimetric calculations must be conducted before treating patients with Lu-177 PSMA. While the beta rays of Lu-177 treats the tumor, gamma rays and the SPECT system aids in visualizing the process, which is crucial when analyzing critical organs such as the kidney and their bio-breakdown progress over time of due to Lu-177. With this observational measurement (this information) and the MIRD (Medical Internal Radiation Dosimetry), the radiation level critical organs are exposed to can be calculated individually for each patient. In this study, we aim to plan an individual dosimetry for each patient undergoing Lu-177 PSMA treatment. In order to quantitatively visualize Lu-177 in the SPECT/CT system of the Yeditepe University Hospital Nuclear Medicine department, the necessary imaging and reconstruction parameters are determined. Furthermore, count-activity calibration is defined whereas the obtained data is conducted to determine specific dosimetry calculation for each patient individually. Currently, patient-specific dosimetry studies are being done by either SPECT systems used for visualization. Methods of visualization must be calibrated during the adjusting of the visualization parameters. In this thesis, the calibration and parameter are designated in order to plan patient-specific dosimetry studies. This scientific study will also aid another study currently conducted at the Yeditepe University Hospital Nuclear Medicine Department on DOTATATE, a different peptide connected to Lu-177, used for neuroendocrine tumor treatment, by also allowing for the calculation of patient-specific dosimetries.

Additionally, this study will lead to the safe treatment of patients as well as new studies focusing on dose-reaction relationships at tumors in similar treatment modalities.

Key words: Prostate Cancer, Nuclear Medicine Treatment, Dosimetry, Quantitative, Lutetium

ÖZET

ÇELİk, G. Lutesyum-177 PSMA Tedavisinde Kantitatif SPECT/CT ile Hastaya Özgü Dozimetri. Yeditepe Üniversitesi Sağlık Bilimleri Enstitüsü, Sağlık Fiziği ABD., Master Tezi İstanbul.

Kastrasyona dirençli prostat kanseri tedavisinde Nükleer Tıp bölümlerinde uygulanan Lutesyum-177 (Lu-177) ile işaretli PSMA (Prostat Spesifik Membran Antijeni) tedavisi günümüzde yaygınlaşmaktadır. Lu-177 PSMA hastalara damar yolu ile uygulanmakta ve radyoaktivite hastanın vücuduna dağılmaktadır. Vücut içerisinde prostat kanseri hücreleri ve metastazlarına giden Lu-177 PSMA, Lu-177'nin beta ışınlarının iyonizan etkisiyle tedavi sağlamaktadır. PSMA vücut içerisinde böbrekler, tükürük bezleri ve gözyaşı bezleri gibi sağlıklı dokularda da tutulmaktadır. Bu nedenle sağlıklı dokular da belirli oranlarda radyasyona maruz kalmaktadır. Böbreklerde toksik etkinin ortaya çıkmaması için böbrek dozlarının belirli değerler altında tutulması önerilmektedir. Bu nedenle hastalara uygulanan Lu-177 PSMA tedavisinde dozimetrik hesaplamalar önem arz etmektedir. Lu-177'nin sahip olduğu beta ışınları ile tümör tedavi edilirken, gama ışınları ile SPECT sistemlerinde görüntüleme yapılabilmektedir. Bu sayede Lu-177 PSMA'nın böbrekler gibi kritik organlardaki biyo-dağılımının zamana karşı değişimi tespit edilebilir. Bu bilgi ve MIRD (Medical Internal Radiation Dosimetry) yönteminin kullanılmasıyla kritik organların her tedavide maruz kaldıkları radyasyon miktarı, hastaya özgü olarak belirlenebilir. Bu çalışmada, Lu-177 PSMA tedavisinde hastaya özgü dozimetri yapılması amaçlanmaktadır. Bu amaçla, Yeditepe Üniversitesi Hastanesi Nükleer Tıp Bölümünde bulunan SPECT/CT sisteminde Lu-177'nin kantitatif olarak görüntülenebilmesi için gerekli çekim ve rekonstrüksiyon parametreler belirlenecektir. Bunun yanı sıra, fantom görüntülemeleri ile sayım-aktivite kalibrasyonları gerçekleştirilecek ve elde edilen bilgiler yardımıyla hastalara özgü dozimetrik hesaplamalar gerçekleştirilecektir. Nükleer Tıp tedavilerinde hastaya özgü dozimetri çalışmaları, görüntülemenin yapıldığı SPECT sistemine özgü yapılabilmektedir. Başka bir deyişle, görüntüleme sistemlerinin bu amaçla kalibre edilmesi ve görüntüleme parametrelerinin belirlenmesi gerekmektedir. Bu tez çalışmasında, adı geçen kalibrasyon ve parametre belirleme işlemleri gerçekleştirilecek, bu sayede hastaya özgü dozimetrik çalışmalar yapılabilecektir. Bu tez Yeditepe Üniversitesi Hastanesi Nükleer Tıp Bölümü'ne, Lu-177 PSMA ve hatta Lu-177 ile bağlı diğer bir peptid olan ve nöroendokrin tümörlerin tedavisinde kullanılan DOTATATE için de dozimetrik çalışmaların yapılabilmesi yeteneğini

kazandıracaktır. Ek olarak, hastaların güvenli bir şekilde tedavi edilmesine olanak tanıyacağı gibi tümörlerde doz-cevap ilişkisinin ortaya konabileceği yeni çalışmalara imkân tanıyacaktır.

Anahtar Kelimeler: Prostat kanseri, Nükleer Tıp Tedavi, Dosimetri, Kantitatif, Lutesyum

1. INTRODUCTION

Radioisotope treatment in nuclear medicine is important to determine the reliable radiation dose for analysis of benefits and risks of treatment. A lot of radionuclides used in imaging and therapy in nuclear medicine. Dose absorbed by different organs is evaluated in terms of risk and benefit. Internal dosimetry described that stored radiation energy administered intravenously in the body. Nuclear medicine treatment of cancerous prostate cells and metastasis Lutesium-177 marked PSMA (Prostate-specific membrane antigen) successfully applied to radioisotopes. However, Source organs are to be treated organs and target organs are risky neighboring organs that the aim organs for Lutesium-177 with PSMA peptid therapy are the kidney, Parotid glands, and the Liver (1,2). The National Cancer Institute has awarded four contracts to study "three-dimensional treatment planning for high energy photons. Normal tissue tolerance to therapeutic irradiation that TD 5/5 (The probability of 5% complication within five years from treatment) volume 23 Gy (3), TD 50/5 (the probability of 50% complication within five years) volume 28 Gy (3). This dose causes clinical nephritis according to NTCP (Normal Tissue Complication Probability) for Kidney (2). The importance of time-dose-volume factors in radioisotopes treatment is well-recognized. To avoid toxicity, the amount of radiation dose given to target organs has to be estimated that aimed to estimate the radiation absorbed doses to dose-limiting organs after systemic therapy with Lu-177 PSMA in patients with castration-resistant prostate cancer. Post therapeutic dosimetry was performed based on whole body and single-photon emission computed tomography/computed tomography (SPECT/CT) scans system. Images SPECT/CT obtained from three-dimensional volume at around the source organs and tissues. The volume of activity is assumed as a homogeneous distribution that ıt is a real activity. Interactive methods are estimated in real concentration activities. SPECT/CT of patients obtained that activity- count and this information use Medical Internal Radiation Dosimetry (MIRD). The amount of radiation for critical organs of the patient is determined to be specific with the MIRD method. MIRD in terms of organ dose calculations that application of the standard set by the patient-specific parameters in the evaluation of kinetics and anatomy is important (4). As will be explained in detail in the fourth chapter (5). after the applying of treatment for patients, Whole-Body and Spect shots will get the image at 4, 24, 72 and 168 hours. The chart will be drawn on activity-time with this information. The area under the graph will give the cumulative activity.

The cumulative activity is a difficult task to determine. The gain on the data protocols are applied, interactive methods use obtain acquisition for images. SPECT applies for on activity of the patient. In addition, CT applies for a reduction coefficient. All protocols for correct data must be edited. In this study, by adjusting the appropriate parameters that patient-specific dosimetry will be performed quantitatively. This study regulates photon attenuation, scatter correction, resolution recovery, recovery correction, and calibration parameters.

In this thesis, there three main parts; first part are kind of therapy in Nuclear Medicine Department, Radiopharmaceuticals, Lutetium-177 and Dose calibrators, the second part are the SPECT/CT working principles, Reconstruction, Image correction technique and algorithms, and the third part are comparing the experimental MIRD methods and organ dosimetry, Finally are Patient-specific internal dosimetry with quantitative SPECT/CT in Lu-177 PSMA treatment results and conclusion in Yeditepe University Hospital Nuclear Medicine Department.

2. GENERAL INFORMATION

2.1. Nuclear Medicine

The purpose of Nuclear Medicine (NM) applications; to investigate human organism through artificial radioisotopes, to diagnose and treat diseases. The most important components in this function are artificial radioisotopes. Radiopharmaceuticals, which are formed by combining radioisotopes with a bioactive component under special conditions, are given to the body for diagnostic and therapeutic purposes. The gamma camera image of the distribution of radiopharmaceuticals in the body is called scintigraphy. Diagnosis of diseases is made by clinicians interpreting scintigraphic images. Accurate diagnosis of the disease with scintigraphic images is directly related to the success of the treatment. Bioactive agents are selected to transmit the desired radionuclide to the desired target in the body, in accordance with the site of biological behavior. Once marked with the appropriate radionuclide, it must be localized to a particular organ or region of the body. The ideal radionuclide for diagnosis should have a single energy (monoenergetic) gamma-ray in NM. ^{9m}Tc, ^{111}In, and ^{123}I are ideal radionuclides for diagnostic purposes. However, Unlike diagnostic radionuclides, the purpose of therapeutic radionuclides is cell destruction (6). NM imaging is a non-invasive technique that uses radioisotopes to image biological processes within the body. The radioisotope undergoes radioactive decay and emits gamma rays. Gamma rays emitted from are detected by an external radiation detector to produce an image. While the uptake of some radiotracers may show some anatomical information, it is used to high light areas of pathology and biologic processes such as tissue perfusion and glucose metabolism. There are two main types of NM imaging such as SPECT and positron emission tomography (PET). The fundamental difference between the two is the detection of one gamma-ray versus two coincident gamma rays as needed to create an image. SPECT images are acquired from single gamma rays emitted from RTs which are incident on gamma cameras (7). Radionuclide imaging, including planar scintigraphy. Ionizing radiation emitted by peptide-bound radionuclides damages the DNA of cancer cells, killing them and causing tumors to shrink. Best radionuclides suited for tumors are those emitting ionizing radiation with short penetration into the tissue. Internal Quantitative analyses in NM calculating in human is needed for making appropriate activity to patients for maximum therapeutic benefit (8).

2.1.1. Radiopharmaceuticals

The aim of radioisotopes in NM practices through a study of the human organism, diagnose and treat diseases. Artificial radioisotopes are the most important component in this function. Bioactive components created with the merging of radioisotope diagnostic and radiopharmaceutical radioactive substances into the body for therapeutic purposes is called. Radiopharmaceuticals are active molecules containing radionuclides in the structure and used for diagnosis or treatment. Today, having nearly 100 radiopharmaceuticals. They were prepared by using reactors, generators, or cyclotron derived radioisotopes and used in the treatment of certain diseases, including cancer, and in the diagnosis of many diseases. The radiopharmaceuticals consist of two parts, a radionuclide, and a pharmaceutical. During the preparation of the radiopharmaceutical, a drug (pharmaceutical part) localized in the organ desired to be imaged or participating in the physiological function of the organ is identified. The selected pharmaceutical part is labeled as a suitable radionuclide to prepare the radiopharmaceutical. After it is given to the patient, radiation emitted from the radionuclide is detected with detectors and converted into an image with the aid of a computer. Anatomical and physiological information is obtained by visualizing the distribution of the radionuclide in the organism and by determining the changes of this distribution with respect to time. Nowadays, beta (β-) and alpha(α) emitters have been used for RNT in all over the world. Most commonly used 131 I therapy for thyroid cancer, ^{177}Lu are considered efficient for therapy as they emit β- particles and also have diagnostic contribution due to its gamma emission, however, relative risk related to gamma radiation exposure to the patients and environment should be considered. Therefore, all the workers within the radiation field, caregivers, and the general public are invited to commit the rules and regulations of radiation protection. Lu-177 therapy, isolation for 6,7 hours is acceptable for adequate radiation safety. Regarding Yttrium-90 (90Y) therapy which poses no exposure risk to the environment and public, patient admission to hospital is performed only to provide enough monitoring and observation (9).

