ESCOLA SUPERIOR DE TECNOLOGIA DA SAÚDE DE COIMBRA

Instituto Politécnico de Coimbra
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Radiotherapy Planning with PET/CT

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Mestrado em Ciências Nucleares Aplicadas na Saúde

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Dissertação

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Abstract

Radiation therapy planning has traditionally relied very heavily on CT imaging. However, Fluorodeoxyglucose Positron Emission Tomography (FDG PET), more specifically PET fused with Computed Tomography (PET/CT), is emerging as the standard of care for the staging, monitoring of response to therapy and detection of disease recurrence, for numerous malignancies. So that more and more radiation oncologists believe that target volume selection and delineation cannot be adequately performed without the use of PET/CT.

In order to perform high quality examinations, PET/CT imaging protocols used for radiation therapy planning must be rigorous and consistently applied, which is the technician's responsibility. However, when adapting the scanners for these examinations many difficulties appear, since the patient is immobilized and the use of FDG as a radiotracer may not be the appropriate choice for the study of some malignancies. But, there is a promising future for PET/CT in treatment planning, with the development of radionuclides and biomarkers and of new treatment paradigms.

This dissertation is written for technicians and from a technician's point of view, covering the basis of Radiotherapy and Nuclear Medicine and addressing various aspects regarding PET/CT examinations for radiotherapy planning. Exploring the challenges the professionals face during these examinations, this dissertation provides a solid foundation for those who want to learn more about this newly-discovered side of Nuclear Medicine and reflect about what needs to be changed in order for it to become the technique of choice for radiation treatment planning.

Acknowledgments

First and foremost, I would like to express my special appreciation to my supervisor, Professor Francisco Alves, and my co-supervisor, Professor Stefano Fanti, for accepting my invitation and trusting my work to the point of wanting to be involved in this dissertation. My warm thanks for their kind words, support and for always being available for everything I needed.

I would also like to express my gratitude to my internship supervisor, Marco Maccagnani, for his constant help, guidance and dedicated involvement throughout all of the stages of this work.

In September of 2013, I went to Bologna for a six month internship at the Nuclear Medicine Department of the Sant'Orsola-Malpighi Polyclinic. My time at the department was highly productive and working with those professionals was an extraordinary experience. Almost all of the information presented in this dissertation is owed to my time at both the Nuclear Medicine Department as well as several visits to the Radiotherapy Department. I express my warm thanks to all of the physicians and technicians who kindly assisted me and very patiently answered all of my questions.

I also thank the Nuclear Medicine and Radiotherapy Departments of the Sant'Orsola-Malpighi Polyclinic for giving me consent to include pictures and hospital data as a part of this dissertation.

Getting through it required more than academic support, none of this could have happened without my family. Words cannot express how grateful I am to my parents, grandparents and sister for all the sacrifices they made on my behalf and for encouraging me to strive towards my goal.

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Abbreviations

ALARA - As Low As Reasonably Achievable

CT - Computed Tomography

CTV - Clinical Target Volume

DNA - Deoxyribose Nucleic Acid

DRR - Digitally Reconstructed Radiography

FDG - Fluorodeoxyglucose

GTV - Gross Tumour Volume

Gy - Gray

HDR - High-dose-rate brachytherapy

IGRT - Image Guided Radiation Therapy

IMPT - Intensity Modulated Proton Therapy

IMRT – Intensity Modulated Radiation Therapy

IORT - Intraoperative Radiation Therapy

LDR - Interstitial low-dose-rate brachytherapy

Linac - Linear Particle Accelerator

MIP - Maximum Intensity Projection

MRI - Magnetic Resonance Imaging

PET - Positron Emission Tomography

PTV - Planning Target Volume

RT - Radiotherapy

RTP - Radiotherapy Treatment Planning

SBRT - Stereotactic Body Radiation Therapy

SPECT - Single-photon emission computed tomography

SRS - Stereotactic Radiosurgery

SRT - Stereotactic Radiation Therapy

SUV - Standardized Uptake Value

TOF-PET - Time-of-flight Positron Emission Tomography

TPS - Treatment Planning System

3D-CRT - Three-dimensional Conformal Radiation Therapy

4DCT - Four-dimensional Computed Tomography

Introduction

Radiotherapy planning is a complex process, preparing the treatment of a neoplasm; done with the objective of eradicating the neoplastic tissue while preserving normal tissue function and with reduced radiation induced toxicity . In order to be successful, a correct spatial visualization of the tumour and differentiation from the surrounding healthy organs is crucial; with diagnostic imaging techniques playing a key role in this first step to the treatment (1).

Computed Tomography (CT) has been for many years the gold standard in radiotherapy treatment planning, for target volume selection and delimitation, as well as for dose calculation, by providing anatomical and intrinsic information on the electronic densities of tissues. However, CT has several limitations, namely the lack of contrast resolution for normal soft-tissue and tumour extent, causing the tumour not to be seen if it has a similar density to the surrounding tissue. Although it continues to be the base for dose distribution calculation, fusing other modalities with the CT scan has improved significantly the treatment planning (2).

Positron Emission Tomography (PET) due to its capability of showing highly active neoplastic tissues, giving metabolic information, allows the study of intratumoral biology. This type of examination can serve as a base for an exact identification of the target volume and to adapt the dose according to the biological characteristics of the tumour. Furthermore, metastases can be detected during a PET scan, which involves a complete change in the treatment intentions (1).

However, PET images have significantly lower resolution when compared to CT or Magnetic Resonance Imaging (MRI), which can lead to inaccurate delineation of the neoplasm because of the poor anatomical detail provided; this being one of the main reasons why PET cannot be used by itself for radiotherapy planning, since dose calculation requires an accurate definition of the tumour volume and surrounding structures (3).

The association of the two previous techniques (PET/CT) has given proves of excellence in radiotherapy planning. By combining CT and PET data, structural and functional information is provided with only one examination, allowing the evaluation of cancer distribution and physical tumour size, as well as giving indications about metabolic activity levels (1).

18F-Fluorodeoxyglucose (^{18}F-FDG) is the most used radiopharmaceutical in PET, as well as for treatment planning, but others may be more desirable in some situations, such as tumours close to inflammatory areas or infectious conditions, or when studding tissues where there is an uptake of FDG in normal circumstances (1).

Despite of all the positive clinical implications that PET/CT brought to radiotherapy planning in a medical point of view, nuclear medicine technicians face several difficulties when performing the examination; due to the fact that PET equipments are not adapted to the use of immobilization devices, that are essential for treatment planning, as the patient's position during the PET/CT scan must be the exact same as in the treatment unit.

One of the most evident problems in radiotherapy planning with PET/CT is that the gantry is narrow, but the technicians can be confronted with many others.

In this dissertation we will focus on the nuclear medicine technician point of view in radiotherapy planning. The bases of radiotherapy will be explained, along with the differences in the hardware for a PET/CT scan for radiotherapy planning; the protocol of the examination and the problems faced, with cases as example.

Chapter I

Basic Notions about Radiotherapy

Radiotherapy *(RT)* is a medical treatment modality that delivers prescribed doses of ionizing radiation to neoplasms, mostly malignant and solid, with the intention of curing the disease locally and the improvement or prolongation of the patient's life, whilst preserving healthy tissues from the effects of radiation (2). The success of the treatment is dependent on the radiosensitivity of the tumour but also on the tolerance of the surrounding normal tissue (3).

The main objective of radiation therapy is to eradicate the tumour by inducing neoplastic cells mortality, since the deposition of energy damages the nuclear deoxyribose nucleic acid (DNA), causing an irreversible loss of their reproductive integrity and eventual death (Figure 1) (3). For this reason, higher doses of radiation can lead to better tumour control, but can also damage normal tissues, causing unwanted side effects.

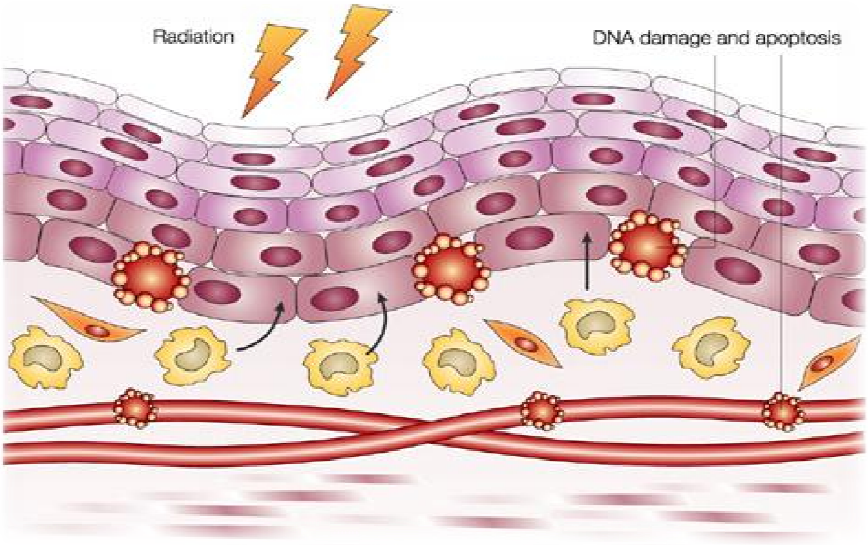


Figure 1 - Radiation induced damage to genomic DNA, thought to be the most important subcellular target molecule (4).

The performance of this clinical modality requires planning and dependents on many factors such as the type of tumour, its location and regional extent, anatomical area of involvement and the geometrical accuracy with which a calculated radiation dose is delivered (3).

When referring to dose in RT, the utilized unit is Gray (Gy). One Gray represents the absorption of one Joule of energy, in the form of ionizing radiation, divided by one Kilogram of matter.

In most cases, RT isn't the only therapeutic intervention that patients are submitted to; but a combination with surgery and radio-sensitising agents, such as chemotherapy and targeted therapy. Radiotherapy can be used as a sole treatment modality for locally advanced tumours, non-resectable, for inoperable patients and for cases where a non-surgical approach is preferred (3,5).

Depending on the condition of the patient, radiation therapy can be performed with different clinical intents:

- **Curative or Radical –** As a definite treatment, usually in association with systemic therapy (concurrent or sequential) and combined with surgery (preoperative, postoperative, intra-operative). High doses are required in these cases, normally above 60 Gy (lymphomas are the exception, normally between 20-50 Gy) (6);
- **Adjuvant –** Performed after an operation, to prevent cancer from recurring. Intermediate doses are used in this situation, around 30-50 Gy (6);
- **Palliative –** To relieve/treat symptoms caused by advanced tumours, such as pain, difficulties while swallowing or breathing and bowel problems. Low doses are effective in this approach, usually not more than 30 Gy (7).

All patients diagnosed with cancer, before starting the treatment with ionizing radiation, have their clinical case evaluated by a physician that has to, among the many treatment options available, decide the best for the patient's condition.

1.1. Treatment Delivery

Different forms of radiation can be used in radiotherapy, such as photons, electrons, protons, neutrons and light ions. For cancer treatment, photons and electrons are more commonly used (5). Electron radiation is mostly applied to superficial tumours, as they produce a higher dose on the skin but exhibit a falloff after a few centimetres; while proton radiation is used for deep-seated tumours (2).

The most frequently used equipments to irradiate tumours are medical accelerators for photons and electrons, named ***linear particle accelerators*** (linacs) that deliver high energy radiation.

A beam of electrons is accelerated through an accelerator tube using electromagnetic waves, being their energy increased from the keV to the MeV range. After, these electrons collide with a high-density target, producing X-rays (Bremsstrahlung effect).

The standard radiotherapy equipment is a **megavoltage linear accelerator**, with an energy range from 4 to 20 MeV (Figure 2). Most of these units also have electron-beam capacities, by moving the target away from the path of the beam (2).

Figure 2 - Patient being treated with a linear particle accelerator (6).

Other types of equipments, called **orthovoltage units** generate X-rays from 125 to 500 keV and are used to treat superficial lesions, as the maximum dose is found on the surface of the patient (2).

In other kinds of therapies, like **proton therapy**, the particle beam is produced in a cyclotron, which increases the cost. One of the advantages of this treatment modality is that the majority of the absorbed dose is deposited at a specific depth, ensuring that the dose received by healthy tissues is overall low, but it's very sensitive to movement and set-up uncertainty (5).

1.1.1 Radiotherapy Techniques

Treatments using radiation can be divided into three categories, depending on the way the radiation is administered.

Conformal therapy

Conformal radiation therapy is a treatment modality based on the geometric shaping of the radiation beam to match it to the contour of the tumour (2). Nowadays, it has many variations:

- External radiation therapy
- Three-dimensional conformal radiation therapy
- Intensity Modulation radiation therapy
  - Image guided radiation therapy
  - Dynamic conformal therapy
  - Serial Tomotherapy
- Intensity modulation proton therapy
- Stereotactic radiosurgery
  - Fractionated stereotactic radiotherapy
  - Stereotactic body radiation therapy

External radiation therapy or Teletherapy is the most used form of RT, being the golden standard for radical radiotherapy. As the name suggests, a radiation beam is administered externally to the patient, 80 to 100 cm away, with a high enough energy to penetrate to the depth of the neoplasm. The beam can be produced by an equipment containing a radioactive source emitting radiation (cobalt-60) or a linear accelerator (5). When produced by a linac, the shape and intensity of the beam can be modified or collimated by a variety of resources (2).

Three-dimensional conformal radiation therapy (3D-CRT) uses an array of beams individually arranged to conform to the shape of the volume to be irradiated, delivering the dose from several directions. The goal is to have a uniform dose distribution throughout the target and as conformal as possible to the shape of the tumour, respecting dose constraints to normal tissues (8).

The treatment is previously planned using images from diagnostic examinations and software that precisely maps the localization of the neoplasm in three dimensions (8). This modality is more useful for tumours that are close to important organs and structures (3).

Therapeutic interventions with photon beams or particles, such as protons, can be used in this way.

A disadvantage of this method is that if the full extent of the tumour was not well visualized and studied, which in some cases can be very difficult, it will not be treated (7). Also, the target needs to have a relatively simple shape for the 3D-CRT to conform well and a large number of beams are required (8).

If the neoplasm has a concave shape, wrapped around a sensitive structure, this treatment modality cannot give a satisfactory result, as the angles needed to avoid/minimize the dose to the normal tissue can be impossible to achieve clinically (8).

Intensity Modulated Radiation Therapy

IMRT is an advanced form of conformal therapy, that besides shaping the array of beams to the contour of the neoplasm, also adapts the intensity of the radiation beams (3). This improvement is especially important when there is not a clear separation between the target and the surrounding normal tissues (2).

The combination of multiple intensity-modulated fields, arriving from different beam directions, allows a better control over the dose, maximizing the dose delivered to the tumour while decreasing the values in adjacent sensitive tissues (7). With this method, dose constraints can be designated by the physicians (3).

To achieve a uniform dose distribution around the tumour and a minimal exposure of the surrounding normal tissues, the fluence of radiation, when exiting the accelerator, can be altered by either modulating the intensity of the beam during its path through the linear accelerator or by using multileaf collimators; improving significantly the risk-benefit ratio (2).

Multileaf collimators are eighty or more individual collimators ("leaves") located at the head of the linear particle accelerator, that can be adjusted to the shape of the target (Figure 3) (2).

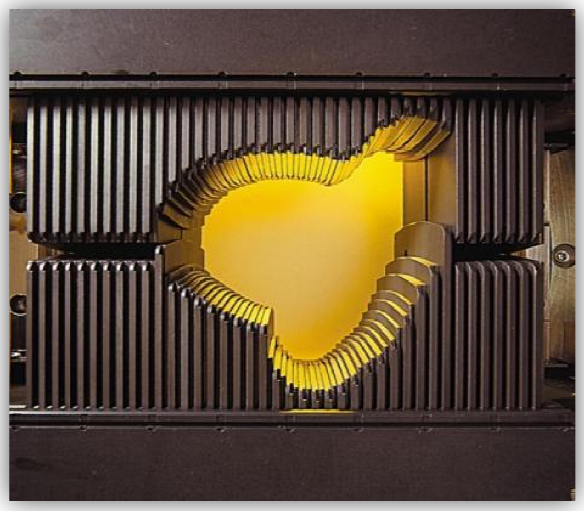


Figure 3 - Multileaf collimator: Varian's 120- leaf (9).

Some linear accelerators have an integrated automatic system that uses high-resolution X-rays to acquire contrasting images of the tumour and adjacent soft tissue, allowing physicians to target the neoplasm more accurately during treatment. This variation is called **Image Guided Radiation Therapy (IGRT)**.

Before, a larger area would have to be treated to compensate for any movement, exposing normal tissue to radiation. Therefore, IMRT improves the precision in the irradiation of the target and IGRT improves the delivery accuracy, decreasing the volume of healthy tissue being irradiated (3).

Because of the precision of this modality, one of the disadvantages is the stringent patient set-up and immobilization and the fact that, by using a higher total dose, the risk of developing new tumours is increased (3).