2.1.1.1. Diagnostic Radiopharmaceuticals

Immediately after radioisotope imaging used for diagnosis is an important excretion from the body. Diagnostic radiopharmaceuticals can be used to examine blood flow of the brain, functioning of kidneys, liver, heart, lungs.

diagnostic medical imaging that uses radionuclides to examine the metabolism and physiology of the body is a method. The choice of radionuclide, each radionuclide and each of the disease processes or the biological half-life is very important because it will be different. Positron-emitting or gamma photon of radioactive used for diagnostic purposes. Each radionuclide has a unique type of decomposition, Half-Life, chemical properties, and production method. which must decide which is appropriate for the display of the radionuclide to be measured or disease.

Technetium-99 radioisotope is widely used in NM medicine. It has a half-life for enough to examine metabolic processes and minimize the radiation dose for the patient. It is low-energy gamma rays emits and low energy electrons. GC is detected the gamma rays photons escape of body. Making a cap of lead into a glass tube containing the radioisotope emitted from a nuclear reactor is moved to hospitals. Molybdenum-99 has half-life is 66 hours. A similar generator is used to produce fluoro-deoxy glucose (FDG) incorporating F-18 for PET.

2.1.1.2. Nuclear Medicine Treatment

Therapeutic use of radioisotopes is gaining importance day by day. Radionuclide therapy (RNT) are used beta emitter at the same time that gama emitter for imaging. Lutetium-177 is used peptits for neuroendocrine and prostate tumours. Lu-177 has low-energy beta emitter. Other new therapy is alpha therapy. It has short range and energetic alpha emitter for cancer cells. Another Examples are Yttrium-90 using for treatment of lymphoma and liver cancer that Actinium-225.

2.1.2. Lutetium

^{177} Lu (PSMA-617) is an important radioisotope used for targeted therapy. It has got beta and gamma emissions and half life is 6.65 day that decay hafnium Max kinetic energy is 498.3 keV. It have two of these γ photons energies 112.9 (6.17%) and 208.4 keV (10.36%) (10, 11). Gamma rays of ^{177}Lu isotope allows dosimetry during treatment, beta damage tumor. Whole body imaging uses two energies with 6% abundance have 113 keV and with 11% abundance have 208 keV. As shown Figure 2.1. Moderate beta energy of 177 Lu leads us using this radionuclide in small tumor theraphy such as neuroendocrine tumors.

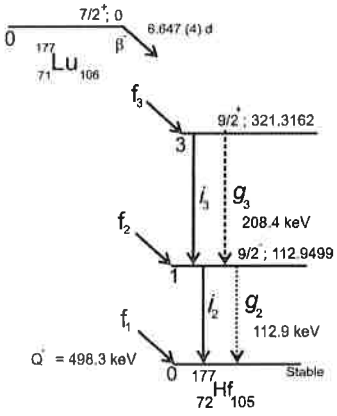


Figure 2.1. ^{177}Lu decay scheme

2.2. SPECT/CT (Single Photon Emission Computerized Tomography) Working Principles

In the SPECT imaging technique, the gamma camera collects data at certain angles as it rotates around the object to be displayed. Today's modern SPECT systems generally consist of systems with a two-head detector. SPECT systems with two detectors are the most suitable design for planar, whole-body scans and tomographic examinations. Two-detector SPECT systems, planar, whole-body CT scans, and examinations the most appropriate design. SPECT cameras actually collect with planar images. The data is processed mathematically to create cross-sectional images from the organ. This technique allows three-dimensional images from each set of two-dimensional images. The scintillation camera must rotate around the patient and collect data at each rotation angle. The gamma camera detector gathers data at certain angles as it rotates around the object to be displayed. The information received on the gamma camera is stored in the image matrix. The image formed by these data collected from the direction the detector sees the object is called the projection image. In each case, only photons moving perpendicular to the detector plane pass through the collimator. Since most of these photons reach the detector from different depths in the patient, the resulting scintigraphic image reflects the sum of all photons released from organs along the specific path. Gamma photons emitted from organs within the body after injection of the imaging agent pass through tissues of varying density on their paths to reach the detectors and are absorbed at certain rates. A SPECT study consists of planar images (projection images) collected at various angles. Data from each viewpoint is stored on the computer. The three-dimensional image is recovered from the projection images using the reconstruction programs. Figure 2.2 Illustrates the principle and basic components of Gamma Camera. The detector element

that collimator of gamma cameras is NaI (T1). NaI crystal especially affected by humidity. The crystal size is 3/8'' that is for general purposes. Emitting gamma photons from the organ are directed by the collimator and dropped onto the detector in gamma cameras, The collimator is used suitable imaging in NM. There are holes in the collimator for the passage of rays. The thickness between the holes is called septa. Septa thickness is designed as thin or thick according to the energy of the radionuclide. Another function of the collimator is to stop the photons coming from the environment and unwanted to enter the image field. A box of the image matrix is called pixels. The volume of each pixel is called voxel. The NaI (T1) crystal stops the gamma photons directed by the collimator, producing scintillation photons proportional to their energy. The scintillation photons are focused by the light guiding layer and struck in the photocathode at the entrance of the photomultiplier tubes (PMTs), causing an electron rupture therefrom. The released electrons are accelerated by the effect of high voltage between the dynodes in the PMT and gradually increase in numbers. The outputs of the PMT are then processed using logic electronics that produce output signals representing the spatial position and energy of the individual detected gamma rays (x, y) on a case-by-case basis. The counts in the pixel corresponding to this position for each x and y signal from the camera are increased by SPECT/CT . Thus, the electrons are collected in the anode at the PMT output. Gamma photons emitted from the organ are transformed into scintillation photons in the NaI (Tl) crystal and electrical signals through PMT. The signals from three different dimensions come the PMT: signals from the x-dimension, signals from the y-dimension and signals from the z-dimension (energy dimension). These signals are amplified and shaped in various electronic units and then converted into images. (Figure2.2) (12).

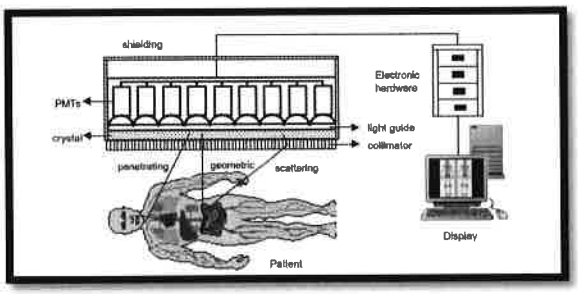


Figure 2.2. Components of Gamma Camera.

2.2.1. Reconstruction

The main problem of the first model radionuclide imaging systems was to obtain two-dimensional projections from three-dimensional source distribution. Over time, tomographic imaging was developed as an alternative to this condition. The information received at every angle is called "projection". Number of projectorsstating how many different angles to stopIt is the parameter. If tomographic information is taken at 64 degrees of 360 degrees that is 64 projection. In these systems, the projection data collected by the detection system revolving around the object, and the reconstruction of the image was made possible by using mathematical algorithms. Common reconstruction techniques are back projection and iterative (repetitive) reconstruction techniques (13).

2.2.1.1. Simple Back Projection

This technique, projection images are taken from the angles of rotation of the camera and stored in computer memory. After all projection data have been collected, they are folded backward from the last image and the three-dimensional structure of the image is obtained. As the camera rotates around the patient, data that hits the same pixel is encoded into consecutive boxes. Computer projection information in this matrix will not be able to predict from which depth the organ comes from all pixels are evenly reflected. Projection dept information is available this a projection in the mirroring process that comes against the point all the pixels are applied. (Figure 2.3.) As a result of the mirroring process, the information overlaps the real image of the object in place is obtained. The projection of future projections changes the object by 1 / r. That is, the recovered image is a convolution of the actual image with 1 / r (14).

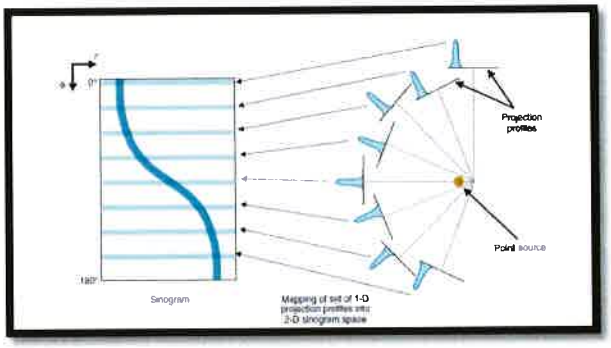


Figure 2.3. Projection Known as Synogram (6).

r: Distancecenter of point-source (1/r: blurring), f '(x, y) = f (x, y) * (1/r)

This the distortion is called the "star effect. Below is the shape of simple back projection. (As shown Figure 2.4.)

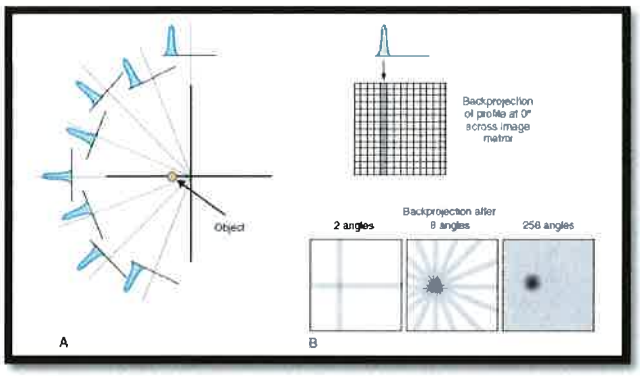


Figure 2.4. A) Projection for a pointsource for different angles. B) repeating build up the backprojected image.

2.2.1.2. Direct Fourier Transform Reconstruction

Projections to eliminate that avoid the blurring effect (1/r) the impact of a number of mathematical operationsthese processes are called filtering. This filtee is Fourier transform (FT) reconstruction (13) .

$f(x)$: 1-D image is variable function

k: Summation of sin and cos functions

$$F(k) = F\,[f(x)] \tag{1}$$

The 2-D FT by,

$$F(k_x, k_y) = F\,[f(x, y)] \tag{2}$$

A inverse FT by,

$$F^{-1}[F(k_x, k_y)] = f(x, y) \tag{3}$$

2.2.1.3. Filtered Back Projection

Projection acquire profiles at N projection angles. Calculate the 1-D FT of each profile and then Apply a ramp filte to each k-space profile. $|kr|$, the absolute value of the radial

k-space coordinate at each point in the FT. Thus, value of the FT is increased linearly. $P(kr, \Phi)$ is the unfiltered FT (13,15).

$H(k_r)$: filter amplitude denoted by,

$$P'(kr, \Phi) = |kr| \; P(kr, \Phi) \tag{4}$$

Calculate the inverse FT of each filtered FT profile to obtain a modified projection Profile by,

$$P'(kr, \Phi) = F^{-1} [\, |kr| \; P(kr, \Phi) \;] \tag{5}$$

Perform conventional backprojection using filtered by,

$$f(x,y) = \frac{1}{N} \sum_i^N p'(x \cos \Phi i + y \sin \Phi i \; , \Phi i) \tag{6}$$

FBP is applied measurind noise-free data, exact value of the true distribution and have short time. High-frequency signals are caused by noise sometimes (Figure 2.5) .

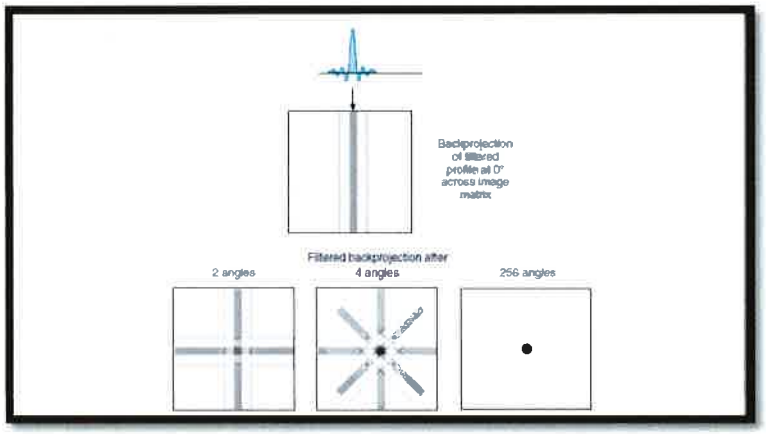


Figure 2.5. Filtered Backprojection Different Angle.

2.2.1.4. Iterative Reconstruction Algorithms

The biggest restriction is that the analytic algorithm physical effects such as photon noise and the reduction is not reflected in the algorithm. Iterative method can be modeled directly noise in the algorithm. In addition, interactive methods position reduction bound depens on the distance coefficients and the power of allocation such as (Figure 2.6.) emission and detection complex physical models of the problem it is suitable to solve.

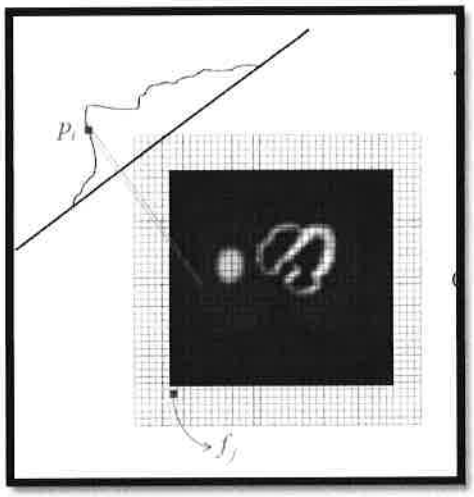


Figure 2.6. fj: Initial and Guess the Value of the Pixel j of Image, pi: Pixel value of i of Image.

P_i: *Forward projection* , $P_i = \sum a_{ij}. f_j$

f_i: *Back projection,* $f_i = \sum a_{ij}. p_i$

a_{ij}: *Transition* matrix

2.2.1.5. Algebraic Reconstruction Technique (ART)

ART start an initial forecast image as such, all interactive method. Initial image projections are calculated using forward projection. The initial image, the measured and calculated compansate for the difference between the projections will is modified with a different compensate for the difference between the projections.

A correction factors of the perspective projection pixel values after calculating factor is reflected. These new values for the next projection as the startup image is taken. Update for all projections a completed iteration is completed.

$$f_j^{new} = f_j^{old} \frac{P_i}{\sum_k a_{ik} \; f_k^{old}} \tag{7}$$

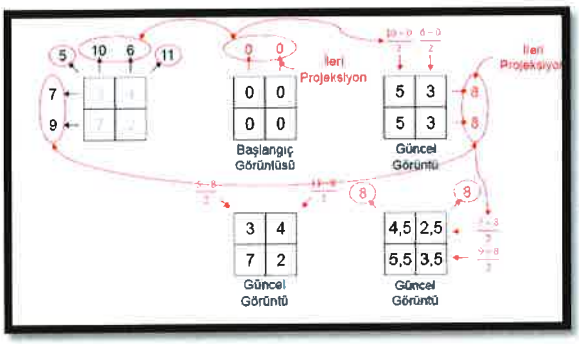


Figure 2.7. Algebraic Reconstruction Technique.

ART method, the correction factors for the multiplication applied as a method to is known Multiplicative ART. (Figure 2.7) The correction factors applied a total Additive ART of other factor. The counting rate relatively the information in nuclear medicine that is collected due to being low in noise ratio is high.

2.2.1.6. Expectation Maximization Reconstruction Algorithm

Maximum uncertainty in determining are used many approaches such as, Expectation-Maximization (EM) and Maximum Likelihood (ML).

$$f_j^{new} = \frac{f_j^{old}}{\sum_l a_{lj}} \sum a_{ij} \frac{p_i}{\sum a_{ik} f_k^{old}} \tag{8}$$

The number of iterations is obtained the actual image close to an image increases. The number of iterations causes increase the too noise. This study was used 16 iteration number.

2.2.1.7. Ordered Subsets Expectation Maximisation(OS-EM) Reconstruction Algorithm

Number of sub-groups is very small unless, OS-EM is almost the same ML-EM. The computation time is almost the same. Thus, If the projection 128 selected for sub-groups of the number 4 according to OS-EM algorithm with ML-EM runs 32 times faster. In practice, the sub-group the calculation of the number 4 selecting speed provides a good balance between image quality.

2.2.2. Image Corrections Parameters

2.2.2.1. Photon Attenuation Correction

An important effect of CT on SPECT images is Linear atenution coefficient. Photons extracted from X-rays or gamma rays according to the unit thickness of the material are called linear attenuation coefficient. (cm^{-1}). The photons coming out of the organ pass through the tissues of different density each time they come to the detector and are subjected to different attenuation each time. When CT images are taken, these different density tissues are normalized and attenuated. The X-ray tube rotates around the patient while it is active. In the meantime, the patient's table moves at a constant speed, which is called a spiral CT scan. As X-rays pass through body tissues, some of the rays are absorbed and weakened. The CT system also measures the intensity of the rays emanating from the tube and the intensity of X-rays emanating from the body tissues. The ratio of these two intensities gives the attenuation coefficient. The CT computer calculates this process separately for each tissue and performs attenuation correction. One of the most important functions of CT on SPECT images is this attenuation correction.(16,17).

Φo: Incident photon fluences

Φ: Transmitted photon fluences

dr: Differential of thickness of tissue

μ : the linear attenuation coefficient (LAC).

$$\Phi = \Phi o \exp [- \int \mu(x,y)\, dr] \quad (9)$$

In order to present the measured linear attenuation coefficient as targeting the tissue type, it calculate the pixel value in Hounsfield Units (HU) with CT options.

$$HU(X,Y) = \frac{\mu_{CT} - \mu_W}{\mu_W} \text{ x } 1000 \quad (9)$$

μ_{CT} (x,y) : Linear attenuation coefficient from CT (x,y) coordinate,

μ_w: LAC of water.

One of the contents of CT in Hounsfield is scaled, the air equal to -1000 HU, the water equal to 0 HU, the bone represents equal 1000 to 2000 HU.

By converting CT data to a map of attenuation coefficients, the energy of the radionuclide photon is directly translated into a map of attenuation coefficients. This conversion can be accomplished by performing x-ray CT calibration measurements of a calibration phantom containing known materials, where it is possible to measure the CT scan (in HU) of the CT number directly from the phantom.

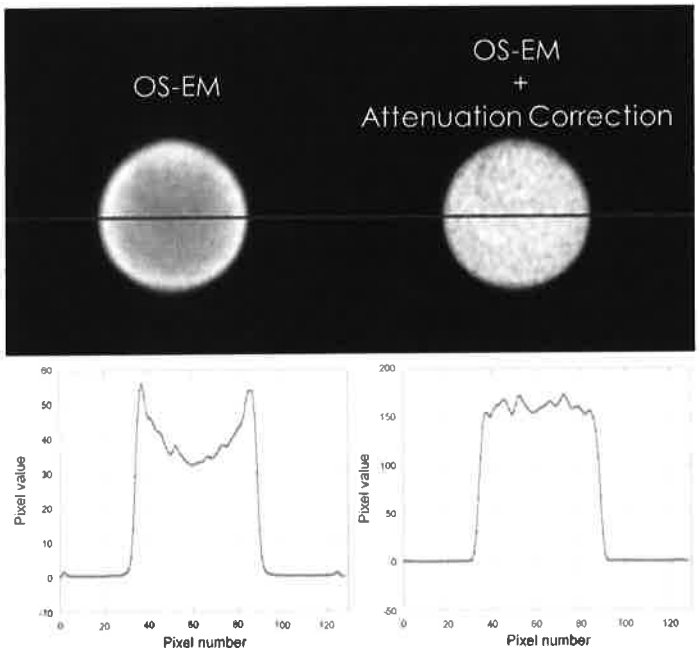


Figure 2.8. Linear Atenuation Correction and OS-EM

An important effect of CT on SPECT images is Linear Atenuation. Because the most anatomic regions in the body are heterogeneous in tissue composition, Nonuniform Density of human body is important to do for patient-specific attenuation compensation map with CT images. When CT images are taken normalized. As shown in the Figure 2.8 , Only Os-Em algorithm was used as seen imege. Osem and atenuation correction was used as seen image.

2.2.2.2. Mass Attenuation Coefficient

The probability of interaction depends on the density of the material and the number of atoms per volume, which can be overcome by normalizing the attenuation coefficient (18).

$$Mass\ Attenuation\ Coefficient\ \left(\frac{\mu}{p}\right)\left[\frac{cm2}{g}\right] = \frac{Linear\ Attenuation\ Coefficient\ (\mu)[cm^{-1}]}{Density\ of\ Material\ (p)\ [g/cm^3]} \quad (10)$$

2.2.2.3. Scatter Correction

As a result of the interaction of photons with body tissues, incorrect information is transmitted to the image and distort the image quality. Scatter correction varies according to as distribution: energy resolution of gamma camera used, radionuclide energy, collimators, target organ size, chemical content of radiopharmaceutical, activity, and source. If the binding energy is too high, the electron energy from the photon, then the electrons and this interaction is called Compton scattering. The most commonly SC techniques are double or triple energy window techniques. These techniques have used Monte Carlo simulations. Many of the scattered photons are radioactive, including the patient's bed. It comes from the structures (organs and tissues) around the source. Some scattering is in the collimator and crystalline, but this scattering is less important in addition to patient scattering and are often neglected. 10% selected in gamma camera applications considering the window width, unlike low-energy photons, high-energy photons are not included in this window. It is observed (19).

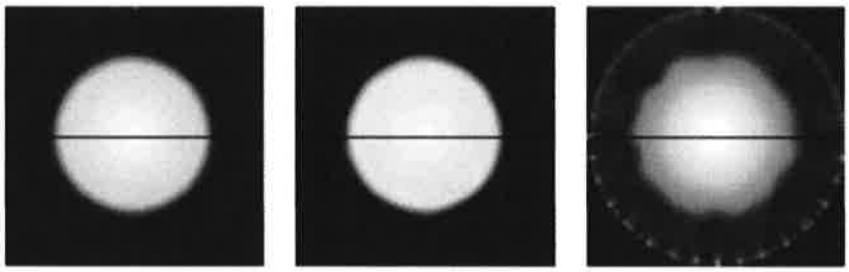


Figure 2.9. Scatter Correction

Dual energy window was called a double photopic window method. For the detected gamma rays, a given range of energy spectra is divided into sub-windows of equal width (20).

2.2.2.4. Colimator Detector Response (CDR)

CDR is one of the basic factors of the image resolution. It is one of the most important disturbing factors in quantitative SPECT imaging. CDR great sensitivity extent can be said to be determined by collimator sensitivity. As a result, collimator efficiency depending on the arrival of the most system sensitivity, collimatoroffers a large difference

according to the type. Lesions of lesions in a gamma camera image contrast is a key to image quality. The spatial resolution varies with the collimator detector distance. CDR makes the image smoother. OS-EM algorithms are used for this. CDR should be defined for the radionuclide since both septal penetration and scattering (21). Collimator-Detector Responses have 4 features intrinsic response function, The geometric response function, The septal scatter function and septal penetration function. Most important this one is geometric response function. Because with the increasing distance resolutaion of the system are getting worsen. You shown Figure 2.10. :The intrinsic response function (upper left) describes the effects of interactions in the detector crystal itself (the point source is collimated to form a pencil beam). The geometric response function (lower left) models source-to-collimator distance effects (the measured response in the crystal varies with source-to-collimator distance). The septal scatter function (upper right) and septal penetration function (lower right) model the interactions between gamma radiation and the collimator.

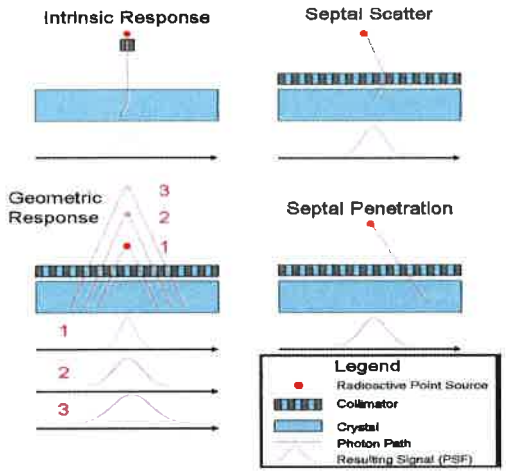


Figure 2.10. The geometric response function, The septal scatter function and septal penetration function

The effects of collimator detector response can be see in the Figures 2.11 it is very important corrections for quantative imaging. (A) LEGP at 113-keV window. (B) ME at 113-keV window. (C) LEGP at 208-keV window. (D) ME at 208-keV window.
The image of D is clearer than the others.