Dynamic conformal therapy is another type of IMRT, in which the collimators conform to the volume to be irradiated while the treatment unit is rotating around the patient, being the radiation delivery completely controlled by computer (2).

Serial Tomotherapy is another method of IMRT, in which the accelerator contains small multileaf collimators forming a "slit" of radiation, typically 2 x 20 cm. In this modality, the treatment is given through a modified CT ring, not a linear accelerator, while performing simultaneously a conventional diagnostic CT scan (Figure 4). While the gantry is rotating through an entire arch around the patient, the collimators are driven in and out of the field, modulating the intensity of the beam. The treatment is extended to the next arches by advancing the treatment couch a few millimetres until the whole area has been irradiated (2).

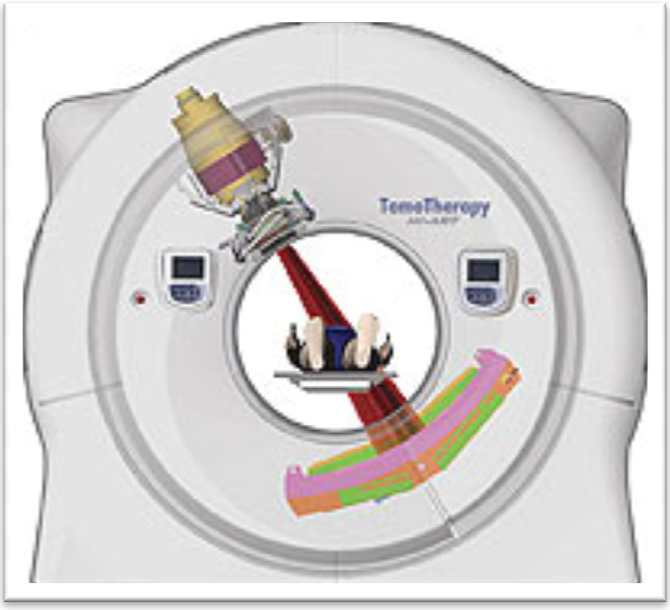


Figure 4 - To perform Tomotherapy an x-band accelerator is mounted on a gantry of a helical CT scanner (10).

A new approach, to ensure that the true extent of the tumour is being treated, uses small implants placed into the area, that send out to the RT equipment radio waves, helping to deliver maximum radiation directly to the tumour, as the slightest tumour movement is detected. This sensor system, named **Calyso®**, also lets the machine compensate for movement, for example respiratory movements, but it hasn't given real proofs yet to be a better option than other treatment modality (7).

Intensity Modulated Proton Therapy

IMPT is a form of Intensity Modulated Therapy applied to proton beams, instead of photon beams, and is commonly used when the tumour is near critical structures, such as eyes, brain or spine (7).

Stereotactic Radiosurgery

SRS is a treatment technique that also uses multiple radiation beams converging in three dimensions, precisely focusing on a small (usually about 3 cm of diameter), well-defined volume to be treated. This modality delivers a high dose, using specially designed collimators attached to a linear accelerator. Multiple stationary beams or several rotational arches, concentrate the radiation dose on the lesion, while sparing adjacent normal tissue (2).

The dose can be delivered in just one fraction or spread out over several doses, being called in this case **Fractionated Stereotactic Radiotherapy** (7).

The ***Gamma Knife*** works by this process. It is a neurosurgery tool that treats by administering high-intensity cobalt radiation therapy, concentrated over a small volume. This device normally contains two hundred and one low-intensity cobalt-60 sources, of 30 Curies (approximately), placed in a circular array in a heavily shielded assembly (Figure 5). The cobalt sources meet at one single focal point, accurate to tenths of a millimetre (11).

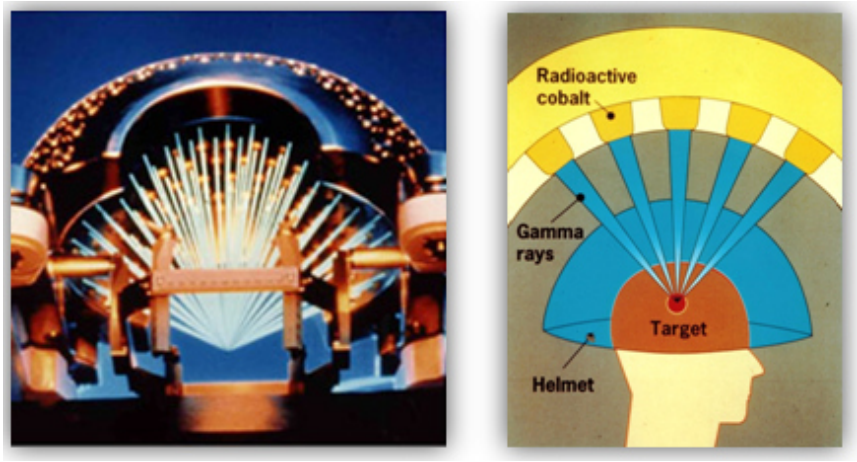


Figure 5 - The irradiation unit (on the left) and a detailed schematic view (right) (11).

As a preparation for the treatment, a stereotactic frame (Figure 6) is surgically fixed to the patient's skull to provide an exact reference with the aim of pinpointing the target area, with the help of imaging procedures. This is necessary to achieve accuracy down to fractions of a millimetre.

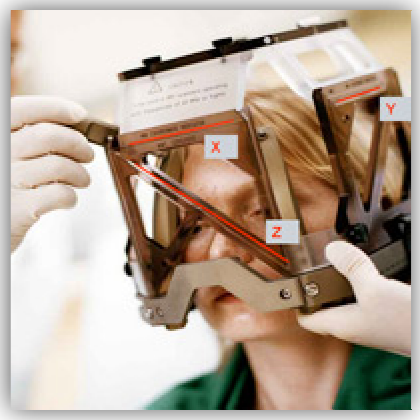


Figure 6 - Stereotactic frame (11).

A CT or MRI scan is performed and the images are sent to the Gamma Knife's planning computer system to calculate the exact correlation between the target lesions and the frame (3). Once the exact localization of the tumour is mapped, narrow radiation beams are focused at the target from hundreds of different angles for a short period of time (Figure 7) (7). An ablative dose of radiation is directed to the tumour in, usually, one treatment session, with minimum adverse effects on the surrounding tissue (11).

Figure 7 - Patient positioned for the treatment, with a detailed visualization of the cobalt sources (11).

A more advanced technique, named ***Robotic Radiosurgery*** or ***Cyber Knife*** is a frameless robotic radiosurgery, image guided in real time and controlled by computer robotics; which delivers a very high dose to a precisely defined target, in one up to five

fractions. The main advantage of this treatment is that it can be completed in one week and it's painless, but the high cost is a drawback (3).

Stereotactic Radiosurgery can be used for a variety of problems, including arteriovenous malformations, benign brain tumours; malignant tumours that started in the brain or spread to it, or functional problems (trigeminal neuralgia) (2,3).

Stereotactic Body Radiation Therapy (SBRT) is a variant used to describe the technique when it's used for tumours in other parts of the body, such as the spine, liver, pancreas, kidney, lung, or prostate (7).

Intraoperative Radiation Therapy

IORT is a therapeutic technique that irradiates the neoplasm during surgery. The dose can be delivered externally or internally and this modality is frequently complemented with sessions of External Radiation Therapy, performed previously or after the operation. It is mostly used for abdominal or pelvic tumours that can't be fully removed and for tumours that have a tendency to reappear after treatment. The cancerous mass is removed as much as possible and, after, a high dose of radiation is directed to the tumour site. Because the radiation therapy is performed during surgery, the adjacent normal tissues can be taken out of the beam's path and protected; so this technique has the advantage of reducing the exposure of healthy tissues (7).

Brachytherapy

Brachytherapy is a form of radiotherapy in which the radiation source is in direct contact with the neoplasm, inside it or adjacent (2,5).

This treatment is performed by using either temporary or permanent implants; the difference is that the ones that are temporary normally have longer half-lives and

higher energies than the permanent implants. The temporary radiation sources are inserted into catheters that are placed on the tumour during an operation.

In this therapy, dose distribution is almost entirely dependent on the inverse square law, since the source is normally within the tumour volume (2).

Brachytherapy can be divided into two categories, according to the dose that is given during treatment. **Interstitial low-dose-rate brachytherapy (LDR)** is frequently used for tumours in the oral cavity, oropharynx and sarcoma; as well as in gynaecology (in which are used temporary insertions) and prostate cancer (using permanent seed implants) (Figure 8) (2,8). **High-dose-rate brachytherapy (HDR)** is administered using remote afterloading techniques (2).

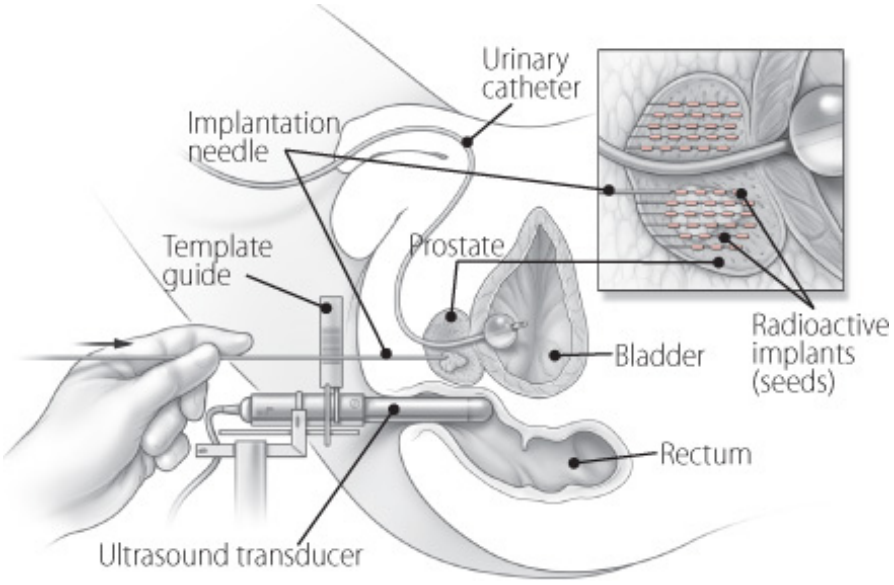


Figure 8 - Scheme demonstrating the implantation of seeds into the prostate using Brachytherapy (12).

For LDR, the radiation source is left in place up to seven days and in HDR for about 10 to 20 minutes at a time (7).

This clinical intervention has the advantage that the dose outside of the tumour can be kept very low, usually around 100 times less than that used in external beam radiation, with penetration depths measured in millimetres rather than centimetres. However,

accessing the tumour, in order to place the radiation source, may be a difficult procedure (5).

Systemic Radioisotope Therapy (Metabolic Therapy)

Systemic Radioisotope Therapy is different from the other techniques, in the sense that it involves the injection of radioisotopes with certain chemical proprieties to study a specific gland; or the use of isotopes attached to particular molecules or antibodies to target the affected areas (5).

Radio-labelled antibodies are employed in the treatment of some non-Hodgkin lymphomas, especially when there is no response to other treatments (7).

Some examples of radioisotopes used in this type of therapy are:

Yttrium-90 (90Y) is a pure beta emitter and the principal radionuclide used in non-invasive therapies, such as Peptide Receptor Radionuclide Therapy (PRRT) for the treatment of neuroendocrine tumours, Radioimmunotherapy (RIT) in non-Hodgkin's lymphomas, Transarterial Radioembolization Therapy (TARET) in unresectable hepatocellular carcinoma and in the treatment of liver metastatic colorectal cancer (mCRC) (13).

Zevalin (*Ibritumomab tiuxetan*), is a monoclonal antibody radioimmunotherapy treatment used for non-Hodgkin's lymphoma, that conjugates an antibody (*ibritumomab*) and a radioactive isotope (yttrium-90 or indium-111) added to a linker (*tiuxetan*) (14).

Radioactive iodine (Iodine-131) can be used with the objective of destroying the thyroid gland and thyroid cancer, without major side effects on the rest of the organism. It can also be of great value to treat some types of thyroid cancer that spread to lymph nodes and other organs (7).

1.2. Treatment Planning

It is understandable, after learning about the existent treatment techniques, that planning is an essential step when dealing with high doses of radiation, in order to achieve our goal of locally controlling the neoplasm, minimizing possible damages on healthy tissues.

Therefore, after the diagnosis, the patient has to go through several phases until the start of an external beam radiotherapy treatment:

1.2.1. Evaluation of the clinical case

Once aware of the need to perform radiation therapy, the patient has an appointment where the Radiation Oncologist, based on the documentation, evaluates the feasibility, objectives and type of treatment more adequate to the case (15).

The clinical data is carefully analysed in order to clearly define the pathological conditions: if the tumour is confined; possible infiltration of the regional lymph nodes or existence of metastases. The potential risk of developing complications related with the local progression of the neoplasm is also evaluated, as well as eventual contraindications to the treatment with ionizing radiation (16).

1.2.2. Pre-treatment studies

The next step is an appointment in the Radiotherapy Department, where the technician and physician work together to establish the type of immobilizer to be used and perform an imaging study, which will be the base for the definition of the target region.

1.2.2.1. Immobilization of the patient

The use of immobilization devices is imperative during radiation therapy, in order to ensure that the position of the patient is reproducible during every treatment session and that the patient is as comfortable as possible on the couch of the equipment, decreasing the risk of movement due to discomfort and guaranteeing that the dose is delivered precisely.

These tools should be stable, secure; don't create image artefacts; be adaptable to the couch of the CT scanner and linac; not modify the dose distribution in the patient and help to leave anatomical parts not of interest out of the radiation field. Also, they should have the right dimensions to not obstruct the inside of the gantry during the planning process and treatment.

Immobilization devices can be divided into categories, according to their capability of adapting or not to the physiognomy of the patient.

Custom molds

- *Thermoplastic Masks*

Head and neck immobilizers are masks made out of a thermoplastic material, that after being immersed in water heated up to 70-80 degrees Celsius, for a couple of minutes, becomes mouldable. Once dried, while being placed and carefully adjusted to the region, will conserve its shape and immobilize the treatment area.

There are two types of masks:

Head-only Thermoplastic Mask

- With this type of mask three reference points are established on the head;
- It is used for palliative treatments on the level of the encephalon.

Head, neck and shoulder Thermoplastic Mask

- This mask allows the marking of five points for the treatment of the head-neck region (with IMRT), mediastine or cervical spine.

The foundation for this immobilization device is a base plate, fixated to the couch top, where the mask is attached using pins (Figures 9 & 10).

Figure 9 - Carbon fiber base plate for head-only masks and an open 3-point mask, where the fixating pins can be visualized (17).

Figure 10 - Carbon fiber base plate for head, neck and shoulder fixation and a 5-point open mask with the fixating pins (17).

One of the advantages is that, with this method, it's unnecessary to tattoo the skin since the marking is done with a permanent pen on the mask. However, because it is too restraining, patients that suffer with claustrophobia may feel uncomfortable.

Also, a headrest is necessary to provide enhanced positioning accuracy, as well as comfort to the patient. There are several options for headrests, with different colours; being selected the one that puts the patient in the desired position, in the most comfortable manner (Table 1).

Red cushion - Positions the head with the neck straight, to prevent anterior curving of the spinal cord in the treatment field;
Black cushion - Used for neck tumours, and has the same curvature as the red one, but it's extended to move the oral cavity and mandible out of the radiation field or to obtain a cranial field border, which avoids the orbit (ear and parotid treatment);
Yellow and white cushions - Enable the chin to be more or less extended to move the oral cavity and mandible out of the radiation field or, as the black cushion, to obtain a cranial field border;
Blue cushion - Allows the chin to be fixed towards the breast.

Table 1 – Examples of headrests and their specific functions (17).

- *Vac-Lok*

Vaccum bags are filled with small polystyrene beads that mold to the patient's shape when emptied; creating a rigid, comfortable cradle around the body (Figure 11) (18). They are reusable, radiotranslucent and available with treatment windows to avoid build-up.

The Vac-lok cushions are important instruments in the treatment of the rectum, abdomen or chest.

Figure 11 - Vac-lok cushion placed on top of the linac's couch (17).

- *Foam cradles*

This type of chemical immobilizer, known as beta-cradle, consists on a polystyrene support that is filled with a polyurethane foam, that is prepared by mixing two chemical substances, which, by an exothermic reaction, heat up and expand. When warm, the foam can be manipulated and adapted to the shape of the body. Then, as it starts cooling, it solidifies (Figure 12) (16).

They have the advantage of being restraining, while allowing the patient to be relaxed; however, they have a high cost and release toxic vapours.

Foam cradles can be used for breast, rectum or limbs.

Figure 12 - Beta-cradle made to immobilize a leg.

Mechanical immobilizers

❖ Wing Board

The Wing Board is a support system made out of a rigid plastic, with two side flaps to rest the arms, a headrest (that can be changed) and an adaptable support for the patient to hold on to, that can be modified for the comfort of the patient. It has a graduated scale that is a reference for the positioning in every treatment session (Figure 13).

Figure 13 - Extended Wing Board (17).

❖ Combifix

The Combifix is a base plate that is placed on the couchtop and combines two cushions, the Feetfix and the Kneefix (Figure 14). The Kneefix cushion contributes to better stability in the supine position and provides comfort. The Feetfix is a universal patient support cushion for radiotherapy and diagnostic procedures and has been designed to provide comfortable positioning with enhanced immobilization (17).

This device is mostly used for the treatment of the prostate and female pelvis and can be combined with other immobilization devices to treat the abdominal region (15).

Figure 14 – Combifix and possible positioning of its components (17).

- *Bellyboard*

The Bellyboard is a thick mattress used to support the patient when positioned in prone. It was fabricated with the aim of reducing the volume of small bowel irradiated in patients undergoing treatments for the pelvic region. To increase comfort, its lower portion was adapted to support the thighs (Figure 15) (17).

Clear scales on both sides of the equipment, allow an easy verification of the longitudinal position of the patient.

Figure 15 – Bellyboard (17).

As seen on Figure 15, the Bellyboard has two apertures:

- The caudal aperture (1) is for the positioning of the pubic bone;
- The central part (2) is for the compression of the small bowel in order to push it cranially, towards the major aperture (3). The pubic bone must be positioned in the caudal aperture for an optimal reduction of the small bowel volume (17).

1.2.2.2. *Imaging studies*

The first step of this appointment is the immobilization and positioning of the patient, in order to perform an imaging examination, which will be the base for the specification of the area to be irradiated (Figure 16).

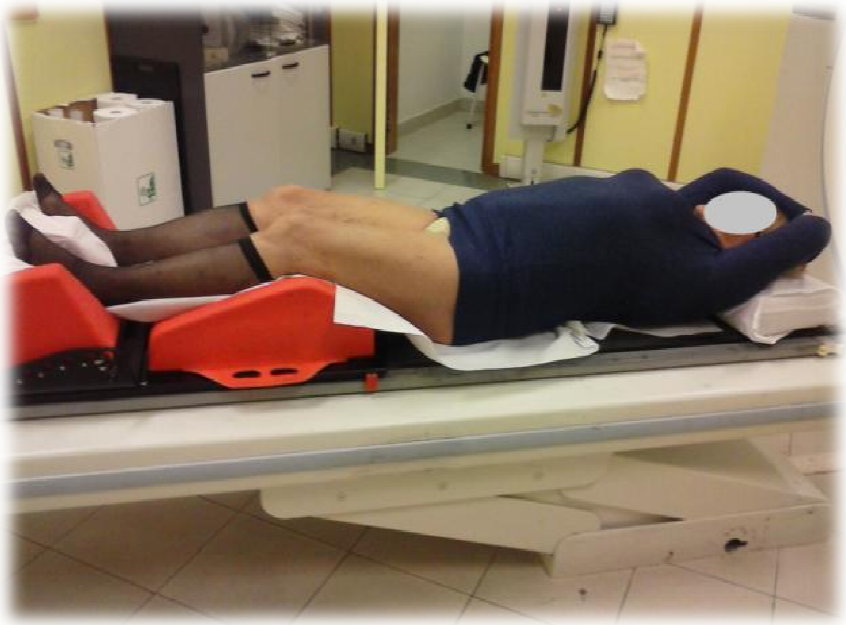


Figure 16 - Patient positioned and immobilized with a Combifix, in the CT scanner for treatment planning.

Computed Tomography is the imaging technique of choice for the majority of cases and it's commonly available in Radiotherapy Departments.

CT was chosen as a standard procedure for radiotherapy planning, essentially for four reasons:

1. Gives an accurate evaluation of the patient's anatomy, allowing a precise identification of the structures of interest, target volume and critical organs;
2. Properly calibrated and free of artefacts, CT images provide accurate data regarding the electronic density of the tissues, necessary for a correct distribution of the dose that takes into account the shape and the presence of inhomogeneities;
3. Allows 3D reconstruction of the images;
4. Allows the creation of a DRR (Digitally Reconstructed Radiography) that has the same geometric perspective of a port film taken in the treatment unit (images that are generated by the radiotherapy beam) (16).

Another positive aspect, is the possibility of combining CT images, that aren't good to study soft tissue and don't provide morphologic or functional information, with other imaging techniques (such as MRI or PET) able to provide additional and complementary information for precise definition of the target and surrounding healthy tissues.

It's the Radiation Oncologist who decides which imaging technique is the most adequate to study the target area with satisfactory details, aiming the elaboration of the best treatment plan possible for that specific case.

Generally, to plan the treatment for breast or prostate, the physician opts for just a CT scan. However, in cases where the target is the head and/or neck, pancreas, gynaecologic or thorax (mediastinum), PET/CT is the technique that they normally prefer. The patient still has this first appointment in the Radiotherapy Department for the preparation and trial of the immobilization devices, as well as an explanation regarding the next steps; but then he is taken to the Nuclear Medicine Department to be injected with a radiopharmaceutical and perform a PET/CT scan.

The CT scan performed is very similar and both equipments, the CT scanner existent in the Radiotherapy Department and the PET/CT scanner used for Radiotherapy planning,

had both to be adapted to satisfy the demands of this kind of study (Figure 17). Further on, these adjustments will be explained in detail.

Figure 17 - Better view of the CT scanner used for Radiotherapy planning.

Basically, the physicians that decide to plan the treatment just using the images acquired with the CT scanner available in the Radiotherapy Department, will study the anatomic region to be treated; identify the target volume and select a slice that will be used as a reference for the establishment of coordinates, that will allow the posterior definition of the final isocentre[1]. These coordinates, given by the localization of the external lasers, are marked on the patient's skin.

The images acquired during this first step of the planning, by CT or another imaging technique, are, after being worked on and evaluated by the Radiotherapist, sent to the Health Physics Department that will define the final isocentre, establish the dose levels to be administered and all of the parameters regarding the treatment method.

[1] The isocentre refers to the point that will be the centre of gantry rotation of the treatment machine. The gantry of the linear accelerator can rotate 360° around this designated point. An isocentric technique is based on the fact that the patient and/or isocentre are at the same position for all the treatment fields.

At the end of this appointment is created a personal file for each patient, where will be kept record of the acquired data, adopted positioning and immobilization; as well as future procedures done in the department.

1.2.3. *Contouring*

The Radiation Oncologist has also the responsibility of processing the acquired images, segmenting the organs at risk. Therefore, guided by the Report 50 (1993) and 62 (1999) defined by the International Commission on Radiation Units and Measurements (ICRU), the physician will use the CT data to define the established number of target volumes.

When studying the tumour, besides outlining the tumour volume microscopically evident (Gross Tumour Volume - GTV), it's included a margin around it, containing areas at risk for microscopic involvement, named Clinical Target Volume (CTV), that will be irradiated with a lower dose than the GTV. To the CTV, another margin is added because of internal organ motion or possible day-to-day positioning variations, the Planning Target Volume (PTV).

The real volume to be treated, which will be irradiated with the prescribed dose for the cure, is an additional border to the PTV; in order to adjust to the physical characteristics of the beam, penumbra, as seen on Figure 18.

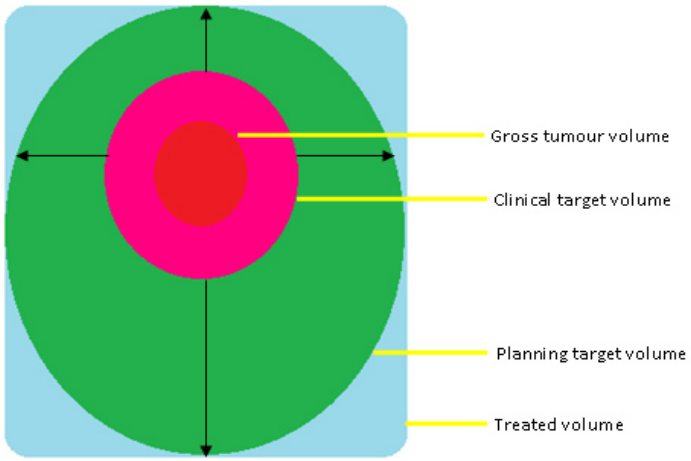


Figure 18 – Different regions outlined when planning the different doses to be received by the tissues.

Then, the images of the tumour and surrounding tissues, marked by the physician, are sent to a Treatment Planning System (TPS), software where the Health Physicist will have access to the images and develop the treatment plan.

1.2.4. *Development of the treatment plan*

This very important step, for the treatment of a patient with cancer, summarizes what was previously explained. It results from the collaboration between the physician and the health physics technician, with the purpose of defining the technical and geometrical details of the treatment process.

The health physics technician prepares the plan, based on the chosen CT slice; determines the spatial dislocations that need to be applied to the previously defined coordinates to situate the final isocenter. Also, he configures the perimeters that will be irradiated with different intensities, optimizing the dose distribution, with the aim of protecting healthy tissues. In cooperation with the doctor, the optimal plan is chosen.

In addition, it's produced a DRR image; a planar image (2D) obtained by processing the image series "CT data set" (3D) acquired with the patient in the treatment position.

1.2.5. *Simulation*

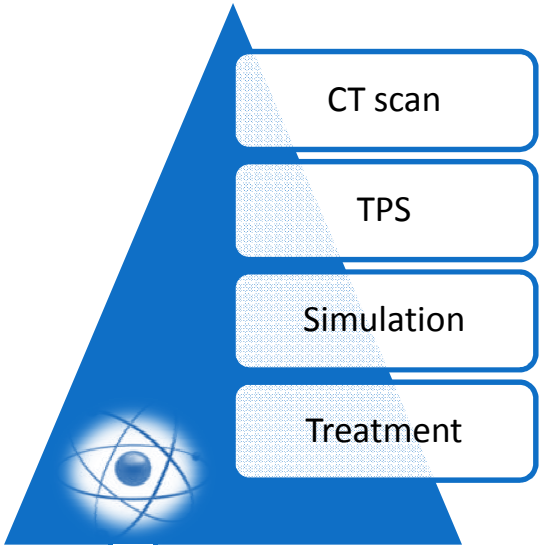
Once all the aspects regarding the treatment method, positioning, immobilization technique and exact spatial coordinates to guide the deposition of ionizing radiation have been defined, the patient is called for one last appointment, completing the treatment planning.

The performance of an imaging study, followed by the elaboration of a treatment plan with the collaboration of health physics, and the need to make one last visit before starting the cure, is part of a procedure called "Conventional Simulation". However, due to the noticeable technology development, all of the actions taken after the scan

can now be executed just using a specific software, naming this new planning methodology “Virtual Simulation”.

Essentially, in the process of simulation, the target volume (the area that will receive the maximum amount of dose) is localized and the organs at risk (the volumes and organs that must receive the minimum dose) are delineated. Once these structures have been well defined, the next step is the delimitation of the irradiation fields in relation with the target volume and organs at risk. Because, during the treatment, the therapy is fractionated, there must be a confirmation that the irradiation orientation and structures localization remain unchanged.

- *Conventional simulation*



After deciding on a treatment plan and on all of the aspects that it involves, they need to be verified. For this purpose is used a digital radiotherapy simulator that mechanically mimics the treatment machine.

A radiotherapy simulator is formed by a gantry, collimator, X-ray tube, imaging unit, patient support/positioning system and a remote control console. The gantry consists of a C-arm, which can rotate along the longitudinal axis passing through the isocenter. One end of the C-arm holds the collimator subassembly and the X-ray tube. The

imaging subsystem is mounted on the other end and comprises an image intensifier coupled with a CCD camera system, providing sharp digital images in fluoroscopy, as well as a radiography mode (Figure 19).

Figure 19 - Radiotherapy Simulator (19).

Another characteristic of this equipment, is that it has a radiation source with energy around 60-150 kV, while a linear accelerator can reach between 6 to 25 MV; because the main objectives of the simulation is to plan or 'simulate' the beam angles and positions. Images of the beams are acquired to be approved by the Radiation Oncologist and compared with the DRR taken during the treatment on the linac.

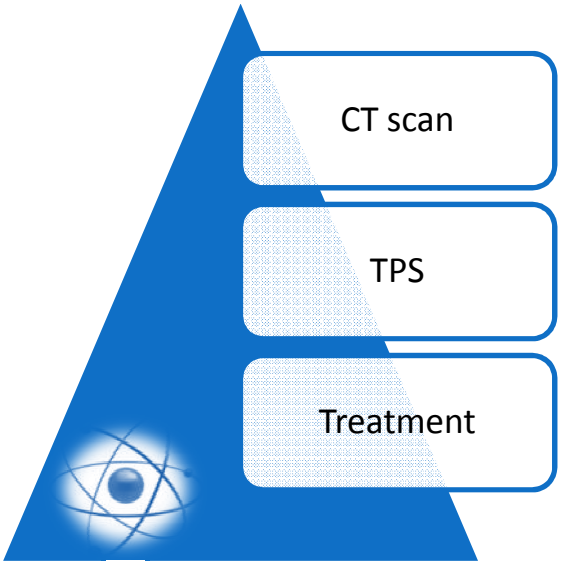
During this appointment, the position and immobilization system adopted for the CT scan is reproduced on the digital simulator. The lasers are positioned where the patient was previously marked and the height of the couch, as well as its longitudinal and transversal position, are altered according to what was established on the treatment plan; obtaining in this way the final isocenter, that is also marked on the patient's skin (16).

Then, the dimensions of the treatment perimeters and the rotation of the collimators and gantry are inserted on the simulator's software and, through fluoroscopy, is acquired an image that will be compared with the DRR. This image will be a reference

throughout the treatment, being confronted with the portal images, with the purpose of following the development of the cure process (16).

The conventional method has the advantage of allowing the physician to track, in the moment, the motion of various organs due to respiratory movement; enabling to proceed to small alterations in the treatment plan. On the other hand, it's difficult to identify with precision the limits of the tumour and the surrounding healthy tissues (16).

- ***Virtual Simulation***



As the number of CT scanners in radiotherapy departments is increasing and there is a constant improvement of the software, it's now possible to elaborate the majority of the treatment plan in just one visit.

In order to meet the new requirements in radiotherapy, virtual simulation uses an advanced simulation system that allows a precise contouring of the patient's anatomical structures, as well as a complete visualization of the area of interest in the three spatial dimensions. With this method, it's not necessary to use a simulator, because it uses the Computed Tomography dataset of the patient, including the external landmarks on the skin, without the patient being present; which saves time to

the radiotherapy team and most of all to the patient, that sees the time of planning reduced and can start the treatment earlier (16).

The objective of simulation, in general, is to mark on the patient's skin the specific coordinates that we have, with which we will intuit the isocenter. By using an advanced treatment planning system (TPS), right after the CT scan, tasks like the delineation of volumes, definition of the isocenter, elaboration of the treatment plan, as well as the composition of reference images, can be completed in a shorter period of time (15).

A virtual simulation system comprises:

- A **CT scanner** to acquire images, perform a 3D reconstruction of the studied section and help with the definition of the volumes of interest;
- An **external laser system** to center and to simulate the treatment;
- A **virtual simulation software** to determinate the aspects regarding the treatment and elaborate the DRR;
- A **TPS** to estimate the dose and the effects of the radiation on the tumour and surrounding organs, providing a 3D visualization.

Basically, a complete protocol consists of seven steps: welcome and prepare the patient; immobilization and positioning followed by the acquisition of a CT scan; identification of the radiation isocenter; marking; preparation of the patient's personal file and development of the treatment plan.

For the development of the treatment plan, the virtual simulation software allows the physician to:

1. Position beams around a virtual representation of the patient, with different gantry and collimator angles, as well as table rotations, warning if the position is not possible to deliver on the linac;
2. Set field sizes and multileaf collimator shapes;
3. Produce digitally reconstructed radiographs;
4. Visualize the patient's surface, showing the treatment field and marks that have been placed on during the planning CT scan;

5. Contour anatomic structures acquired on the CT scan, that can be used by the TPS to calculate dose statistics for the separate organs;
6. Calculate doses and display the dose distribution on the planning CT scan;
7. Elaborate a dose versus volume histogram and/or a plot of the dose versus the amount of tissue receiving that dose, which may be for the whole patient or for individual anatomical structures previously studied (Figure 20).

Figure 20 - Image from the virtual simulation software *syngo®* VSim, from Siemens (20).

Despite this type of software being so complete and reliable, it's indispensable to verify the estimated parameters before the irradiation in the linac.

1.2.6. *Treatment in the linac*

This is the final step of the radiotherapy journey, in which the patient starts the cure process by following the treatment that has been planned since his first visit to the department.

The patient is prepared and positioned on the linac table and the immobilization method chosen for his case is reproduced. By following his personal file, the equipment is manipulated, in order to comply with the established parameters in the plan, and the affected area is irradiated with the determined dose.