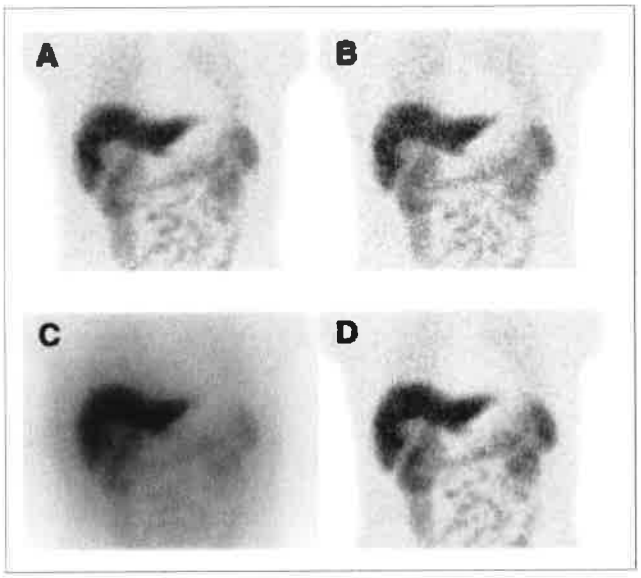


Figure 2.11. Simulated Projections of ^{177}Lu in XCAT Phantom.

2.2.2.5. System Volume Sensivity

With IEC cylindrical phantom, we measured an activity by injecting it into the known volumes. The system volume sensivity is then determined by dividing the total reconstructed counts within the target volume of interest by the product of the known activity and the SPECT acquisition time. SPECT/CT system using a cylindric homogen phantom (Volume:5640 ml) filled with a uniform dilution of activity We calculated the system volume sensitivity. Homogen Cylindrical Phantom has 5640 cc volume that was filled with a Lu-177 solution 7,07 mCi. Used MEGP collimator. Place the Lu-177 homogen phantom source data set type during 12 minute and phase frame duration 1440000 second (22).

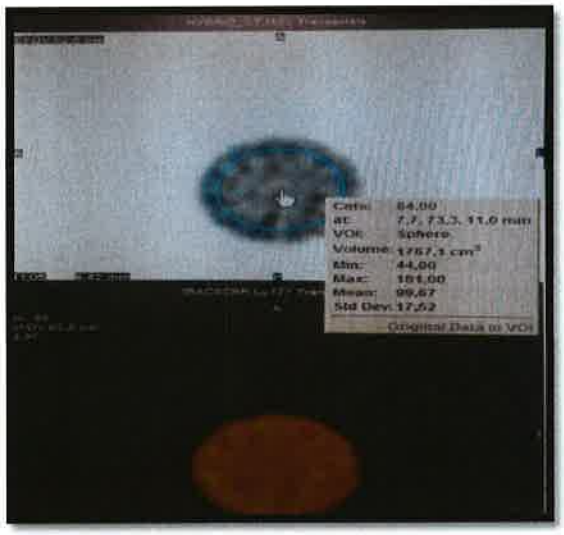


Figure 2.12. Homegen Phantom Count Data.

System volume data calculated for (Figure 2.12) Yeditepe University Hospital has used GE mark Discovery NM/CT 670 SPECT/CT device and GE xeleris software (23, 24).

R: Decay-corrected counting rate

R*:Counting rate (counts/dwell time)

$\mathbf{T_0}$: start time of the acquisition

$\mathbf{T_{cal}}$: the time of the activity calibration

$\mathbf{T_{1/2}}$: half-life of the isotope

$\mathbf{T_{acq}}$: time duration of the acquisition.

After imaging conditions and cylinder phantom filled with activity, calculated the system CF with equation (17) and (18) .

$$R = \exp\left(\frac{To-Tcal}{T1/2}\ln 2\right)\left(\frac{Tacq}{T1/2}\right)\frac{1}{\left(1-\exp\left(\frac{Tacq}{T1/2}\ln 2\right)\right)} \quad (17)$$

$$R* = R \text{ x count rate(cpm)} \quad (18)$$

Count rate (cpm) calculate derived from the reconstructed image (Total VOI count rate/ Time duration of the acquisition) as follows equation (19)

$$\text{Count Rate (cpm)} = \frac{\text{Total VOI count rate}}{\text{Tacq.}} \quad (19)$$

Total VOI count rate calculated as follows Eq. (20)

$$\text{Total VOI count rate} = \text{Mean VOI count x Total Voxel} \quad (20)$$

The system volume sensitivity is deriveded equation (21) ,

C_A: Activity concentration in homogen phantom

$$S_{vol} = \frac{R*/Vvol}{CA} \quad (21)$$

Yeditepe University Hospital, SPECT/CT system volume data calculated for Table 2.1. and equation (21) **: 501,05 cpm/MBq (18.54 kcpm/µCi)**

Table 2.1. Yeditepe University Hospital, SPECT/CT System Volume Sensivity Data.

Time of the activity calibration (T_{cal}):	11.01.2019 13:50
Measured activity (mCi):	7,07
Phantom volume (ml):	5640
Start time (T_0):	11.01.2019 17:37
Time duration of the acquisition (minute) (Tacq):	12
Half-life (day) ($T_{1/2}$):	6,7
VOI mean count:	99,67
Total VOI count:	362000
VOI volume(ml):	1320
Count rate (cpm):	30166,66667
Decay corrected R (cpm):	30675,89273
Activity concentration (MBq/ml) :	0,046381206
Svol (cpm/MBq)	501,05

2.2.2.6. System Planar Sensitivity Measurements

Quantitative SPECT imaging, conversion of pixel values from counts to radioactivity concentration per unit volume (Bq/ml) requires measuring a conversion factor, often referred to as System Sensitivity. This factor should be measured for each combination of camera, collimator and radioisotope, usually presented either in counts per minute per

μCi (cpm/μCi) or in counts per second per MBq (cps/MBq) units (25). Camera sensitivity should be measured according to the NEMA standard for System Planar Sensitivity (For example, System planar sensitivity measurements for NM GP 600 series)

The system planar sensitivity is the ratio collimated counts detected in one acquisition plane to activity of a specific planar to plane source. The planar sensitivity must be measured for each collimator being in use with the appropriate isotopes. The sensitivity is represented counts per minute/μCi or in counts per second/MBq. This measurements rely o n the accuracy o f the calibration o f the radionuclide activity, and therefore it is important to use standard calibration devices the same for sensitivity and for clinical dose measurements (26).

Test conditions: Count rate must be less than 30 kcps through an energy window used in appropriate clinical protocol.

Test equipment:

- 1-5 cc plastic syringe
- 30-50 c c plastic syringe
- 150 mm diameter Petri plastic dish
- Calibrated dose calibrator (well counter), the same that is used for clinical dose measurements.

Measurement procedure:

1) Fill the Petri dish with water using the large plastic syringe to at least completely cover the bottom o f the dish to 2-3 mm depth.
2) Fill the small syringe with an amount o f activity o f about 3 -5 mCi. Measure exact amount o f activity $\mathbf{A_{SR}}$ with the dose calibrator. Record the time $\mathbf{T_0}$ of the measurement.
3) Disperse the source from the syringe to the Petri dish.
4) Measure the residual activity **Ares** remaining in the syringe. Calculated amount o f activity in the Petri dish as $\mathbf{A_0 = A_{SR} - A_{res}}$ at the time o f preparation.
5) Rotate the gantry such that detector 1 surface is perfectly horizontal and facing up. Place the prepared Petri dish at the approximate center of detector 1 FOV, such that the bottom of the dish is at 100±2 mm from the detector surface. To minimize effects of scattering and attenuation, the dish should be placed on a

holder with negligible attenuation. Make sure the dish is leveled such that the fluid solution in it is distributed evenly (27).

6) Set the following static acquisition parameters: energy session appropriate for the isotope, matrix 256x256, zoom **1.0**, stop on time $\mathbf{T_d}$, such that the total acquisition counts is at least **4000 Kcnts.**
7) Run the acquisition. Record the acquisition start time $\mathbf{T_s}$. Send the acquired image to Xeleris and use the available tools to measure the total counts number ***N***.
8) Calculate the system planar sensitivity of detector 1 as follows (Equation 22)
9)

$$S = \frac{N}{Td\ xA0}\ X\ e^{\left[\frac{\ln(2)x(Ts-T0)}{Thalf}\right]} \qquad (22)$$

10) Repeat steps 1 -8 for detector 2,
11) Calculate Camera Sensitivity (to be entered in Q. Metrix or Dosimtery toolkit application) as the mean of the sensitivity parameters of detectors 1 and 2: Camera Sensitivity = $(S_{det1}+S_{det2})/2$
12) According to the data in the following Table 2.2. ,
13) Our results derive (S) :14,04 cpm/ μCi
14)

Table 2.2. System Planar Sensitivity Measument Data

A_0 (mCi)	A_{SR} (mCi)	A_{res} (mCi)	N (Count)	T_d (min)	T_s	T_0	T_{half} (day)
4,07mCi	4,14	0,07	4,000.000	70	15:09	14:47	6,65

2.3. MIRD (Medical Internal Radiation Dose) Method

MIRD is a method to calculate the dose in NM. In MIRD pamphlets published since 1968 the formula for calculation of absorbed dose rate by developing equation 23 to become has provided. MIRD 16 located at the absorbed dose rate equation is expressed as. It has standard size models of the human body and its organs is based on the calculation of the dose on that in the method, the source of radioactivity in the target organs dose-dependent attenuation that causes in the organs is calculated (5, 29, 30)

$$D = k\tilde{A} \sum_i niEi\,\Phi i/m \quad (23)$$

D = Absorb dose

$\tilde{A}$ = Cumulative activity

n_i = Number of particles

E_i : Energy per particle

f_i = Fraction of absorbed energy

m = Mass of target region

k = Constant

Cumulated activity ($\tilde{A}$) is the area under the time-activity curve for a source organ. Absorbed dose in the MIRD system is a deceptively simple representation of

$$D = \tilde{A}.S \quad (24)$$

S factor:

$$S = k \sum_i ni\ Ei\,\Phi i/m \quad (25)$$

(r_h) : source region and as follows:

(r_k) : target region

(A_0): activity administered

(τ): residence time.

$$Dr \leftarrow k = \sum k\ \tilde{A}\ S(rk \leftarrow rh) \quad (26)$$

$$\tau = \tilde{A}\ /A_0 \quad (27)$$

Using this definition the dose equation may be written as:

$$Dr \leftarrow h = Ao\ \tau\ S(rk \leftarrow rh) \quad (28)$$

Radionuclide dose conversion factors to be used in the calculations are given in reference to the organs (29).