The patient goes through several treatment sessions, where the effectiveness is evaluated through the comparison of port films and the DRR, until the purpose is achieved.

Chapter II

PET/CT

According to *Phillip H. Kuo et al* (2008), even though radiotherapy is an effective method fighting cancer, more than 50% of the patients will die from the disease, frequently in consequence of local failure. Several factors contribute to this outcome, such as inaccurate identification of the tumour, inadequate staging of nodal involvement or metastatic spread, insufficient tumour targeting due to unidentified nodes, imprecise definition of the borders of the tumour, inadequate dose or tumour resistance (1). These errors can be overcome with the combination of different imaging modalities when planning the radiotherapy treatment, which can improve significantly the accuracy of the acquired data by providing different information about the disease. With the acquisition of more detailed information about a particular tumour, better can be planned a treatment strategy that will efficiently eradicate it.

2.1. Evolution of treatment planning in Radiotherapy

Radiation therapy has been in use for the treatment of cancer and other diseases for approximately 100 years. Around 1897, it was concluded that X-rays could be used not just for diagnostic purposes but also with therapeutic intentions (Figure 21). The investigation of X-ray radiation for patient therapy moved into the clinical routine in the early 1920s (21).

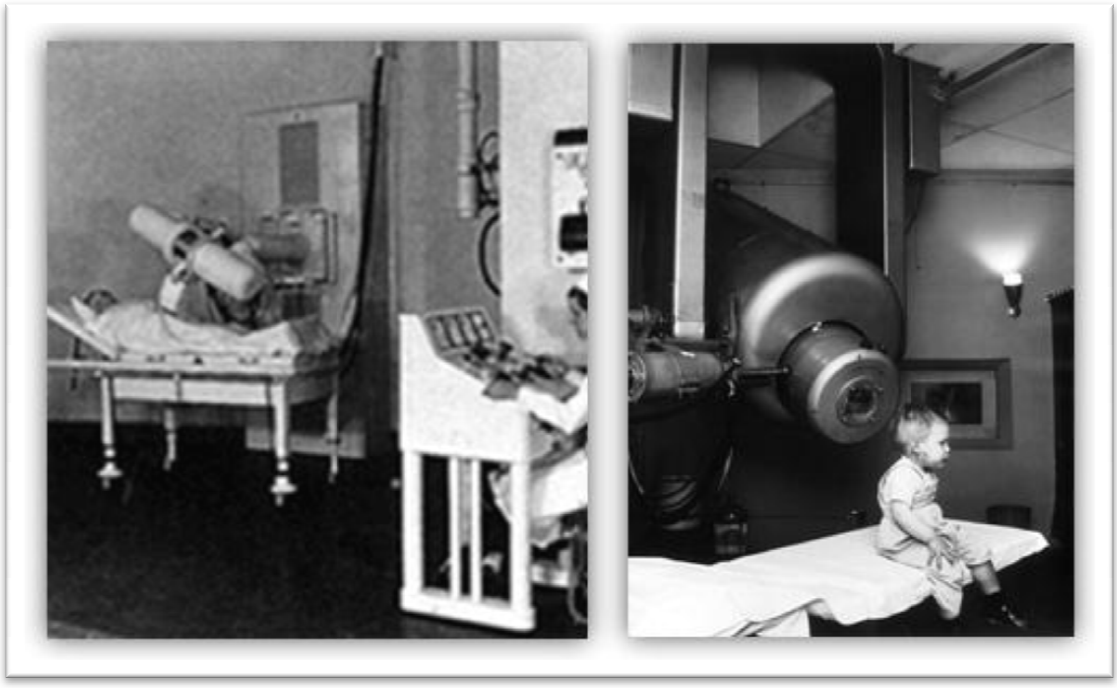


Figure 21 – On the left: An original X-ray cancer therapy system in use circa 1922 (22). On the right: A two-year-old boy suffering from retinoblastoma, was the first patient to be treated using a research linear accelerator modified by physicists for medical use, in 1957 (23). A year later, was introduced the first commercial medical-use linear accelerator.

Radiation oncology was born not long after the discovery of X-rays in 1895. By then, the detection of tumours was based simply on **clinical examination** and **radiographic imaging**. But these methods had major drawbacks, such as a lack of quality to distinguish between soft tissues and difficulties in interpretation, due to the fact it's a superimposed two-dimensional (2D) image of a three-dimensional (3D) volume. Besides that, in conventional 2D imaging, it's not possible to perform a quantitative analysis of the tumour volume (24) .

Computed Tomography overcame all the limitations of conventional 2D imaging, becoming the primary imaging modality for image based radiotherapy treatment planning. CT images provide data about the X-ray attenuation characteristics of the patient and allow a good identification of structures and organs for the specification and delineation of treatment volumes (25). The images have good anatomic detail, without geometric distortion, which is ideal for the definition of target volumes. By

providing intrinsic information on the electronic densities of various tissues, that information can be used for dose calculations (26). However, CT lacks contrast resolution to differentiate between normal soft-tissue and neoplasm, affecting the precise definition of the GTV; in addition, the image quality can be compromised by the presence of metallic structures (27).

With the introduction of advanced radiotherapy treatment techniques, like 3D Conformal Radiotherapy (3D-CRT) and Intensity Modulated Radiotherapy (IMRT), it is of maximum importance to delineate the target volume precisely, in order to achieve a good tumour control, since any error during the delineation of the tumour volume will lead to tumour underdosage (24). The improved dose conformity and steep dose-gradients, underpinning these techniques, require more accurate structure definition to avoid the chance of geographic miss, seeing that high-precision radiotherapy is poorly tolerant to set-up errors (28). Since anatomical cross-sectional CT images do not reflect the underlying cellular and biochemical processes of the diseases, that are essential factors for the success of the treatment, investigations were held to supplement the purely anatomical information of X-ray imaging by providing data regarding molecular function (25).

Magnetic Resonance can provide functional information and together with CT, despite into a lesser extent, are the most widely used modalities (25). However, MRI isn't as sensitive to biochemical processes as techniques that use radioactive tracers, being Positron Emission Tomography one such technology.

PET utilizes short lived positron emitting radioisotopes, such as Flourine-18, Carbon-11, Oxygen-15 or Nitrogen-13, tagged to a substance that is specific to the study of interest. The majority of these special radioactive isotopes are produced in cyclotrons. Once injected into the body, the positrons emitted by these radiopharmaceuticals undergo annihilation with the electrons in the tissues, converting their mass into two 511 keV gamma rays emitted in opposite directions (Figure 22).

The PET camera consists of a ring of detectors. When two gamma rays, within the appropriate energy and time window, interact with detectors oppositely aligned, is registered that a "true" count occurred along the line between the two detectors (line

of response). Counts are rejected if they fall outside the energy window, since the gamma-ray may have been scattered; or outside the time window, since the two gamma-rays may have been originated from separate annihilation events. The coincident photons are collected by a scintillation detector and processed by computer to form an image. An algorithm, such as filtered-back projection or iterative reconstruction, is in that case used to generate the image from the collected "true" counts (1).

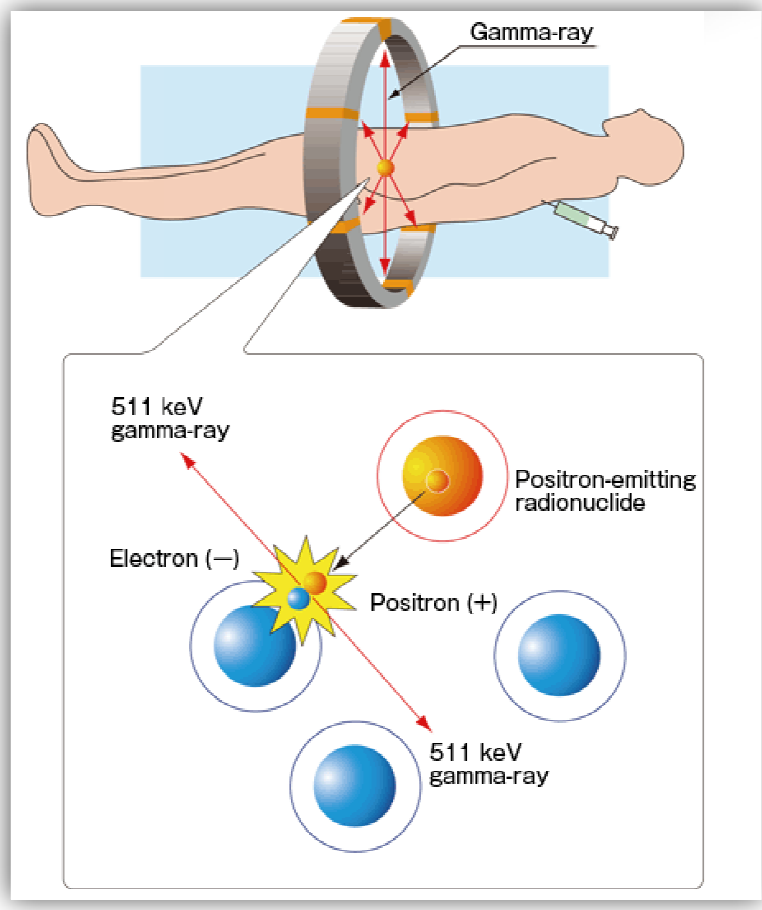


Figure 22 – Principles of Positron Emission Tomography (29).

As with all of Nuclear Medicine, the PET scan is defined by the injected radiotracer. FDG is by far the most widely used PET radiotracer. It is a modified glucose molecule (fluorodeoxyglucose) labelled with radioactive fluorine (^{18}F-FDG). This tracer is an indicator of glucose metabolism within the body and is driven primarily by the expression of the glucose transporter molecule (GLUT-1) at the cell surface (25).

FDG is injected intravenously into the patient, being the role of the PET camera to localize and quantify the accumulation of radiopharmaceutical within the patient. Tumours have higher rates of glucose metabolism, so have increased FDG uptake in comparison with the normal surrounding tissue. The substitution of the fluorine into the glucose molecule results in biochemical trapping of FDG in the malignant cells. FDG is initially phosphorylated like glucose, but then doesn't proceed further down the metabolic pathway, remaining "trapped" within the tumour (Figure 23)(1).

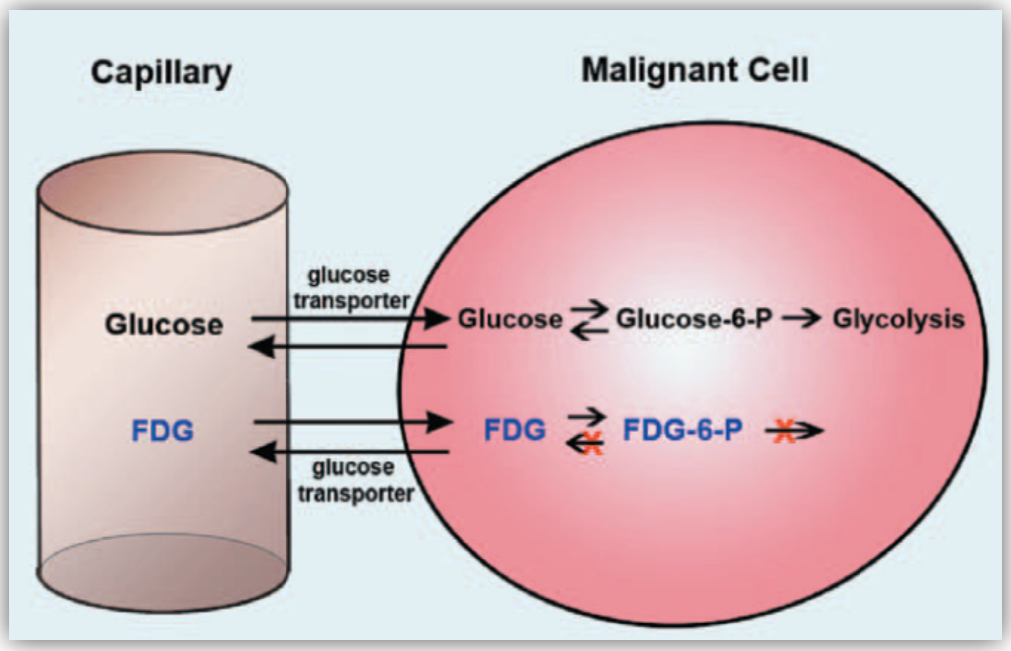


Figure 23 – Comparison between the pathway of glucose and FDG in a malignant cell (1).

Malignant tumours require an energy source to fuel their growth and metastatic spread that often occurs. Many tumours preferentially use glucose as their energy substrate, allowing us to use FDG to identify abnormal sites of metabolic activity, making FDG-PET a sensitive imaging modality for the detection of many types of tumours (30).

Imaging the metabolic activity of a tumour provides more sensitive and more specific information about the extent of disease than morphologic/anatomical imaging alone, presenting substantial advantages in oncologic imaging. PET is able to provide

additional information on the tumour extent, lymph node involvement and putative distant metastases (31). It can also add information on different biological characteristics of the tumour itself and help on the differentiation between malignant and benign growths, as well as between tumour recurrence and radiation necrosis. In addition, PET is also capable of identifying slow growing tumours and hypoxic regions (24).

For all of the above, the incorporation of PET into radiotherapy treatment planning has revolutionized the field of radiation oncology. It has found its role in diagnosis, staging, prognostication, treatment planning and evaluation of treatment response (24).

Specifically, in treatment planning, the functional data provided by PET examinations has the potential to modify treatment volumes and to guide treatment delivery to cells with particular metabolic characteristics. The addition of PET into radiotherapy treatment planning has reduced significantly inter-observer variability, when identifying gross tumour volumes, than just using CT images (25). This biological information can be used to delineate a biological target volume and to adapt a treatment, in terms of volume as well as dose (24).

Although this is a welcomed outcome, it does not necessarily mean that the volumes are being defined any more accurately. One important limitation of PET is the fact that the exam is not absolutely specific for cancer, and false-positive findings can occur in inflammatory or infectious conditions, where is also seen an increased uptake of glucose by the cells. Another major drawback is the substantially lower resolution of the images when compared with the ones obtained with CT or MRI, providing poor anatomic detail, which creates difficulties during the definition of the peripheries of the tumours. Since dose calculation requires accurate definition of external body and normal structures surrounding the tumour volume, PET cannot be used alone for radiotherapy treatment planning. To be used in radiation therapy, PET should be fused either with CT or MRI, being an integrated PET/CT or PET/MRI the best option (24).

2.2. The influence of PET/CT in Radiotherapy Treatment Planning

With the inclusion of many newer imaging modalities, each with unique diagnostic capabilities, multimodality imaging is the current buzzword in radiotherapy.

The advantages of PET/CT, over stand-alone PET and CT, are that it offers a more accurate localization of FDG uptake and improvements in treatment monitoring (24). PET examinations are able to identify areas of disease not readily visible on CT alone and the CT images can provide improved spatial resolution, helping to anatomically localize sites of involvement. In addition, the low noise CT data can be used to generate a patient-specific map of attenuation coefficients to correct PET data errors from photon attenuation, scattered radiation, and other physical degrading factors, such as partial volume effect. That's why dual-modality PET/CT can improve both the visual quality and the quantitative accuracy of the correlated radiotracer data, providing a much better basis for human judgment. On the other hand, this improvement comes at a cost in terms of increased radiation dose compared to a simple PET examination (28).

The concept of multimodality imaging improves the ability of earlier detection of the tumour volume and plays a vital role altering treatment decisions, improving treatment planning, and as a tool to assess response to therapy (1).

2.2.1. PET/CT optimizing the treatment plan

PET/CT can optimize the treatment plan by improving the delineation of the entire extent of the disease, so that the treatment field can be appropriately increased or decreased. Even a single positive node that may be left outside of the treatment field will result in therapy failure. At the same time, PET/CT can lead to a minimization of toxicity, by decreasing elective nodal irradiation and irradiation of normal tissue, that by conventional anatomic imaging could not be distinguished from diseased areas (1).

In recap, PET/CT combined with IMRT allows:

- Dose escalation;
- Decrease dose to normal tissues;
- Decrease acute toxicity;
- The possibility of better tumour cure;
- Less long-term toxicity (1).

2.2.2. *PET/CT altering the treatment plan*

PET/CT alters radiation treatment planning in up to 45% of patients and leads to changes in tumour volumes in 30% to 50% of patients (Figure 24). All because increased uptake of FDG can clearly show neoplastic involvement of subcentimeter nodules that otherwise would have been missed on a simple CT scan (1).

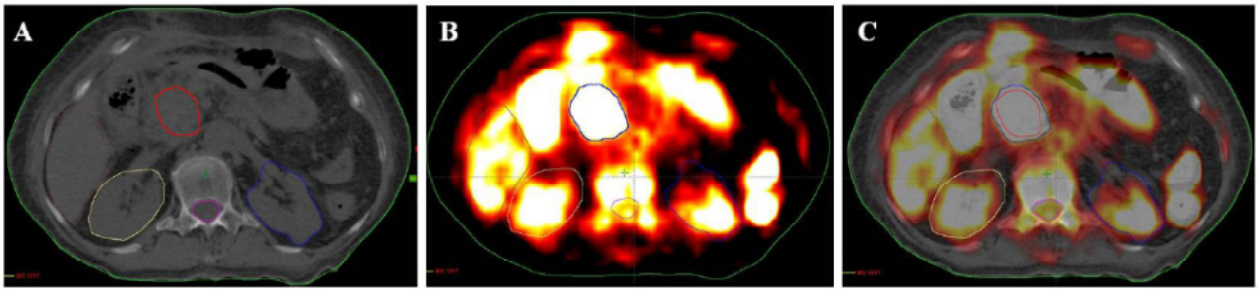


Figure 24 – Representative image of a patient where different GTVs where delineated using CT (A), PET (B) and co-registered PET/CT (C) (32).

Detection of residual tumour in a mass after treatment can be rapidly assessed using PET, rather than relying on serial anatomical imaging to assess for any change in size. Obviously, accurate disease staging is crucial to treatment planning and to establish a goal for the radiation therapy, since the discovery of widespread or distant spread of disease could change the goal of RT from curative to palliative or no treatment. A more accurate staging will spare the patient from the potential morbidity and mortality associated with the toxicity of the therapy. PET/CT has also the capability of assessing early response to RT and can also be used to detect disease recurrence (1).

2.2.3. *The role of PET/CT in the diagnosis of different types of malignancies*

PET/CT is primarily used for staging different types of cancer, including head and neck cancer, lung cancer, breast cancer, colorectal cancer, melanoma; as well as in the assessment of chemotherapy response in many conditions, particularly lymphoma (24). Extensive literature has stated the ability of PET/CT in staging lung cancer, detecting nodal involvement and distant metastases, significantly better than any other non invasive imaging tool; although, false positives can happen, caused by inflammatory or infectious processes (Figure 25) (30).

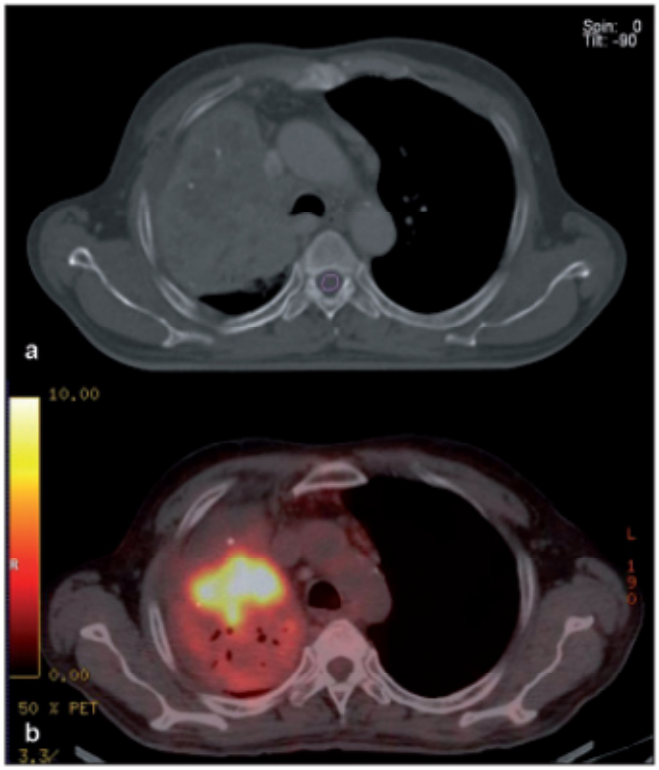


Figure 25 – Images from a patient with lung cancer. The axial CT scan (a) showed a large mass in the upper lobe of the left lung. The corresponding FDG-PET/CT image (b) revealed an increased uptake only in the central portion of the mass, representing viable tumour with adjacent areas of atelectasis that clearly lack FDG-avidity (28).

Several studies that have examined the role of PET/CT in the context of radiotherapy planning, have concluded that there are significant quantitative and qualitative differences between PET/CT-derived tumour volumes in a large proportion of patients

with head and neck squamous cell carcinoma (HNSCC).The decision to designate a node as involved or not with disease, translates into the difference between delivering tumouricidal doses applicable for gross disease (66-70Gy) versus delivering prophylactic dose (54-56Gy) for elective at-risk nodes (Figure 26) (28).

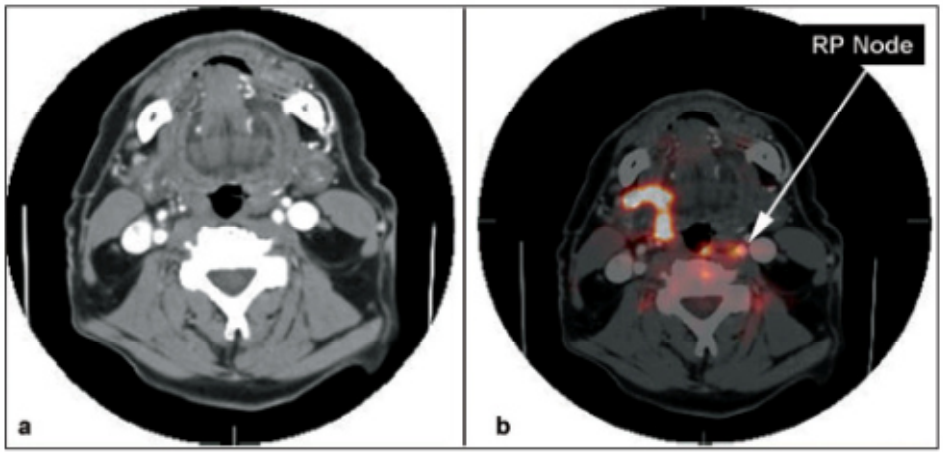
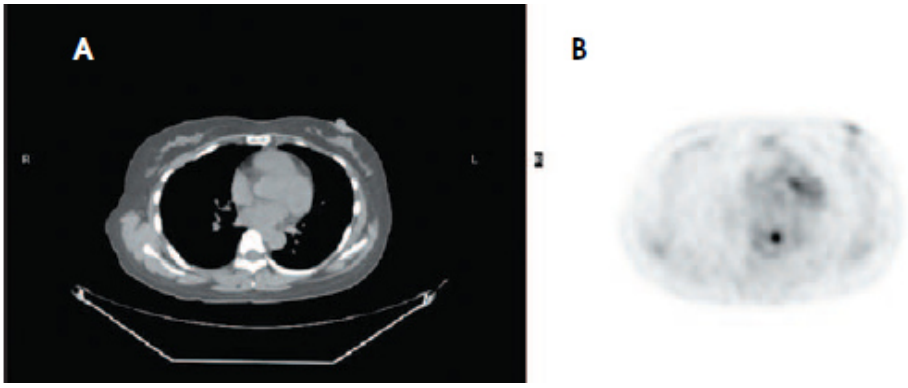


Figure 26 – Contrast enhanced CT scan (a) showing a large oropharyngeal lesion on the right side. A FDG-PET/CT scan (b) identified a small FDG-avid retropharyngeal lymph node (arrow) in the contralateral neck, equivocal on CT alone. This necessitated the delivery of high tumoricidal doses to the involved retropharyngeal nodal region that would have otherwise received only prophylactic doses as low-risk elective volume (28).

Also, PET/CT brought great advantages for cervical cancer, in the detection and inclusion in the target volume of gross para-aortic and pelvic lymph nodes, which might have been equivocal on CT imaging (Figure 27). Besides, it provides valuable additional information for brachytherapy planning in patients with gynaecological tumours (28).



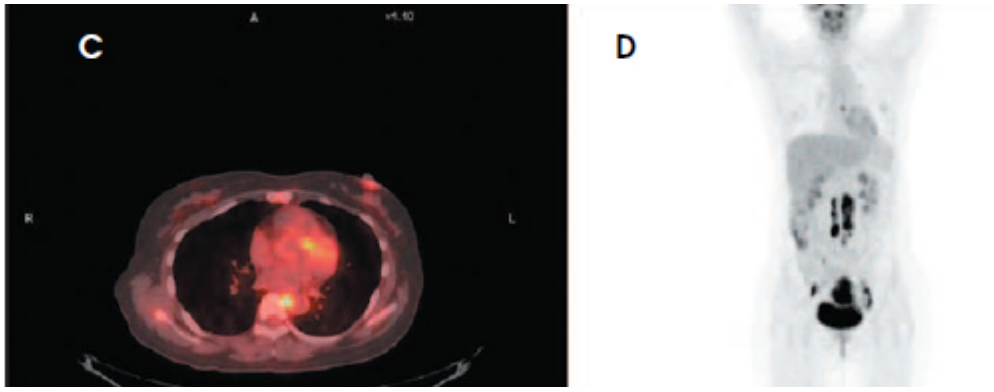


Figure 27 – Images from a patient with cervical cancer: (A) axial CT scan, (B) FDG-PET image, (C) fused PET/CT image, and (D) an anterior maximum intensity projection (MIP) image. Distant metastasis of cervical cancer to a paraesophageal node was evident on the FDG-PET (B) and PET/CT image (C), that was not detected on a diagnostic CT scan, performed previously (not shown). The anterior MIP image (D) showed extensive disease burden in the pelvis, as well as retroperitoneal adenopathy (1).

2.3. The PET/CT equipment for Radiotherapy Treatment Planning

Initial studies, for treatment planning of three-dimensional conformal radiation therapy, used PET and CT images that had been acquired on different scanners and registered afterwards. Accuracy of image registration is an important factor in radiotherapy treatment planning and any discrepancy in the fused images would have a significant impact on the probability of tumour control and cause problems to healthy tissues (24).

Making a software fusion of the PET and CT images, had what was thought to be an advantage, that the acquisition of the PET data didn't necessarily need to be performed in the treatment position and could be obtained from the diagnostic scan. However, a major downside is that the simulation scan and the PET examination will be acquired at different times, most likely on different couch tops and potentially with the patient in different positions; which could bring potential problems associated with organ motion when treating the patient. The use of a conjoined PET/CT scanner provides a hardware solution to image registration, reducing uncertainties in patient positioning (25). Because CT and PET images use the same DICOM coordinates, images are automatically fused and manual correction is avoided (27).

2.3.1. The PET/CT scanner

A PET/CT camera is essentially a PET camera and a CT scanner placed back-to-back into one machine, allowing the scan to be performed with the patient in a single position (Figure 28). The data set of attenuation coefficients, that constitute a CT image, will provide information for attenuation correction of the PET images, resulting in reduced acquisition time and in scans with little organ movement between the PET and CT portion, since the physiologic data from the PET and the anatomic data from CT are acquired nearly simultaneously (24).

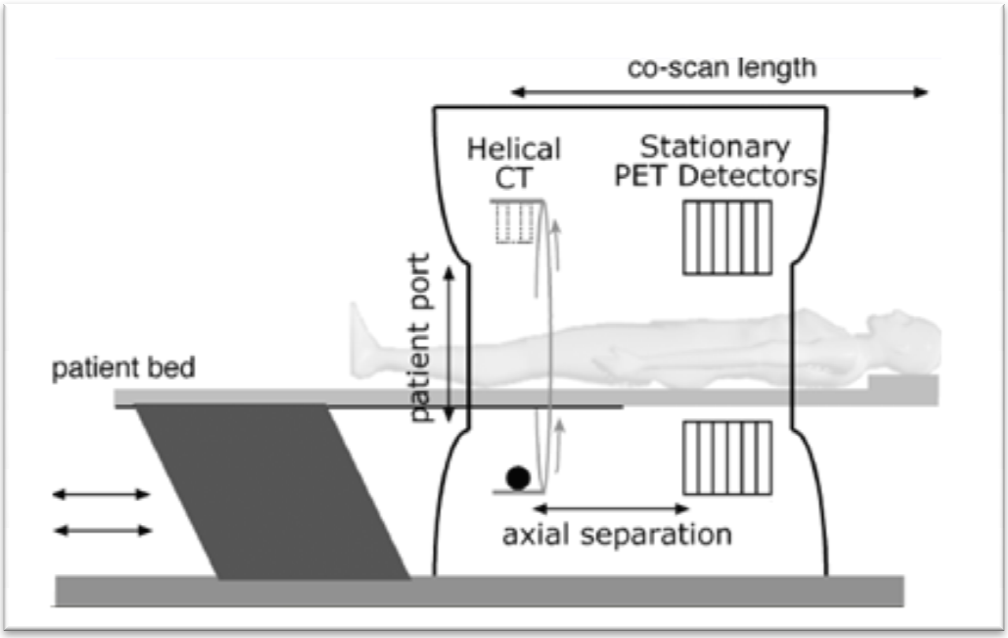


Figure 28 – Scheme of the hardware (33).

The final images are the result of the overlay of colour PET images onto the CT images (Figure 29) (1).

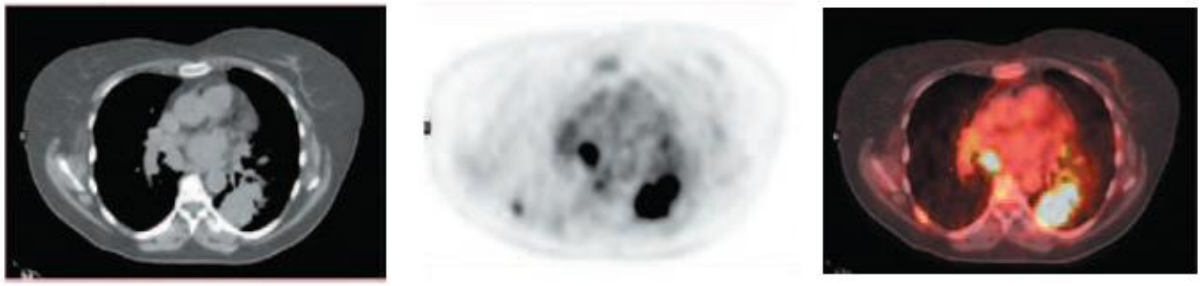


Figure 29 - The CT scan is acquired first, followed by the positron emission tomography (PET) scan (without attenuation correction). The CT is then used for attenuation correction of the PET scan. The PET and CT scans are fused by overlaying the PET image, converted with a colour scale, onto the CT (1).

Images for radiotherapy treatment planning (RTP) purposes must be acquired differently from those for use in diagnosis and staging of patients. The introduction of any new imaging modality for RTP requires a close teamwork between professionals,

in order to develop appropriate protocols and adapt the scanning procedures. Therefore, the protocol for the exam, as well as the PET/CT equipments that are used for planning, have some differences from the ones used for diagnostic (Figure 30).

Figure 30 – PET/CT scanner prepared for radiotherapy planning (34).

2.3.2. Additional hardware

Couchtop

An essential adjustment, required for the PET/CT equipments, is to switch the couchtop of the scanner; since having an equal couchtop to the treatment unit is the key for the reproducibility of the position of the patient in every treatment session.

In radiotherapy it's used a couchtop with a flat surface, rigid and made out of a carbon fiber. Carbon fiber couchtops are a radiation-friendly base, creating fewer image artefacts. These have an indexing system, as well as supports for patient positioning and fixation accessories (Figure 31).

Figure 31 – Better view of the carbon fiber couchtop used in radiotherapy (17).

External Laser System

The PET/CT equipment has an internal laser system, but the positioning of the patient for radiotherapy planning is more complex, in part because the patient is immobilized and these devices occupy a large part of the gantry, due to their considerable dimensions. For this reason, the immobilization and positioning has to be done when the patient is still outside; so, the scanners had to be adapted with an external laser system to achieve precise patient alignment and set up external reference points.

These positioning lasers are high intensity beams of light, parallel and perfectly collimated, projected from three sources, with directional precision instruments (Figure 32).

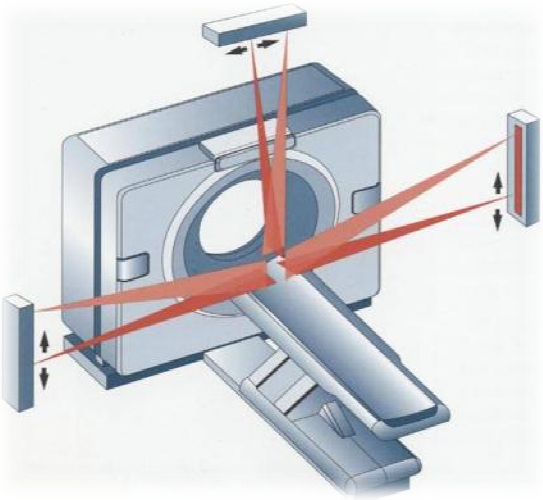


Figure 32 - Scheme of the external laser system (35).