2.3.1. Organ Dosimetry

PRRT, in the treatment of neuroendocrine and prostate tumors with ^{177}Lu-DOTA/PSMA peptits with beta emitting radioisotopes, such as marked with is performed. ^{177}Lu are widely used in the treatment of prostate cancer with PSMA marked. Both treatments, which limits the value that can be given to patients with the highest activity of the two organs: the kidneys, and bone marrow. National Council on Radiation Protection and

Measurements (NCRPM), according to the kidneys of 23 Gy like-dose exposure, 5% of patients within 5 years give rise to deterministic effects. Gamma rays of the isotopes ^{177} Lu, with or without dosimetry during treatment. The activity of the patient's medical status and usually the first treatment is determined by considering the literature data. MIRD method is widely used for dose calculation. According to the source and target organs of the treatment is determined (31). The determination of cumulative activity is significant. In the calculation of the cumulative activity for each organ, after the injection 4, 24, 72 and 168 hours received in the anterior and posterior whole body and SPECT/CT images are used. Whole-body imaging isotopes ^{177} Lu in 6,8 % of 113 keV energy or abundance factor by 10,4% of 208 keV gamma rays with two energy abundance factor can be used. High photon energy s of isotope can cause star artifect. 208 keV peak has a higher incidence than 113 keV. It is lower attenuation in the tissue, MEGP collimators are used for imaging with ^{177}Lu. In addition to the 208 keV window will improve the count statistics and so increase contrast resolution, makes more accurate dosimetry and short scanning time. Appropriate scatter correction techniques have to be applied in order to be able to use both Windows. Each organ and the whole body for 4, 24, 72 and 168 hours are drawn to the images obtained in the corresponding fields on. This is used in the related fields other images taken of the same patient after treatment. Patient's organs and thickness is most importand calculations for dosimetry. Images of the thickness of each body part is determined by LAC with the help of the reduction factor μ multiplied by the linear value. In a study in relationship between LAC and CT HU unit using radionuclides for SPECT (18). By combining SPECT and CT images, anatomical and functional information is more localized in terms of clinical. Linear attenuation coefficients referred. Patient-specific reduction map was determined after SPECT/CT imaging. Thus, taken together the cumulative activity for each CT and SPECT images in the determination of patient-specific linear attenuation coefficient is determined and is included in the calculation. Another important parameter for organ dosimetry is calibration factor. Gamma camera calibration factor detail was described in the section 3. We draw VOI for relevant organs that obtain corresponds to the count to activity. VOI is calculated by the multiplication count and activity. The area under the count activity-time curve gives cumulative activity. D is calculated by multiplying S factor in the tables, which is available with, For example;

$$D_{\text{kidneys}} = \tilde{A}_{Kidneys}\ x\ S_{kidneys \leftarrow kidneys} + \tilde{A}_{\text{liver}}\ x\ S_{kidneys \leftarrow \text{liver}} + \tilde{A}_{\text{the rest of the body}}\ x\ S_{kidneys \leftarrow \text{the rest of the body}} \quad (29)$$

D: Absorned dose of kidneys

$\tilde{A}$: Organ received activity

S: Dose conversion value (Gy/MBq-s)

2.3.2. Lesion Dosimetry

Dosimetry in radyonuclid therapy has been based on the S-value developed by the MIRD. Organs for various age groups, children or adults are modeled with phantoms. Based on the determination of the cumulative activities of the critical organs in the neighboring environment from the origin of the organ to be treated by S values. *S values* for calculations were initially determined by Monte Carlo methods for stylized models representing reference human anatomy and for all sex, age (30). Also, Unit density sphere model is used for lesion dosimetry. Lesion density is assumed to be spherical and 1g/cm ^{3} that only because of the activity of the lesions, the lesion frequently asked doses can be calculated. Lesions dose of organs dose, other source and other source of lesions is not calculated. One of volume and cumulative activity are important for Unit density sphere model (32).

$$D_{\text{target} \leftarrow \text{source}} = \tilde{A}_{source}\ x\ S_{target \leftarrow source} + \tilde{A}_0\ x\ \tau\ x\ S_{target \leftarrow source} \quad (29)$$

A_0 : Activity İnjected into the patient

τ: Residence time (s)

S : Dose conversion value (Gy/MBq-s)

3. METHODS AND MATERIALS

From January 2018 to September 2019, among the 22 patients treated for 9 patient with ^{177}Lu PSMA or DOTATATE using for patients affected by somatostatin receptor positive tumours prostate. The patients were given by intravenously radionuclides on of treatment planing day. The amount of activity planned by physicians doctors. First whole-body and SPECT/CT images were taken 4 hours after treatment. Whole-body and SPECT shots will get the image at 4 24,72, and 168th hours after the radiopharmaceutical is given to the patient with transfuse (33). The volume drawn (VOI) of kidneys, liver and spleen organs of all patients had been marked with GE Xeleris functional imaging workstation (Version 3.1) the software program, I used multi SPECT/CT technic that can you see Figure 3.1.

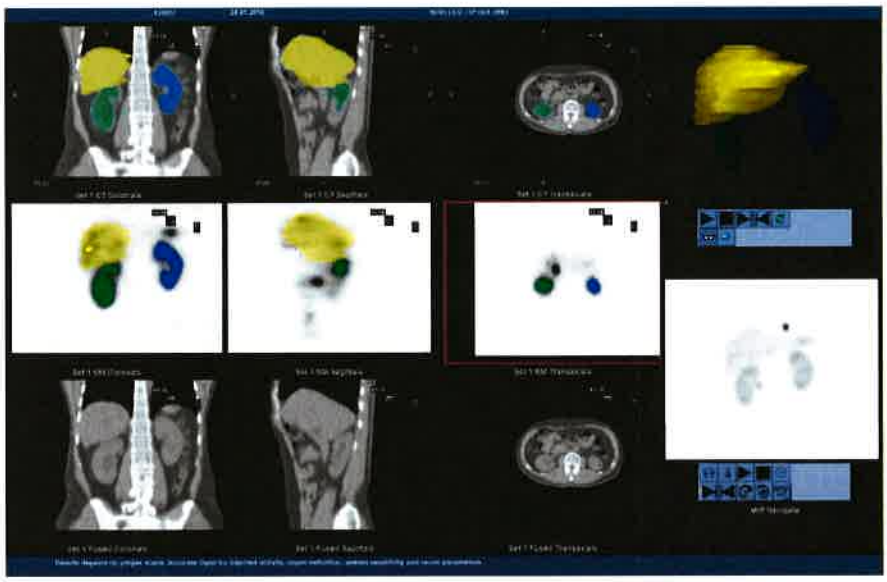


Figure 3.1. VOI at SPECT/CT GE Xeleris Functional Imaging Workstation

3.1. Whole Body Imaging

GE Discovery NM/CT 670 Pro SPECT/CT was used this study. Whole body scan speed was 30 cm/min, Energy window: 208 keV ± 10%, was used Medium Energy Genaral collimator. The counts of the organs were calculated with SPECT imaging. Anterior and posterior whole-body counts were calculated with GE Xeleris software program and geometric mean was calculated. Because the energy of Lu, 208 keV is medium energy range of nucleer medicine imaging.

3.2. SPECT/CT Imaging

Dual Energy window (scatter photon) is 160 keV ± 10%, It was used 120 projection, 20 sec./ projection. Matrix size was 128×128, OS-EM had 2 iteration, 10 subset. Slice of slice volume of the organs were calculated by drawing with CT and images received at all hours have been confirmed. For those who do not match, the program is fully aligned. A given amount of activity of all treatment patients, weight, height, time of treatment, and the imaging time were noted. Only CT images do not give us information about how much activity in the kidney. Kidney, liver and Spleen volume were drawn with CT that Region of Interest (ROI) and the GE Xeleris program was created slices combined with VOI. SPECT imaging was not used in the program for kidney, Liver and Spleen volumes, only used counts. Our goal is to draw weight of each patients organs with CT, because the structure of the reduction map is drawn with HU and overlap with SPECT to calculate the reduction of the photon's interaction with the other tissue and bone followed by the photon to the detector. This is called photon attenuation correction. ^{177}Lu abandance is low, dead time has not been. The program has been corrected for the collimator detector response as the object will change when the object is near and far away. We have adjusted our FOV to reduce scattered photons. Matrix size is 128x128, 2 FOV and view angle is 5 °. We have taken 2 iterations, 10 subset of shots. All count, volume and system sensitivity were obtained Figure 3.2 .

Figure 3.2. Example Patient's Excel Table

Time calculated by subtracting treatment time to imaging time fixed in shots, 12 minute. Activity = (organ's count x System sensitivity)/time The scan time 80 second for whole body activity. Anterior and posterio scanning were obtained by taking the geometric mean. The Matlab software program was used to transform activity from counts. The area under the activity-time curve plotted with the data obtained was calculated with the Matlab software program. This area give us cumulative activityfor all body (34).

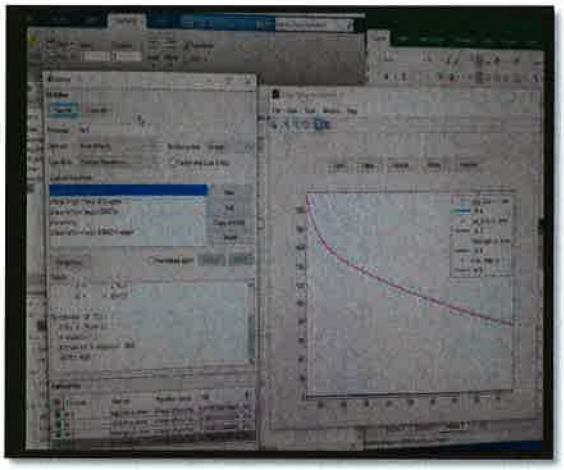


Figure 3.3. Example Patient's Data Calculation for Matlab.

If time is integrated from zero to infinity and $T_{1/2}$ is 6,7 day ($\tilde{A} = Ao.\ e^{-0,693/T1/2}$)
Exponential curve fitting method implemented be calculated for 4 points obtained are not exponential. Exponential functions are usually written in the form $y = a.e^{-bx} + c.e^{-dx}$ As shown Figure 3.3.

Cumulative activities units obtained mCi-h, TIAC (Time-Integrated Activity Coefficient) are calculated. TIACs data were entered to OLINDA/EXM software program (version1.1) that shown Figure 3.4-5 (35). OLINDA /EXM is organ level internal dose assessment code. This code gives doses for stylized model of average individuals results. This program has a lot of different phantom. Such as, Famale, male, ages, pregnat, adult and childeren. The chart will be drawn on activity-time with with this information. Area under the graph will give the the cumulative activity. The cumulative activity is a difficult task to determine. The gain on the data protocols are applied, interactive methods use obtain acquisition for images. SPECT applies for on activity of patient. In adition, CT applies for reduction coefficient. All protocols for correct data must be edited. In this study, by adjusting the appropriate parameters that patient-specific dosimetry will be

performed quantitative. This study regulate photon attenuation, scatter correction, and calibration paramete (36).

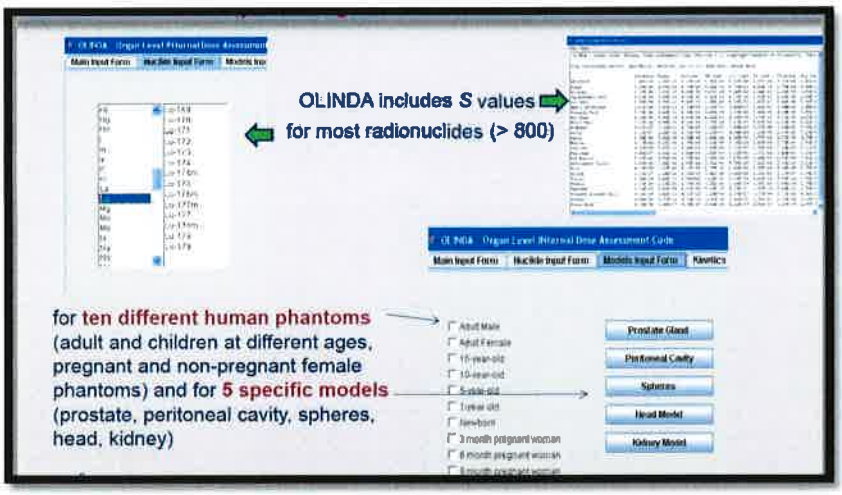


Figure 3.4. OLINDA/EXM Software Program.

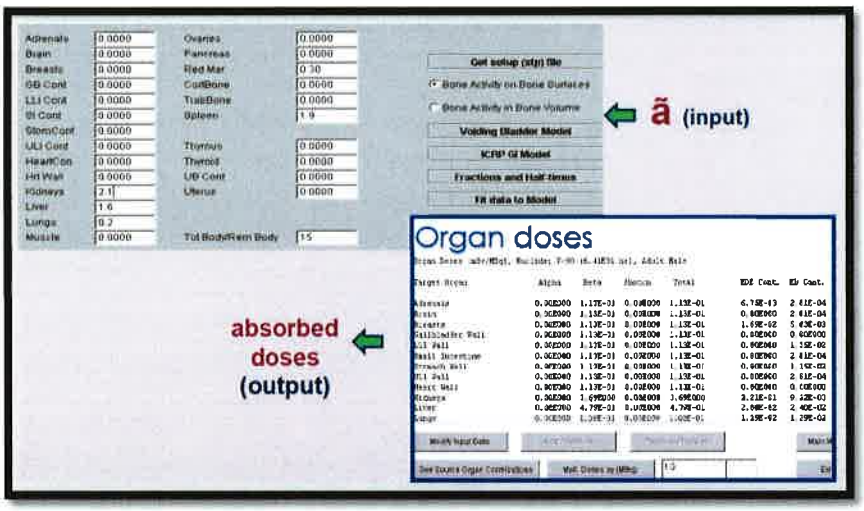


Figure1.5. TIACs input at OLINDA/EXM Software Program.