The first laser is mounted on the ceiling and it's preferably movable. The couch of the scanner can move up/down and in/out but can't move left/right, so the sagital laser should be able to move to the sides to allow marking away from the patient mid line; as well as to help identifying the degree of rotation comparing to his longitudinal axis. The other two lasers are immobile and mounted on opposite sides of the gantry and project luminous bands intersecting the horizontal axis of the beam isocenter, locating the height in the anteroposterior direction.

Chapter III

PET/CT for Radiotherapy Planning – The Protocol

Background story

The initiative to develop a dissertation, regarding the use of PET/CT for Radiotherapy planning, was taken while being an intern at the Nuclear Medicine Department of the Sant'Orsola-Malpighi Polyclinic. Due to my unfamiliarity with this variant of PET/CT, its study complemented my training in Nuclear Medicine, introducing me to the basic principles of Radiotherapy and making me aware of usual problems the Nuclear Medicine technicians face when using the equipment for radiotherapy planning.

3.1. The Sant'Orsola-Malpighi Polyclinic

Figure 33 – Main entrance of the Sant'Orsola-Malpighi Polyclinic in Bologna (36).

With more than 400 years of history, **Sant'Orsola-Malpighi Polyclinic** (official name: *Azienda Ospedaleiro – Universitaria Policlinico Sant'Orsola Malpighi*) was the first hospital in Bologna, being one the best and largest hospitals in Italy (Figure 33). It is a university and public hospital, home of the School of Medicine and Surgery of the *Alma Mater Studiorum* – University of Bologna 1088 (37).

The University Hospital is well-known internationally for its high quality in the study and treatment of various pathologies. Its medical conferences and conventions, organized every year, are attended by professionals of international fame. It has international excellence in various fields, such as hepatology, pediatric surgery and oncologic haematology (38).

The Medical Oncology Unit is dedicated exclusively to the diagnosis and treatment of cancer patients and is part of the Department of Haematology & Oncology that also includes, between others, the Radiotherapy, Radiology and Nuclear Medicine Units (39).

The Radiotherapy Unit

The Radiotherapy Unit is run by a close teamwork between Medical Radiation Oncologists, Medical Physicists, Radiation Therapy Technicians and Nurses, with other medical specialists from different medical fields, with the aim of achieving the best results.

These facilities are equipped with three linear accelerators with multileaf collimators alongside with verification systems, a CT simulator and a traditional digital simulator system for three-dimensional treatment planning.

In collaboration with the Department of Radiological Sciences, the CT images acquired for planning can be fused with other imaging techniques, namely MRI. The Radiotherapy Unit has also developed a partnership with the Nuclear Medicine Unit, performing PET/CT scans for treatment planning in their facilities with strict collaboration with the Nuclear Medicine staff.

The decision to perform a PET/CT scan for radiotherapy treatment planning is responsibility of the patient's physician, depending on the clinical case. The majority of the requests refer to oropharyngeal cancer, lymphomas and inoperable gynaecological malignancies (40).

Figure 34 - The CT simulation room in the Radiotherapy Unit of the Sant'Orsola-Malpighi Polyclinic.

The Nuclear Medicine Unit

The Nuclear Medicine Unit is divided into two branches: a Conventional Nuclear Medicine section and a PET centre. In the Conventional Nuclear Medicine section are performed static and dynamic planar scintigraphy examinations, as well as Single-photon emission Computed Tomography (SPECT), with three whole-body scanners available for the studies. The unit also comprises a hot lab, where are prepared radiopharmaceutical injections for Conventional Nuclear Medicine and a PET radiopharmacy, with a cyclotron equipped with six targets for the production of the most used radionuclides (^{18}F, ^{11}C, $^{18}F_2$, ^{13}N, ^{64}Cu, ^{89}Zr) as well as generators for the preparation of ^{68}Ga-DOTANOC (41).

The high-tech PET centre consists of four PET/CT scanners, one of them being a time-of-flight (TOF) PET system and another that doubles as a diagnostic and a radiotherapy treatment planning scanner. The room where this last scanner is located was adapted with the additional hardware needed for radiotherapy planning and once a week, during the afternoon, is exclusively used for these studies (Figure 35). The technician assigned for that equipment that afternoon, has the responsibility to prepare the room, scan the patient and assist the radiotherapy team, composed by one or more doctors, two Nuclear Medicine technicians and other medical staff if needed.

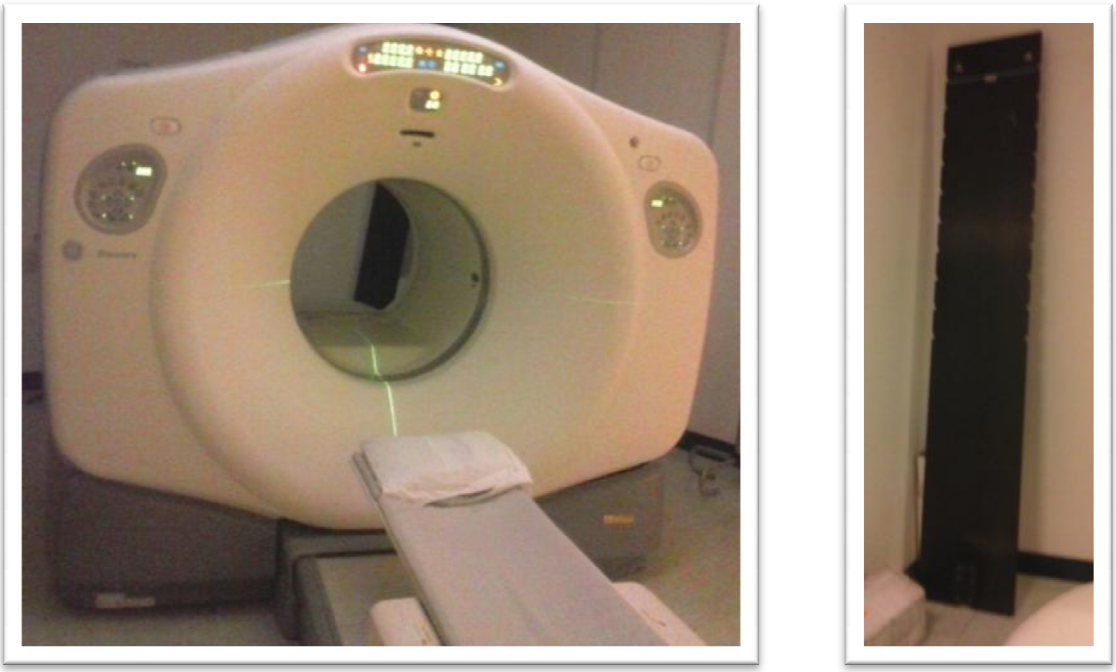


Figure 35 – Pictures from the PET/CT room designated for RT planning (on the left) and a more detailed view of the carbon fiber couchtop, stored in the back of the room when is not being used (on the right).

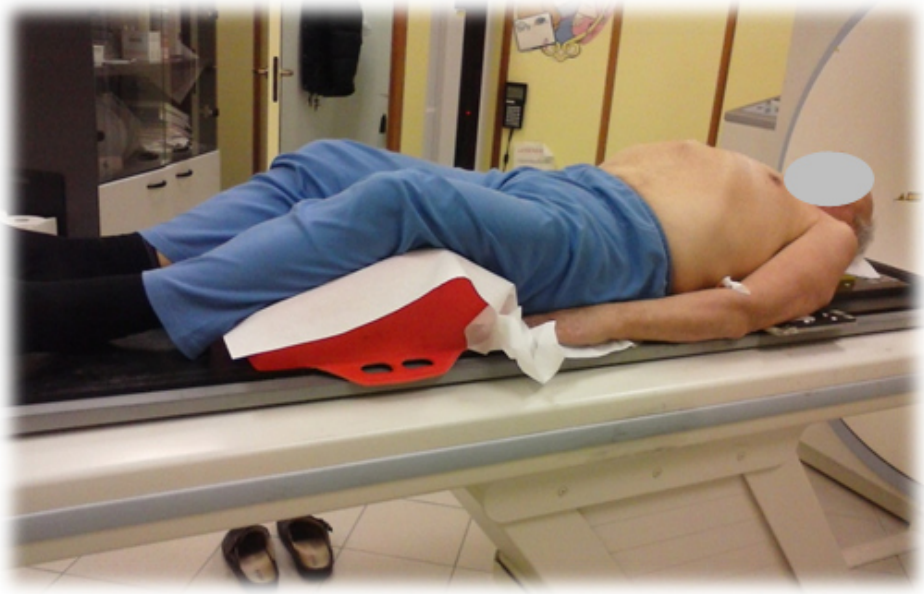
This institution performs routinely this type of examination with specialized Nuclear Medicine and Radiotherapy professionals and is well aware of common problems. In this chapter will be described the hospital's protocol for a PET/CT scan for Radiotherapy planning, explaining problems that frequently occur with real cases as example.

3.2. A Protocol for Radiotherapy planning with PET/CT

The protocol adopted by this institution for a standard RTP examination without sedation or anaesthesia, consists:

3.2.1. Appointment in the Radiotherapy Department

The start of the preparations for the scanning takes place in the Radiotherapy department. The patients are first called for an appointment with the Radiation Oncologist, to receive all of the information about the treatment plan and give their consent. Then, in the room for treatment planning, all of the aspects regarding the preparation for the PET/CT scan are organized. Depending on the clinical case, immobilization devices are chosen and made to fit the individual patient. A mask is used for head/neck cancer and a vacuum-form body immobiliser for lung, stomach and colorectal cancer. For patients with ovary, penis or testicle cancer, an outer/extremity fixation is normally used. The PET/CT procedure is also explained briefly, as well as the advantages that the scan will bring integrated into the treatment plan.



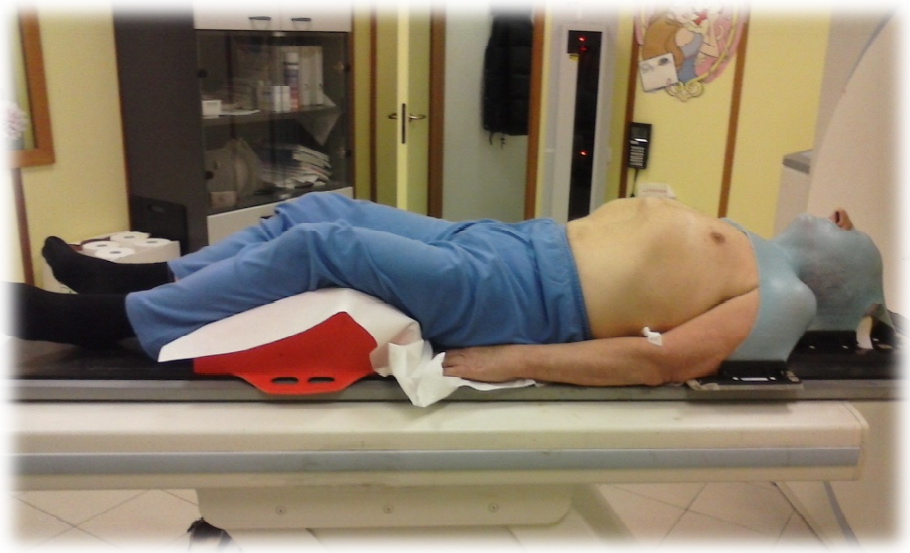


Figure 36 – Pictures taken at the Radiotherapy department of the Sant'Orsola Polyclinic. The first image shows the patient experiencing the position that he must keep during the PET/CT scan and trying on the kneefix, as a preparation for the placement and adjustment of the thermoplastic mask. The image above shows the patient now with the mask on, waiting for it to dry to maintain its shape. When it is dry, the technician identifies the mask with the patient's personal data and all of the set of immobilization devices will be brought to the Nuclear Medicine department for the PET/CT examination.

At this point, the radiotherapy team can also identify potential problems that can occur during the therapy PET/CT scan. For example, for patients who suffer with claustrophobia, suitable medication can be provided prior the examination.

Since these two departments aren't connected in this specific hospital, before leaving this first appointment, the patients are informed about the necessary requirements for the PET/CT examination, as well as the day and time they need to be in the Nuclear Medicine Department to start the preparation for the scan.

To perform a PET/CT scan, patients should fast for a minimum of six hours prior to an FDG injection. Children should fast for six hours before the scan and infants for four hours. For that reason, it's very important that the patient is informed and has understood these preparatory measures.

3.2.2. Preparation for the PET/CT scan

Radiotracer injection

At the scheduled time, the patients should present themselves at the Nuclear Medicine Department. Their identification is confirmed with the name and/or unique personal number and they are asked about their fasting period.

Approximately one hour (between 45 to 90 minutes) before the PET/CT scan, ^{18}F-FDG is injected intravenously (the protocol for this hospital is that the injection of the radionuclide is performed by a physician specialized in Nuclear Medicine). For an adult, the dosage is calculated as 4MBq/kg and in paediatric cases as 3MBq/kg.

Infants not having anaesthesia or sedation should be injected with the tracer as close to the next meal as possible. A meal may be given 30min after tracer injection at the earliest.

It's the Nuclear Medicine Technician who controls the time of injection. The technician asks the radiopharmacy to start preparing the doses and send them to the department, based on the number of scheduled patients and the exact time that each examination is programmed. Since a PET/CT examination requires a close teamwork between the Nuclear Medicine and Radiotherapy staff, it's important to respect the time of those specific examinations as the Radiotherapy staff will purposely be in the NM department for the planning scan.

The patients are also advised to drink water in order to maintain a good hydration and reduce radiation exposure of the bladder; the same for children not having anaesthesia or sedation.

Preparation of the PET/CT scanner

Before the arrival of the Radiotherapy staff, the PET/CT scanner needs to be prepared, as referred previously. The Nuclear Medicine Technician needs to turn on the external laser system and to replace the couchtop with the one made out of carbon fiber.

At this point the technician has already received a file prepared on the patient's arrival to the department filled with different data, such as name, date of birth, height, weight, injection time, dosage, as well as a brief medical history. It is important to be familiar with the patient's medical history prior the scanning, as this ensures the treatment region is clear to all staff members. The data is needed for the patient's identification on the PET/CT scanner software and is also essential in order to provide to the Nuclear Medicine Technician more information about the case, allowing him to be better prepared when supporting the Radiotherapy team for the performance of a quality examination.

When the room is ready and the Radiotherapy team has arrived in the department, the patient is called from the waiting room and asked to empty the bladder.

While the Nuclear Medicine Technician calls the patient, the Radiotherapy team enters the room, bringing the immobilization devices designed for the individual patient and start positioning them (Figure 37).

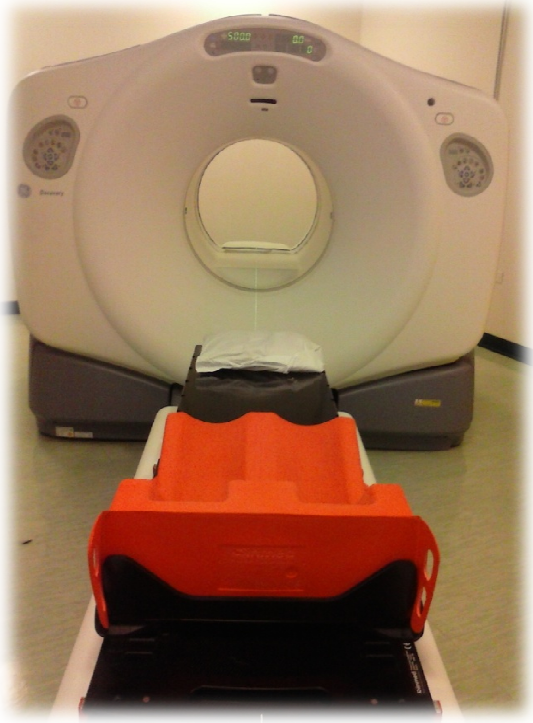


Figure 37 – Picture taken at the PET/CT room specifically used for Radiotherapy planning, after the equipment has been prepared for the planning scan. The couchtop was changed, the external laser system was turned on (one line of the laser is visible on the gantry) and the fixation devices were positioned.

Once the patient enters the room, he/she is asked to take away any metallic objects, prostheses, clothing and shoes, depending on the type of scanning and target area.

Positioning the patient

The most crucial part of the procedure is to position the patient on the exam table. Since during the previous appointment in the Radiotherapy department the fixation devices were already prepared and fitted, this procedure can now be concluded more rapidly.

It is very important to inform the patient that he/she must lay down still throughout the scan. It is particularly important to ensure that patients with head/neck cancer understand that they must lie perfectly still with their fixation mask on the entire scanning. The mask is uncomfortable but it will prohibit any movement, so that the radiation therapy can be given as accurately as possible.

There should always be two technicians positioning the patient and checking that he/she is properly positioned in the fixation devices, as well the patients' physician supervising the whole process (Figure 38). They must constantly maintain a sufficient distance and need to work efficiently. While prepping, a further short explanation of the scanning should then be provided, encompassing why it is necessary and how it will be done.