Absorbed Dose (Gy/GBq) = Kidney Total Dose (Sv)/ Giving Treatment Activty (GBq)

3.3. CT Imaging

CT was performed at 4, 24, 72 and 168 th hours in order to have an effective dosimetry study in terms of the benefit and effectiveness of the treatment, All in all considering that the existing patients are cancer, even if the diagnosis is not appropriate. Tomographic irradiation parameters are shown in the Figure 4.6. Diagnostic tomography was performed at 24. Hour. At the 4, 72, 168th hour, ultra low dose tomography was performed. For the purpose of just for attenuation correction

IMPACT CT patient Dosimetry was used that application can be downloaded from the Windosis. Exa web page. This application work with database and excel sheet. IMPACT CT patient Dosimetry Calculator (version 1.0.4) made according to ICRP-103. There are registered fields in which various devices and parameters can be changed in Excel. It helps to calculate total effective dose and organ dose by entering information such as attraction parameters (CTDI vol, DLP) and irradiation distance. Figure 3.6 shown the irradiation distance in the phantom. We are dealing with kidney doses in this study. The reason for the calculation of CT doses in this study, accurate treatment plan with correct dosimetry, receiving full treatment that causes incomplete treatment. Figure 3.19 contains the parameters of the irradiation parameters and calculations of 4, 72 and 168th. hours, Figure 3.20 contains the parameter of the irradiation parameter and calculations of 24. hours. CT shooting parameters for 4, 72, 168 th hours. Hours that thickness is 5mm, Thick speed is 0,938 (spiral pitch), tube voltage is 120 kV, Tube current is 20mA, CTDIvol is 1,5mGy, DLP is is 68 mGy.cm. CT shooting parameters for 24 th. Hour that thickness is 5mm, Thick speed is 1,375 (spiral pitch), tube voltage is 120 kV, Tube current is 222 mA, CTDIvol is 11,7 mGy , DLP is 513 mGy.cm .

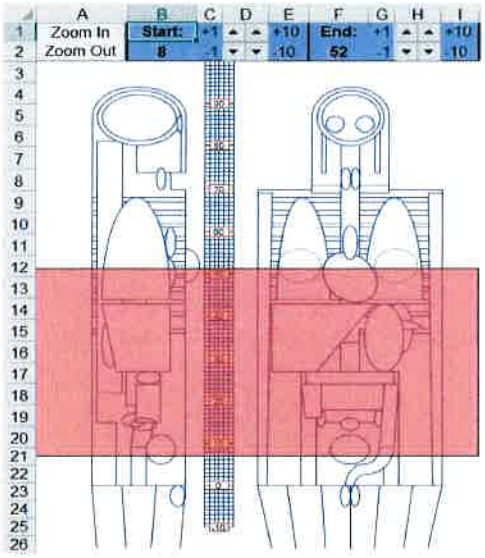


Figure 3.6. IMPACT CT Patient Dosimetry Phantom.

4. RESULTS

4.1. Patients

Patient-specific dosimetry was successfully performed in the treatment of ^{177}Lu PSMA and DOTATATE in NM at Yeditepe University Ihtisas Hospital. After radiopharmaceutical infusion, patients were followed up to avoid side effects. Whole body images and SPECT / CT images were taken after 4 hours. Doses were calculated for each organ and for the rest of the body. Kidney, Liver and Spleen dose calculations were made in terms of risk. Evaluation was performed for 9 patients for PSMA, 4 patient (Women is 1, Man is 3) for DOTATATE in Yeditepe University Ihtisas Hospital. Mean age of patients is 67, 6 (56,7-61,6) for PSMA and 47,6 (10,3-47,6) for DOTATATE. PSMA peptide treatments had 14 for 9 patients and DOTATATE peptide treatments had 8 for 4 patients. Some patients were not calculated liver activities and counts because of liver tumors. Demographic information of patients are given in the Table 4.1.

Table 4.1. Demographic Information.

Total Treatment Number	Patient No	Treatment number	Age (y)	Peptide	M/F	Treatment Activity (GBq)
1	1	1	63,4	PSMA-617	M	5,55
2	1	2	63,4	PSMA-617	M	5,55
3	2	1	72,9	PSMA-617	M	5,55
4	3	1	73,2	PSMA-617	M	5,29
5	3	2	73,2	PSMA-617	M	5,48
6	4	1	79,2	PSMA-617	M	7,77
7	5	1	73,1	PSMA-617	M	4,59
8	5	2	73,1	PSMA-617	M	5,55
9	6	1	60,8	PSMA-617	M	5,74
10	6	2	60,6	PSMA-617	M	5,55
11	7	1	70,1	PSMA-617	M	7,62
12	7	2	70,3	PSMA-617	M	5,55
13	8	1	57,0	PSMA-617	M	5,99
14	9	1	56,7	PSMA-617	M	7,40
15	10	1	10,	DATATATE	M	2,92
16	11	1	58,8	DATATATE	M	5,85
17	11	2	58,8	DATATATE	M	6,03
18	11	3	58,8	DATATATE	M	5,92
19	12	1	41,4	DATATATE	M	7,22
20	12	2	41,4	DATATATE	M	8,25
21	12	3	41,4	DATATATE	M	7,22
22	13	1	69,3	DATATATE	F	4,44

Average activities was given 5,9 GBq (4,6-7,7 GBq) for PSMA treatment patients that 6,0 GBq (2,9-8,3 GBq) for DOTATATE (37).

4.2. PSMA and DOTATATE Doses

Organ absorbed doses per GBq were 0,59±0,08 Gy for Kidneys (Table 4.2) that were 0,07±0,03 Gy for Liver and 0,04±0,01 Gy Spleen for PSMA treatment (38,39). 9 Patients' 14 Treatment Number of Kidney Doses at ^{177}Lu PSMA(Table 4.2) . On the other hand, Organ absorbed doses per GBq were 0,58 ± 0,09 Gy for Kidneys that were 0,08± 0,03 Gy for Liver and 0,28± 0,25 Gy for Spleen for DOTATE treatment (Table 4.3).
As seen Figure 4.2, PSMA, dotate treatments for kidneys and liver have been relatively close to each other, while the spleen dotate quite alot compared to PSMA.

Table 4.2. ^{177}Lu PSMA Patients' Kidneys, Liver and Spleen Doses.

Total Treatment Number	Kidney (Gy/GBq)	Liver (Gy/GBq)	Spleen (Gy/GBq)
1	0,56	0,06	0,03
2	0,55	0,05	0,03
3	0,53	0,03	0,08
4	0,59	0,09	0,04
5	0,63	0,11	0,04
6	0,50	0,02	0,06
7	0,79	0,13	0,02
8	0,71	0,05	0,05
9	0,52	0,12	0,04
10	0,54	0,05	0,03
11	0,52	0,03	0,05
12	0,67	0,06	0,04
13	0,58	0,04	0,03
14	0,52	0,02	0,02
MEAN ± SD	**0,59±0,08**	**0,07±0,03**	**0,04±0,01**

Table 4.3. ^{177}Lu DOTATATE Patients' Kidneys, Liver and Spleen Doses.

Total Treatment Number	Kidney (Gy/GBq)	Liver (Gy/GBq)	Spleen (Gy/GBq)
1	0,72	0,17	0,17
2	0,51	0,08	0,08
3	0,43	0,08	0,25
4	0,48	0,07	0,22
5	0,67	0,05	0,19
6	0,61	0,05	0,16
7	0,63	0,05	0,25
8	0,61	0,09	0,93
MEAN ± SD	**0,58 ± 0,09**	**0,08± 0,03**	**0,28±0,25**

In the Table 4.4 and 4.5 shown the cumulative renal doses. None of the patients had an over 23 GY threshold dose.

In the figures we see kidney doses per activity for both peptides. Different colored bars indicate patients. As the doses differ in each patient, we observe dose differences in the treatments within the patient itself. Kidney Gy per GBq is seen in Table 4.4 and 4.5 different colors for different treatments specific to each patient foR PSMA and DOTATATE.

Table 4.4. ^{177}Lu PSMA Patient' Kidney Doses Gy per GBq for Different Treatment.

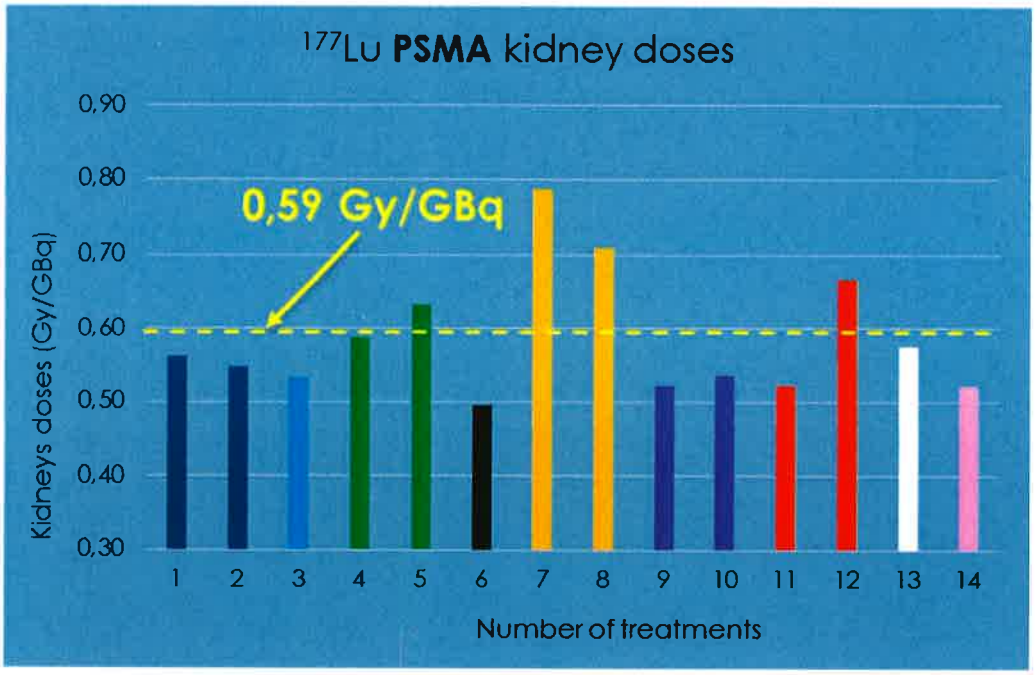
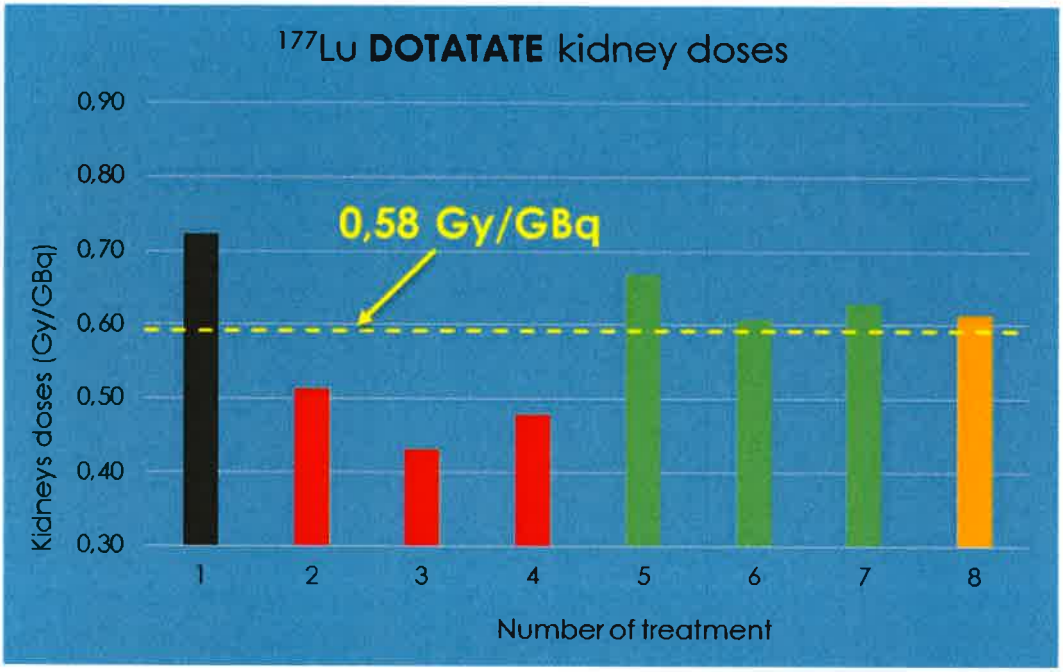