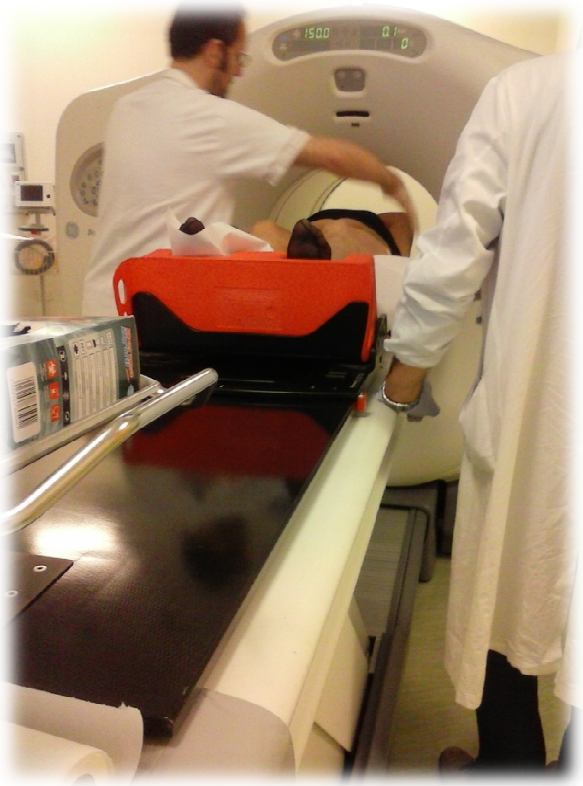


Figure 38 – Radiotherapy technician positioning the patient for the scan, following the directions of the physician.

The technicians must ensure that the patient lies exactly in the middle of the longitudinal external laser. To avoid errors in rotational isocentre, it is important that the entire patient, and not only the target area, is lying in the middle longitudinal line, and is not twisted or rotated.

Then, the table should be positioned at an appropriate height, around the 140 centimetres mark (Figure 39). The height of the table is very important in order to achieve optimal resolution for the scan; the scanner won't start the acquisition until the equipment is set at that required height. This aspect can cause some problems for radiotherapy planning, which will be explained and discussed in the next chapter.

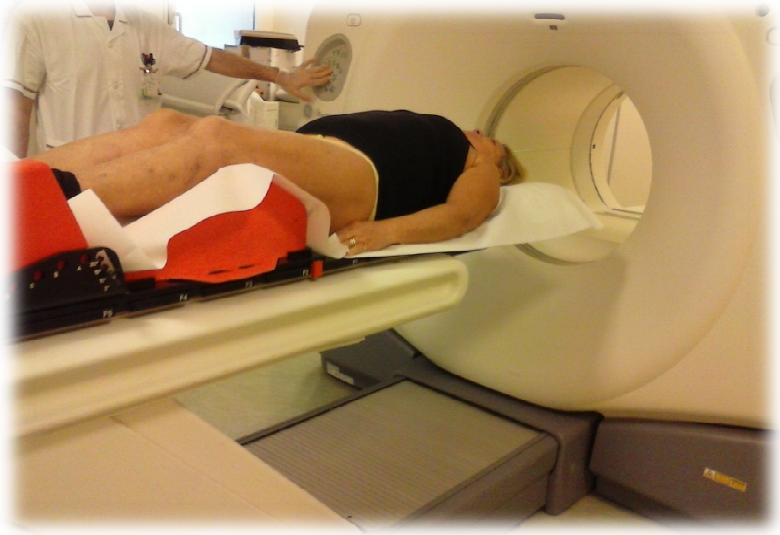


Figure 39 – Adjustment of the height of the table with the patient precisely positioned for the examination.

Afterwards, the table is driven towards the gantry until the external laser system reaches the target region (already identified in previous diagnostic examinations). Placed on both sides of the patient, the radiotherapy technicians guided by the lasers, draw with a permanent pen three vertical lines on the patient's skin, or individual fixation device, that will be alignment points for the coordinates x, y and z. At those marks will also be placed metal pins, in order for those to be visible on the CT scan.

The nuclear medicine technician then moves the couch to the scan's starting position and sets the length position to 0, using at this point the internal laser system as reference (Figure 40).

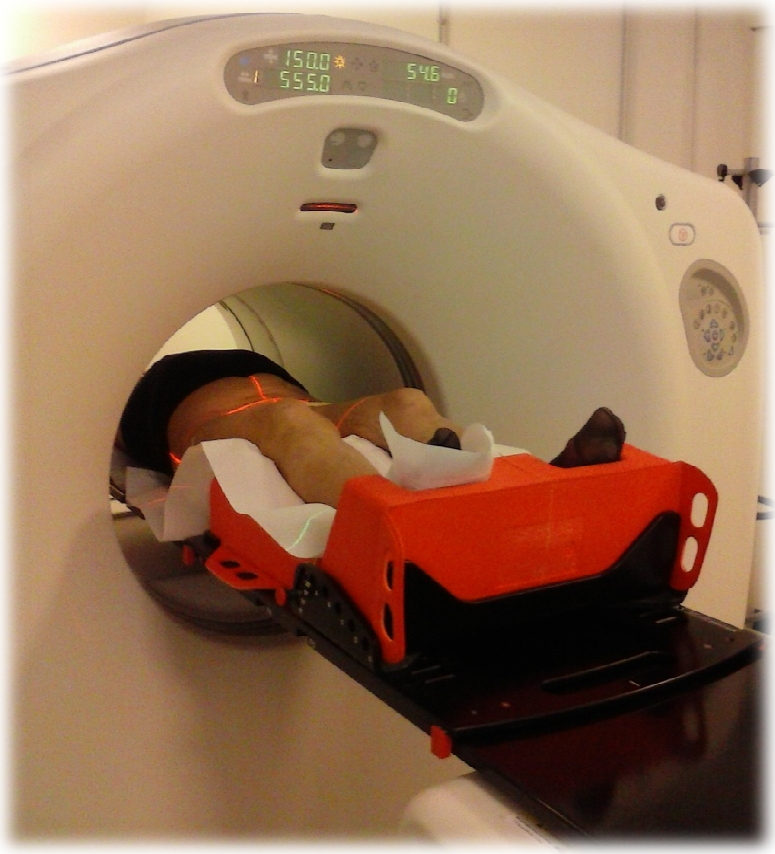


Figure 40 – Patient entering the gantry in order to set the start position using the internal laser system of the PET/CT equipment (red lines visible on the patient's abdomen).

The patient is informed that the scan is about to start and remained about the recommendations. The all staff is accommodated in the control area.

3.2.3. The scan

Since the patient's data was already inserted in the software, the nuclear medicine technician starts the examination by acquiring a scout image of the entire patient, which will be the base for the definition of the length of the scan, based on a number of steps (with 150 mm each) (Figure 41).

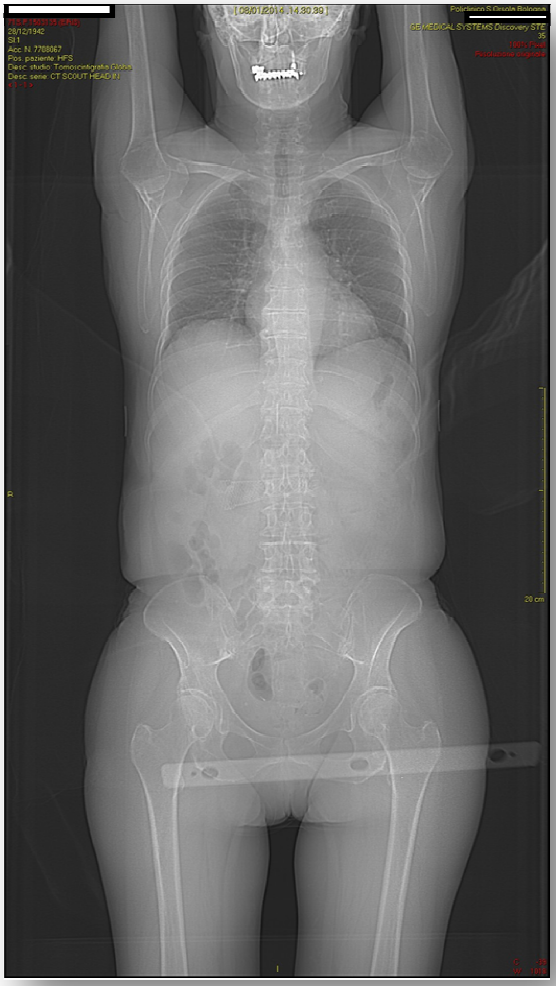


Figure 41 – Example of a scout image. This patient was positioned for a RTP examination, in a Vac-Lok.

Whole-body scans are always performed for radiotherapy planning, owing to the possibility of detection of unknown metastatic disease or new primary cancers which may change the treatment planning. Typically, a PET/CT scan includes the all area between the orbits (if the head is not the target region, if it is, the complete skull is studied) to the mid thigh region. However, there is a limitation regarding the acquisition length and the number of steps that the scanner can acquire, which can be a problem for taller patients.

The next step is the selection of the exposure conditions for the CT scan. A PET/CT scan of an adult or child in the radiotherapy planning setting is based on the ALARA (As Low As Reasonably Achievable) principles regarding both the CT scan and the FDG dosage.

Once performed the CT scan, the acquired data is reconstructed with a 3,75mm slice thickness and can be readily accessed. The PET examination will start right after but, depending on the software, at this point the user can change some parameters regarding the scan, such as the used radiopharmaceutical, the desired acquisition time for step, among others.

During the PET scan, the nuclear medicine technician together with the radiotherapy staff, go through the CT images and choose a slice where all the placed metal pins are visible but which position must end in __,0 mm or __,5 mm or in an approximate value (for example: __ ,98 or __,45) (Figure 42).

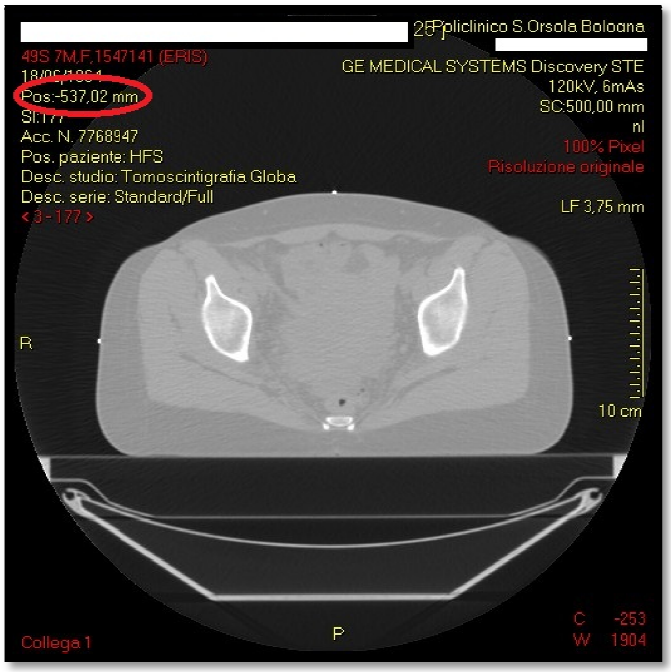


Figure 42 – Example of a slice that was chosen in a planning examination of a patient with cervical cancer. The three metal pins, placed before the scan, are visible and the position approximately ends in _,0 mm (537,02 mm).

This last requirement is important because this slice will be posteriorly established as a new landmark for the equipment, allowing the marking of the patient to be done outside of the gantry, so it must be easily localized.

The PET data is also reconstructed into 3,75mm image slices in three planes and the CT data is used for attenuation correction of these images. At last, the CT and PET images are matched.

3.2.4. Marking the patient

The last step of a PET/CT examination for radiotherapy planning is the marking of the patient or fixation device.

When the team enters the room, the patient is informed that the exam is finished but he must keep his position for a little bit longer. The table is moved until the internal laser system reaches the exact slice that was chosen previously and a new landmark is established as the new zero of the equipment (Figure 43).

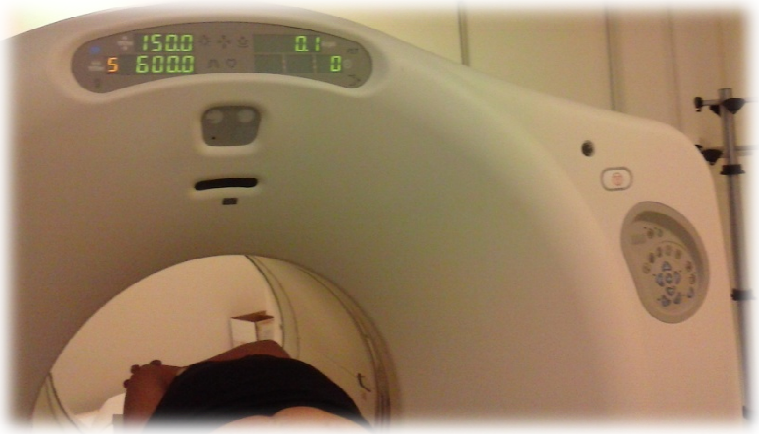


Figure 43 – After the new landmark was set on the chosen slice, the table is moved outside of the gantry 600mm.

Knowing that the internal and external laser systems are 60 cm (600 mm) apart from each other, the technicians know that if the table is moved 60 cm further the established landmark, the external laser system will be placed right on the selected area and the radiotherapy technicians can now tattoo the patient (Figure 44).

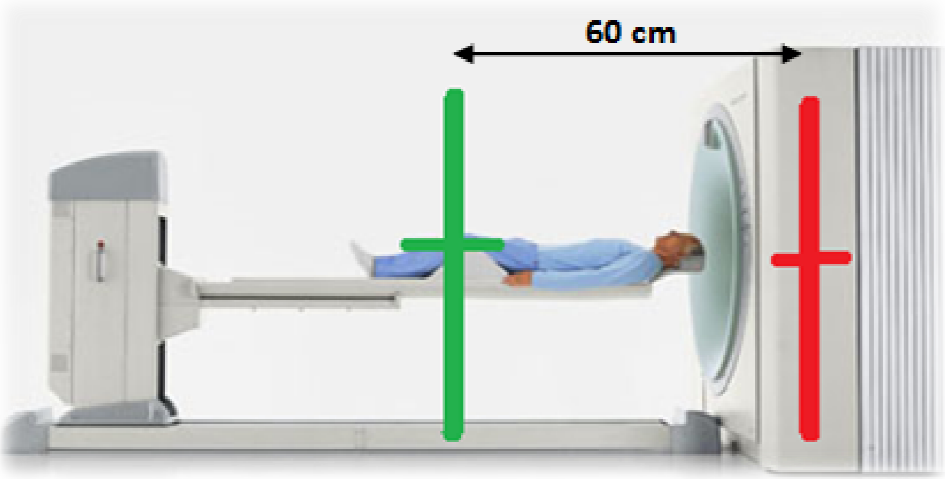


Figure 44 – Representation of the two laser systems needed for radiotherapy planning with PET/CT and the exact distance that separates them.

Guided by the external laser system, the patient's isocentre alignment marks are first defined using a black ink and then, using a small blood sample lancet, the point where the three coordinates meet is marked with a small tattoo, after asking for the patient's consent (Figure 45). If a mask or vacuum-form body immobiliser is being used, the permanent marking can be done on the immobilisers instead, with a permanent pen. Isocentre alignment marks are essential for the reproducibility of the patient's positioning on the subsequent treatment sessions.

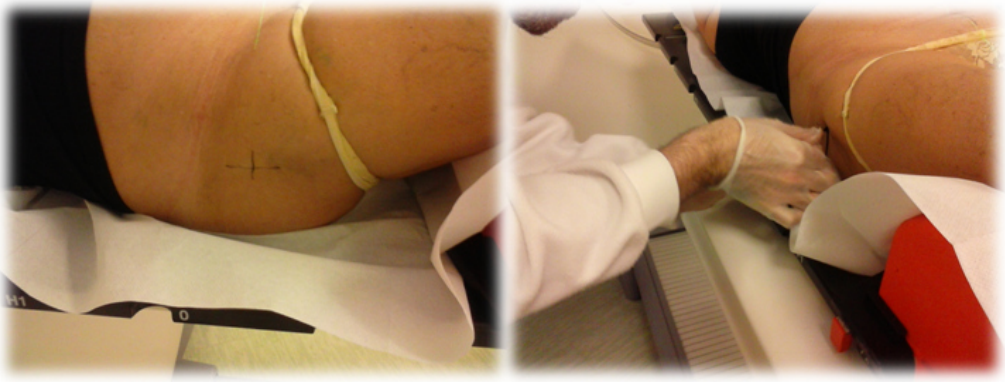


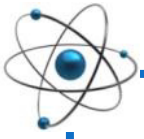
Figure 45 – The alignment marks are first defined with a black ink pen, following the external laser system lights (image on the left) and then the tattoo is made with a single quick, small prick in the middle of the drawn cross. After, the drawn cross must be removed with an alcohol swab and it has to be confirmed that the tattoo can be seen.