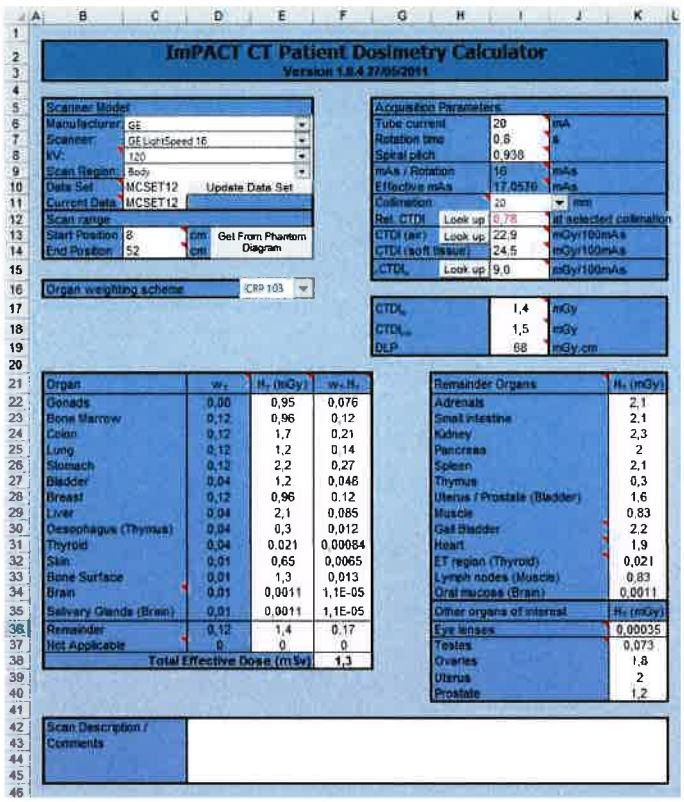
Table 4.5. ^{177}Lu DOTATATE Patient' Kidney Doses Gy per GBq for Different Treatment.



4.3. CT Doses

Other important information, the data Collected with IMPACT CT patient Dosimetry is 17 mGy and total effective dose (mSv) is 9,5 at 24th. Hour CT for Kidney. The data Collected with IMPACT CT patient Dosimetry is 1,5 mGy and Total effective dose (mSv) is 1,3 at 4, 72 and 168th. Hours CT for kidney. Table 4.6 and 1.10 shown at 4, 72 and 168th. Hours dose from CT.

Table 4.6. 4, 72 and 168th. Hours CT Doses Parameters.



ImPACT CT Patient Dosimetry Calculator

Version 1.0.4 27/05/2011

Scanner Model

Manufacturer:	GE
Scanner:	GE LightSpeed 16
kV:	120
Scan Region:	Body
Data Set	MCSET12
Current Data	MCSET12
Update Data Set	
Scan range	
Start Position	8 cm
End Position	52 cm
Get From Phantom Diagram	

Acquisition Parameters

Tube current	20	mA
Rotation time	0.6	s
Spiral pitch	0.938	
mAs / Rotation	16	mAs
Effective mAs	17.0570	mAs
Collimation	20	mm
Rel. CTDI	Look up 0.78	of selected collimation
CTDI (air)	Look up 22.9	mGy/100mAs
CTDI (soft tissue)	24.5	mGy/100mAs
$CTDI_w$	Look up 9.0	mGy/100mAs

Organ weighting scheme: ICRP 103

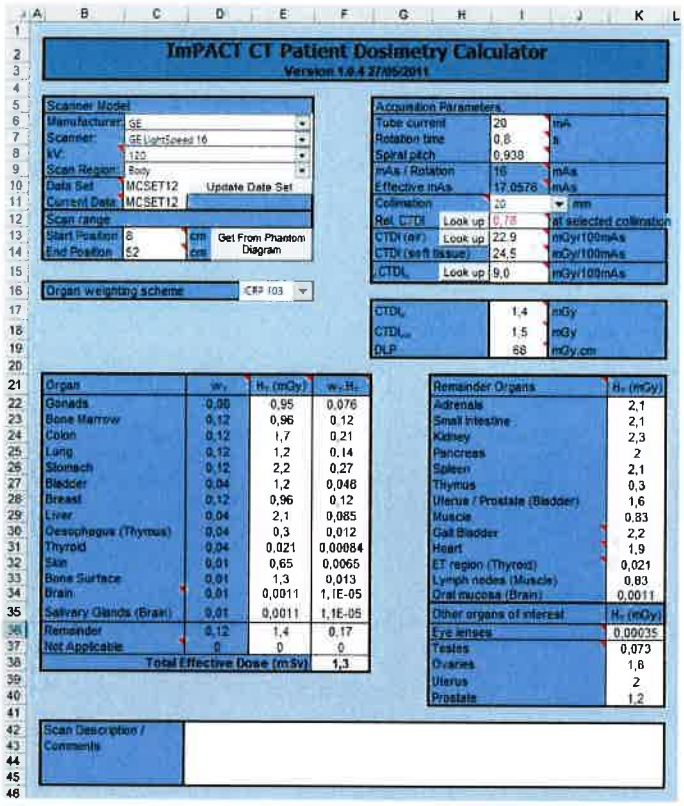
$CTDI_w$	1,4	mGy
$CTDI_{vol}$	1,5	mGy
DLP	68	mGy.cm

Organ	w_T	H_T (mGy)	$w_T.H_T$
Gonads	0,08	0,95	0,076
Bone Marrow	0,12	0,96	0,12
Colon	0,12	1,7	0,21
Lung	0,12	1,2	0,14
Stomach	0,12	2,2	0,27
Bladder	0,04	1,2	0,048
Breast	0,12	0,96	0,12
Liver	0,04	2,1	0,085
Oesophagus (Thymus)	0,04	0,3	0,012
Thyroid	0,04	0,021	0,00084
Skin	0,01	0,65	0,0065
Bone Surface	0,01	1,3	0,013
Brain	0,01	0,0011	1,1E-05
Salivary Glands (Brain)	0,01	0,0011	1,1E-05
Remainder	0,12	1,4	0,17
Not Applicable	0	0	0
Total Effective Dose (mSv)			1,3

Remainder Organs	H_T (mGy)
Adrenals	2,1
Small intestine	2,1
Kidney	2,3
Pancreas	2
Spleen	2,1
Thymus	0,3
Uterus / Prostate (Bladder)	1,6
Muscle	0,83
Gall Bladder	2,2
Heart	1,9
ET region (Thyroid)	0,021
Lymph nodes (Muscle)	0,83
Oral mucosa (Brain)	0,0011
Other organs of interest	H_T (mGy)
Eye lenses	0,00035
Testes	0,073
Ovaries	1,8
Uterus	2
Prostate	1,2

Scan Description / Comments

Table 4.7. 24th. Hour CT Doses Parameters.



Total kidney equivalent dose is 23, 9 mSv. High doses have been observed in treatments such as: 2, 5-5 Sv, but total dose is 2,3 mSv for all CT. More importantly extra tomography is insignificant. One CT is necessary for a good dosimetry that Using general 24. Hours at Hibrit model. Whereas, this thesis has used 4, 24, 72 and 168. Hours CT. Since patients already have cancer, we should not hesitate to take this extra dose, Because If the dose calculation is done correctly, treatment planning is done exactly and the patient gets more beneficial treatment. It may be possible to give the patient one more phase of treatment, but it may lead to early discontinuation of treatment if we do not perform the correct dosimetry. ^{177}Lu dosimetry was performed by quantitative imaging and it was used in clinical routine. In none of the patients, cumulative renal doses did not exceed 23 Gy. In addition to patient-to-patient dose differences, renal doses were also different in different treatments of the same patient. Literature data average is 0.74 GBq per Gy, this study finded 0,59 GBq per Gy. Hybrites models generally used only 24th hors CT construction of whereas this study have been taken 4 SPECT/CT. When we look at the literature studies with the planar images, kidney doses can be calculated more than actual value. In this study, I think that we do a more realistic dose calculation by SPECT and CT at 4 different time (41, 42, 43, 44).

5. DISCUSSION

When we look at the literature studies with the planar images and Hybrites models for kidney doses, Literature reviews for ^{177}Lu-PSMA-617,

- Kabasakal L, et al. 2015 Pre-therapeutic dosimetry of normal organs and tissues of 177Lu-PSMA-617 prostate-specific membrane antigen (PSMA) inhibitor in patients with castration-resistant prostate cancer that was used Hybrid model. Calculated radiation-absorbed doses per meqabecquerel were 0.88 mGy.
- Delker A,et al. 2016 Dosimetry for 177Lu-DKFZ-PSMA-617: a new radiopharmaceutical for the treatment of metastatic prostate cancer that was used Hybrid model. Calculated radiation-absorbed doses per meqabecquerel were 0, 60 mGy.
- Kratochwi C, et al. 2016, PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with 177Lu-Labeled PSMA-617 that was used Hybrid model. Calculated radiation-absorbed doses per meqabecquerel were 0, 75 mGy.
- Fendler WP, et al. 2017, Preliminary experience with dosimetry, response and patient reported outcome after 177Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer that was used Planar model. . Calculated radiation-absorbed doses per meqabecquerel were 0, 60 mGy.
- Yadav MP, et al. 2017, Post-therapeutic dosimetry of 177Lu-DKFZ-PSMA-617 in the treatment of patients with metastatic castration-resistant prostate cancer. That was used planar model. . Calculated radiation-absorbed doses per meqabecquerel were 0, 99 mGy.

  According to the results of this studies, my study organs doses value was lower than other study. When the literature data were compared, they calculated the kidney doses for the same peptide species using different methods. As can be seen in the literature studies done only in using planar or hybrid. In hybrid method only one hour CT was used. CT was applied all the time in my thesis. Also, we used 3 more spect values calculated kidney doses lower than other literature. To do this, the patient was given 7mSv doses by extra 3 tomograpy. I think to calculated more realistic doses in the my thesis with extra 3 SPECT/CT. It is known in the literature that when using planar images, kidney doses can be overestimated.

6. CONCLUSION

This study showed that the volumes of the organs specific to the patient can be calculated optimally instead of dosimetric calculation from planar images which is a traditional method and all the impressive factors can be evaluated by making corrections. Still widely used in planar imaging. 3D dosimetric studies based on SPECT/CT that clinically, is becoming widespread. It is preferred because of the acceleration of protocols. Factors limiting accuracy such as overlap of organs, back-ground activity, and lack of 3D knowledge are limiting.

^{177}Lu dosimetry was performed by quantitative imaging and it was decided to use in clinical routine. For none of the patients, cumulative doses were not exceeded 23 Gy. It is observed that renal doses were different for each patient. In addition it is observed that renal doses were different for the same patient's different treatments. Dosimetric calculations should be performed specific to the patient and the treatment. The extra kidney doses that patients were exposed due to CT scans were negligible when compared to the doses exposed due to treatment. By using SPECT/CT imaging in all time periods, renal doses can be determined more accurately. According to this work higher activities may be administered to patients for more effective treatment results.

REFERENCES

1. Hohberg M, Eschner W, Schmidt M, et al. Lacrimal Glands May Represent Organs at Risk for Radionuclide Therapy of Prostate Cancer with 177 Lu DKFZ-PSMA-617. Mol Imaging Biol. 2016;18(3):437-445. doi:10.1007/s11307-016-0942-0

2. Emami B. Tolerance of Normal Tissue to Therapeutic Radiation. Reports Radiother Oncol. 2013;1(1):36-48. doi:10.1016/0360-3016(91)90171-Y

3. Bodei L, Cremonesi M, Ferrari M, et al. Long-term evaluation of renal toxicity after peptide receptor radionuclide therapy with 90Y-DOTATOC and 177Lu-DOTATATE: the role of associated risk factors. Eur J Nucl Med Mol Imaging. 2008;35(10):1847-1856. doi:10.1007/s00259-008-0778-1

4. Kabasakal L, Toklu T, Yeyin N, et al. Lu-177-PSMA-617 Prostate-Specific Membrane Antigen Inhibitor Therapy in Patients with Castration-Resistant Prostate Cancer: Stability, Bio-distribution and Dosimetry. Malecular Imaging Radionucl Ther. 2017;26(2):62-68. doi:10.4274/mirt.08760

5. Siegel J a, Thomas SR, Stubbs JB, et al. MIRD pamphlet no. 16: Techniques for quantitative radiopharmaceutical biodistribution data acquisition and analysis for use in human radiation dose estimates. J Nucl Med. 1999;40(2):37S-61S. doi:10025848

6. Simon R. Cherry. Physics in Nuclear Medicine. Vol 67. 4th ed.; 2007.

7. Irim, G. Master of thesis Yeditepe Universit, Simulation of gamma camera in Yeditepe University Hospital with GATE 2013

8. Yuni K. D, MIRD Pamphlet No. 23: Quantitative SPECT for Patient-Specific 3-Dimensional Dosimetry in Internal Radionuclide Therapy. 2012

9. Wessels BW. Radiopharmaceutical Dosimetry Professor of Radiation Oncology Case Western Reserve University. https://www.aapm.org/meetings/2001AM/pdf/7196-9326.pdf.

10. Beauregard JM, Hofman MS, Pereira JM, Eu P, Hicks RJ. Quantitative \n 177Lu SPECT (QSPECT) imaging using a commercially available SPECT/CT system. Cancer Imaging. 2011;11(1):56-66. doi:10.1102/1470-7330.2011.0012

11. De Nijs R, Lagerburg V, Klausen TL, Holm S. Improving quantitative dosimetry in 177Lu-DOTATATE SPECT by energy window-based scatter corrections. Nucl Med Commun. 2014;35(5):522-533. doi:10.1097/MNM.0000000000000079

12. Madsen M. Quantitative Analysis in Nuclear Medicine Imaging. Vol 34.; 2007. doi:10.1118/1.2716416

13. Essential Medical Notes. 2014.

14. Zeintl J, Vija AH, Yahil A, Hornegger J, Kuwert T. Quantitative Accuracy of Clinical 99mTc SPECT/CT Using Ordered-Subset Expectation Maximization with 3-Dimensional Resolution Recovery, Attenuation, and Scatter Correction. J Nucl Med. 2010;51(6):921-928. doi:10.2967/jnumed.109.071571

15. Camanzi B. Joint CI-JAI advanced accelerator lecture series Imaging and detectors for medical physics Lecture 3 : X-ray imaging. 2016.

16. Patton JA, Turkington TG. SPECT/CT Physical Principles and Attenuation Correction. J Nucl Med Technol. 2008;36(1):1-10. doi:10.2967/jnmt.107.046839

17. Kism L, Fizik A, Dal A, Program F, Ii K, Dem M. FEN BİLİMLERİ ENSTİTÜSÜ. 2011.

18. Brown S, Bailey DL, Willowson K, Baldock C. Investigation of the relationship between linear attenuation coefficients and CT Hounsfield units using radionuclides for SPECT. Appl Radiat Isot. 2008;66(9):1206-1212. doi:10.1016/j.apradiso.2008.01.002

19. He B, Du Y, Segars WP, et al. Evaluation of quantitative imaging methods for

organ activity and residence time estimation using a population of phantoms having realistic variations in anatomy and uptake. Med Phys. 2009;36(2):612-619. doi:10.1118/1.3063156

20. Zeintl J, Vija AH, Yahil A, Hornegger J, Kuwert T. Quantitative Accuracy of Clinical 99mTc SPECT/CT Using Ordered-Subset Expectation Maximization with 3-Dimensional Resolution Recovery, Attenuation, and Scatter Correction. J Nucl Med. 2010;51(6):921-928. doi:10.2967/jnumed.109.071571

21. Dewaraja YK, Wilderman SJ, Ljungberg M, Koral KF, Zasadny K, Kaminiski MS. Accurate Dosimetry in 131 I Radionuclide Therapy Using Patient-Specific, 3-Dimensional Methods for SPECT Reconstruction and Absorbed Dose Calculation. Vol 46.; 2005.

22. Shcherbinin S, Piwowarska-Bilska H, Celler A, Birkenfeld B. Quantitative SPECT/CT reconstruction for 177Lu and 177Lu/ 90Y targeted radionuclide therapies. Phys Med Biol. 2012;57(18):5733-5747. doi:10.1088/0031-9155/57/18/5733

23. D'Arienzo M, Cazzato M, Cozzella ML, et al. Gamma camera calibration and validation for quantitative SPECT imaging with 177Lu. Appl Radiat Isot. 2016;112:156-164. doi:10.1016/j.apradiso.2016.03.007

24. Ljungberg M, Strand S-E. A Monte Carlo program for the simulation of scintillation camera characteristics. Comput Methods Programs Biomed. 1989;29(4):257-272. doi:10.1016/0169-2607(89)90111-9

25. Li T, Ao ECI, Lambert B, Brans B, Vandenberghe S, Mok GSP. Quantitative imaging for targeted radionuclide therapy dosimetry - Technical review. Theranostics. 2017;7(18):4551-4565. doi:10.7150/thno.19782

26. Date R, Date O, Document C. System Planar Sensitivity measurements. 2014:1-5.

27. IAEA. Chapter 18: Internal Dosimetry.; 2014. https://humanhealth.iaea.org/HHW/MedicalPhysics/elearning/Nuclear_Medicine

_Handbook_slides/Chapter_18._Internal_Dosimetry.pdf.

28. Ljungberg M, Celler A, Konijnenberg MW, Eckerman KF, Dewaraja YK, Sjogreen-Gleisner K. MIRD Pamphlet No. 26: Joint EANM/MIRD Guidelines for Quantitative 177Lu SPECT Applied for Dosimetry of Radiopharmaceutical Therapy. J Nucl Med. 2016;57(1):151-162. doi:10.2967/jnumed.115.159012

29. Feller PA, Sodd VJ, Kereiakes JG. Using the S Tables of MIRD Pamphlet 11. J Nucl Med. 1977;18(7):747. http://www.ncbi.nlm.nih.gov/pubmed/874160.

30. Siegel J a, Stabin MG. Absorbed fractions for electrons and beta particles in spheres of various sizes. J Nucl Med. 1994;35(1):152-156. http://www.ncbi.nlm.nih.gov/pubmed/8271037.

31. Zankl M, Becker J, Eckerman KF, Bolch WE, Behrens R. ICRP Symposium on Radiological Protection Dosimetry. 2016. http://www.icrp.org/docs/2015tokyo/03 - Zankl.pdf.

32. Kabasakal L, AbuQbeitah M, Aygün A, et al. Pre-therapeutic dosimetry of normal organs and tissues of 177Lu-PSMA-617 prostate-specific membrane antigen (PSMA) inhibitor in patients with castration-resistant prostate cancer. Eur J Nucl Med Mol Imaging. 2015;42(13):1976-1983. doi:10.1007/s00259-015-3125-3

33. Sandstrom M, Garske-Roman U, Granberg D, et al. Individualized Dosimetry of Kidney and Bone Marrow in Patients Undergoing 177Lu-DOTA-Octreotate Treatment. J Nucl Med. 2013;54(1):33-41. doi:10.2967/jnumed.112.107524

34. Zanzonico B, Ljungberg M. 3-Dimensional Dosimetry in Internal Radionuclide Therapy. 2012;i(8):1310-1325. doi:10.2967/jnumed.111.100123.MIRD

35. Stabin MG, Sparks RB, Crowe E. OLINDA/EXM: the second-generation personal computer software for internal dose assessment in nuclear medicine. J Nucl Med. 2005;46(6):1023-1027. doi:46/6/1023 [pii]

36. D'Arienzo M, Cazzato M, Cozzella ML, et al. Quantitative \n 177Lu

SPECT (QSPECT) imaging using a commercially available SPECT/CT system. Eur J Nucl Med Mol Imaging. 2012;35(1):772-786. doi:10.1088/0031-9155/57/18/5733

37. Coia L. Original Contribution IRRADIATION. 1991;21:109-122.

38. Emami B, Lyman J, Brown A, et al. Tolerance of normal tissue to therapeutic irradiation. IntJRadiat Oncol. 1991;21(1):109-122. doi:10.1016/0360-3016(91)90171-Y

39. Yadav MP, Ballal S, Tripathi M, et al. Post-therapeutic dosimetry of 177Lu-DKFZ-PSMA-617 in the treatment of patients with metastatic castration-resistant prostate cancer. Nucl Med Commun. 2017;38(1):91-98. doi:10.1097/MNM.0000000000000606

40. Yorke E. Biological Models in Radiation Therapy : Normal Tissue Complication Probability.

41. Ilan E, Sandstrom M, Wassberg C, et al. Dose Response of Pancreatic Neuroendocrine Tumors Treated with Peptide Receptor Radionuclide Therapy Using 177Lu-DOTATATE. J Nucl Med. 2015;56(2):177-182. doi:10.2967/jnumed.114.148437

42. Delker A, Fendler WP, Kratochwil C, et al. Dosimetry for 177Lu-DKFZ-PSMA-617: a new radiopharmaceutical for the treatment of metastatic prostate cancer. Eur J Nucl Med Mol Imaging. 2016;43(1):42-51. doi:10.1007/s00259-015-3174-7

43. Kratochwil C, Giesel FL, Stefanova M, et al. PSMA-Targeted Radionuclide Therapy of Metastatic Castration-Resistant Prostate Cancer with 177Lu-Labeled PSMA-617. J Nucl Med. 2016;57(8):1170-1176. doi:10.2967/jnumed.115.171397

44. Fendler WP, Reinhardt S, Ilhan H, et al. Preliminary experience with dosimetry, response and patient reported outcome after ^{177}Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer. Oncotarget. 2017;8(2):3581-3590. doi:10.18632/oncotarget.12240

APPENDIX A: CV

Özgeçmiş

Kişisel Bilgiler

Adı	GÜLÇİN	**Soyadı**	ÇELİK
Doğum Yeri	EDİRNE	**Doğum Tarihi**	09-06-1983
Uyruğu	T.C	**TC Kimlik No**	22967119052
E-mail	GİRİM@YEDİTEPE.EDU.TR	**Tel**	5375176573

Öğrenim Durumu

Derece	Alan	Mezun Olduğu Kurumun Adı	Mezuniyet Yılı
Doktora			
Yüksek Lisans	FİZİK	**YEDİTEPE ÜNİVERSİTESİ**	2013
Lisans	FİZİK	**ERCİYES ÜNİVERSİTESİ**	2007
Önlisans	BİYOMEDİKAL C. T.	**ERCİYES ÜNİVERSİTESİ**	2002
Lise	FEN BİLİMLERİ	**ARHAVİ LİSESİ**	2000

[#] Başarılmış birden fazla sınav varsa(KPDS, ÜDS, TOEFL; EELTS vs), tüm sonuçlar yazılmalıdır

Bildiği Yabancı Dilleri	Yabancı Dil Sınav Notu ([#])

İş Deneyimi (Sondan geçmişe doğru sıralayın)

Görevi	KURUM	Süre (Yıl - Yıl)
SORUMLU EEG-EMG TEKNİKERİ	YEDİTPE ÜNİVERSİTESİ HASTANESİ	2007-
		-

Bilgisayar Bilgisi

Program	Kullanma becerisi

*Çok iyi, iyi, orta, zayıf olarak değerlendirin

Bilimsel Çalışmaları

SCI, SSCI, AHCI indekslerine giren dergilerde yayınlanan makaleler

Diğer dergilerde yayınlanan makaleler

Uluslararası bilimsel toplantılarda sunulan ve bildiri kitabında (*Proceedings*) basılan bildiriler

APPENDIX B: Ethics Committee Report

Sayı : 37068608-6100-15- 1744 **19/09/2019**
Konu: Klinik Araştırmalar
Etik kurul Başvurusu hk.

İlgili Makama (Gülçin Çelik)

Yeditepe Üniversitesi Sağlık Fiziği Anabilim Dalı. Prof. Dr. Ş. İpek Karaaslan'ın sorumlu araştırmacı olduğu **"Patient – Specitif İnternal Dosimetry With Quantitative SPECT/CT in Lutetium– 177 PSMA Treatment Retrospectively "** isimli araştırma projesine ait Klinik Araştırmalar Etik Kurulu (KAEK) Başvuru Dosyası **(1730)** kayıt Numaralı KAEK Başvuru Dosyası),Yeditepe Üniversitesi Klinik Araştırmalar Etik Kurulu tarafından **18.09.2019** tarihli toplantıda incelenmiştir.

Kurul tarafından yapılan inceleme sonucu, yukarıdaki isimi belirtilen çalışmanın yapılmasının etik ve bilimsel açıdan uygun olduğuna karar verilmiştir (KAEK Karar No: 1091).

Prof. Dr. Turgay ÇELİK
Yeditepe Üniversitesi
Klinik Araştırmalar Etik Kurulu Başkanı