Before ending the appointment, it's recommended to photograph the layout, with the patient still positioned and immobilized, keeping the photographic documentation as reference in the patient's file.

3.3. Problems/challenges regarding PET/CT scans for RTP

When performing a PET/CT scan for radiotherapy planning, there are many challenges that the professionals need to overcome in order to perform a high quality examination, obeying the rigorous positioning of the patient required for radiotherapy planning.

Besides the usual problems that can always occur when dealing with debilitated patients, the fact that it's used a normal PET/CT scanner for examinations where immobilization devices are used, can aggravate the conditions under which the exam is performed, requiring a great preparation of the doctors and technicians involved.



3.3.1. Problems related to the equipment:

- The size of the gantry vs. the size of the immobilization devices
- Adjustments on the height of the couch of the PET/CT scanner
- Adjustments on the length of the scan
- Weight limit of the PET/CT scanner
- The external laser system

3.3.2. Patient-related problems:

- Problems related to the general health and age
- Respiration and organ motion

3.3.3. Other

3.3.1. Problems related to the equipment

The size of the gantry versus the size of the immobilization devices

The most evident challenge when performing a PET/CT examination for radiotherapy planning is fitting the patient, positioned in adequate immobilization devices, inside a relatively narrow gantry (Figure 46).

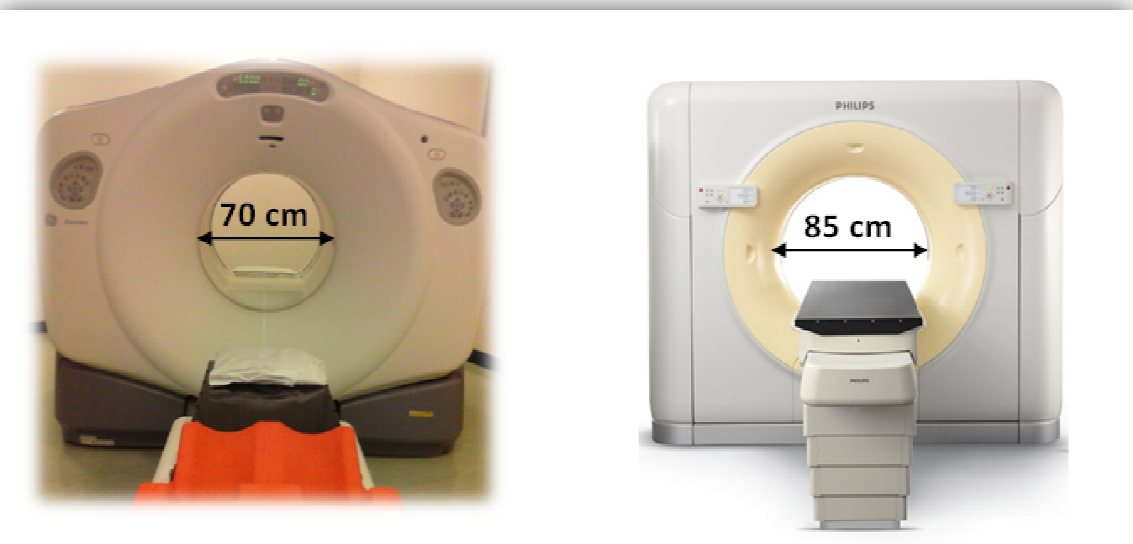


Figure 46 - Comparison between two equipments used for RT planning, with apertures of different sizes. On the left, there is the PET/CT scanner used at the Sant'Orsola Polyclinic, Discovery STE (16 slice) 3D from GE, that has a 70 cm aperture bore. On the right, is presented the Brilliance CT Big Bore from Philips, which is the industry's only 85 cm aperture bore.

Combined PET/CT scanner designs vary among different vendors. The most common PET/CT scanner has a gantry with approximately 700 mm of diameter; however, the PET portion of the scanner can have a gantry opening ranging from 600 to 700 mm in diameter (42). This difference in size is attributed to the importance of optimizing the image quality of the PET scan; that's why stand-alone PET scanners have a relatively small gantry bore opening (typically 550-600 mm) and were not really designed to accommodate radiotherapy patients in treatment positions with immobilization devices (43).

These evidences mean that some of the commercial scanners have a non-uniform gantry opening as the patient travels from the CT portion to the PET side of the scanner (43). This design feature can severely limit the size of immobilization devices that can be used and the patient's adopted position.

Specifically for radiotherapy planning, it would be ideal to use a scanner with an extra-large gantry opening, having the same diameter throughout the scanner. Currently a PET/CT scanner with a 760 mm diameter gantry opening is commercially available (5). However, the majority of the institutions don't think it justifies, just yet, investing on

specific PET/CT equipment for RT planning, once a usual scanner can in most cases be adapted.

The most challenging examinations are the ones where a Wing Board or a Vac-Lok has to be used.

The Wing Board keeps the patient's arms outside of the area of interest for the examination, having the arms to be positioned above the head with the elbows flexed (Figure 47).

Figure 47 – Patient positioned using a Wing Board device for radiotherapy planning (44).

In some patients it can be a problem because in this position he/she may not be able to go through the gantry. So, the technicians have to pay extra attention when positioning the patients in this type of immobilization device, or whenever the arms have to stay above the head, making sure the patient fits comfortably inside of the PET/CT gantry without moving or taking his/her arms out of the device or hitting the gantry.

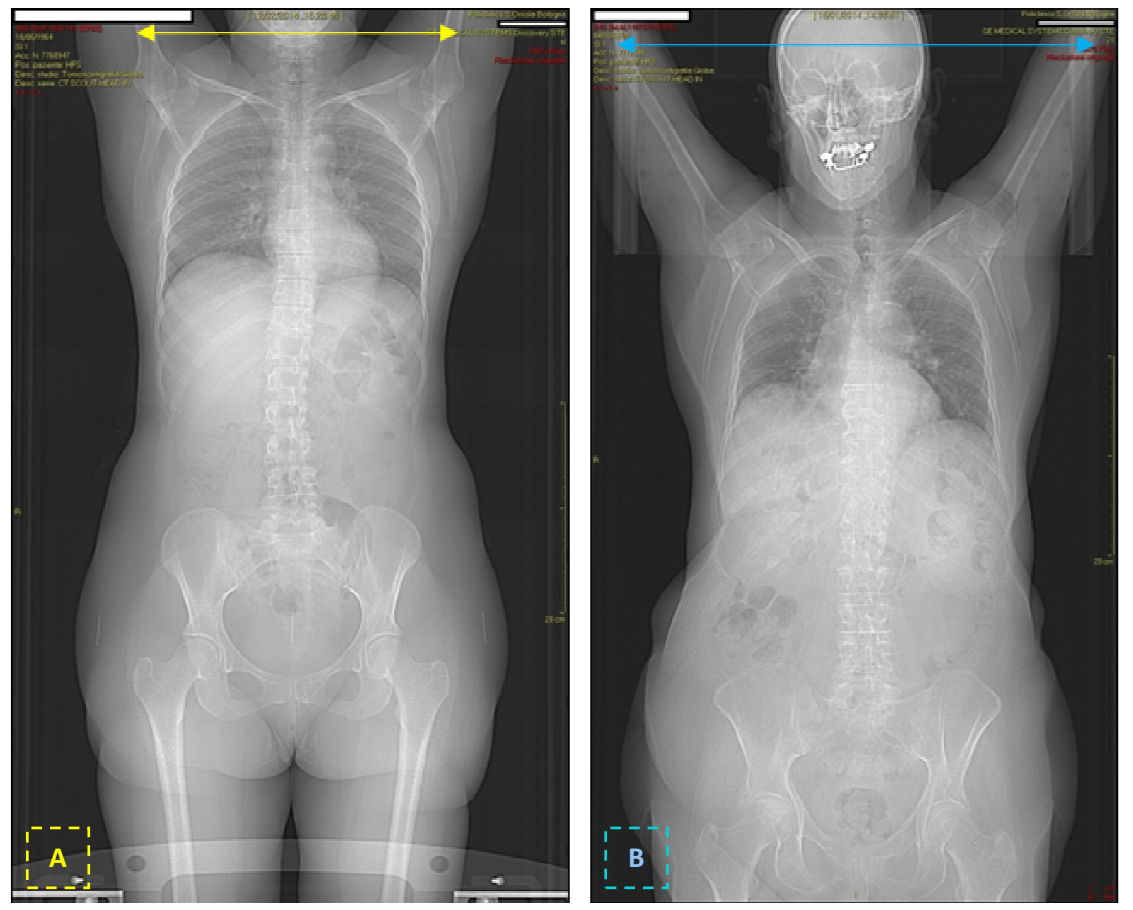


Figure 48 – Scout images of two different patients, positioned with their arms above their heads, without being immobilized (A) and using a Wing Board (B).

Above are shown two scout images of different patients and examinations (Figure 48). The patient from image **(A)** was diagnosed with cervical cancer in stage III and was immobilized just using a Combifix for the treatment planning PET/CT scan and asked to place her arms above the head. The patient from image **(B)** had pancreatic cancer and was immobilized using a Wing Board together with a Kneefix.

To compare the space both patients occupied inside of the gantry of the PET/CT scanner, was used a free software for image processing and analysis in Java, called *ImageJ*. Images from both PET/CT examinations were provided by the Nuclear Medicine Department of the Sant'Orsola-Malpighi Polyclinic for this study, under the condition that the patient's identity would be protected.

Using *ImageJ* and its analysis feature, the scale of the images was set on the software and the distances indicated on the previous images were calculated in millimetres. The results are shown bellow (Figure 49).

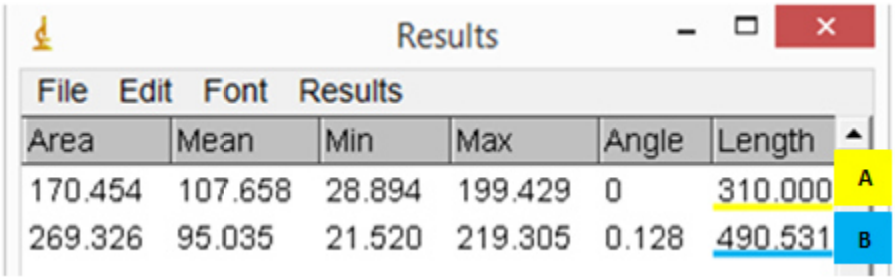


Figure 49 – Measurements obtained with *ImageJ* concerning the indicated distances on Figure 48.

Out of the 700 mm gantry bore, patient B occupied almost 500 mm with his arms positioned on the Wing Board device, while patient A used less than half of the available space; which confirms that there is a risk of a patient not being able to fit in the gantry using this immobilization device, if the patient is larger, has bigger arms or is not positioned correctly.

When using a Vac-Lok, the problems that can occur are much more challenging. Due to its size, it occupies a larger space inside the gantry, comparing with other immobilization devices, which can be a problem causing the patient not to fit through the gantry opening once immobilized (Figure 50).

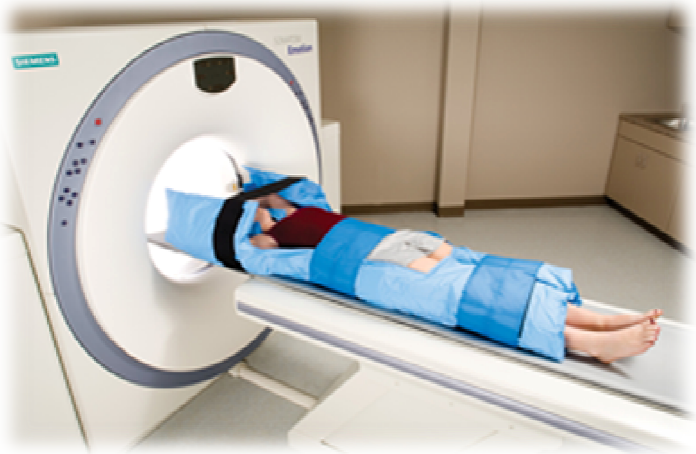


Figure 50 – Patient immobilized with a Vac-Lok, ready to start a planning CT scan. It is visible that the immobilized patient barely fits through the opening (45).

However, the difficulties that the technicians face are not only regarding the width of the gantry or if the patient is able to go through it with his/her arms on the Wing Board. When positioning the patient, the technicians also have to be careful about the patient being able to go through the gantry adjusting the couch in terms of height, especially when a Vac-Lok is being used, considering its thickness. Furthermore, they have to take into consideration that the PET/CT scanner has particularities regarding the height of the couch, as explained previously, which is an additional complication.

PRACTICAL EXAMPLES

Performing an examination for radiotherapy planning requires much more than the use of immobilization devices. As referred, to prepare the PET/CT scanner for this examination, the couchtop has to be changed for one made out of carbon fiber, more rigid and completely flat. However, this change has implications.

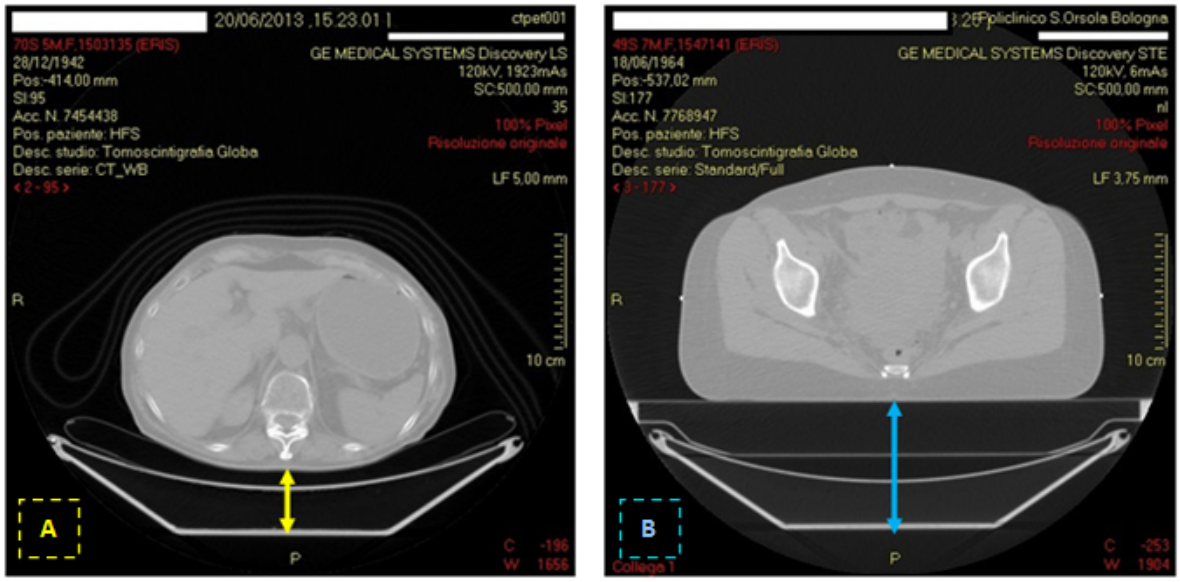


Figure 51 – Images from two different examinations, with a standard couchtop (A) and a carbon fiber couchtop for Radiotherapy planning (B).

Comparing two slices from two different exams, a diagnostic PET/CT scan **(A)** and a PET/CT scan for radiotherapy planning **(B)**, was measured the difference in height when using the two different couchtops (Figure 51). The results are shown on the next page (Figure 52).

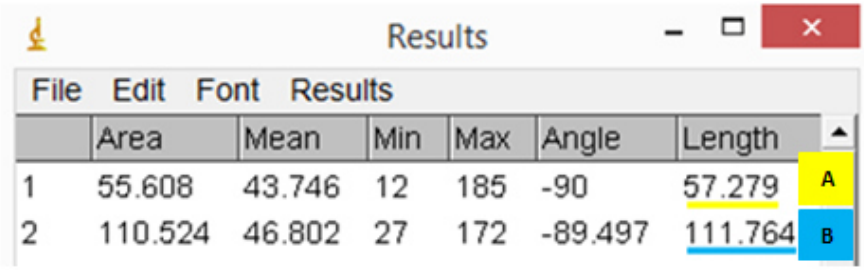


Figure 52 – Results obtained with *ImageJ* regarding the distances indicated on Figure 51.

The results show that when using a carbon fiber couchtop there is an increase in height (approximately 54 mm) that can make a difference when using bigger immobilization devices, like a Vac-Lok, or in obese patients; potentially creating problems for the patient to fit inside the gantry or requiring an adaptation on the height of table, in order for the scanner to start the examination.

The only devices that can be used without any problems are the Kneefix and the Combifix, since a standard examination does not study below mid-thigh.

Adjustments on the height of the couch of the PET/CT scanner

For the PET/CT scanner to start acquiring, the table needs to be at a certain height, normally set around the 140 cm mark; since when it is above or under this value the equipment won't start working because the patient might be at risk.

This may be a problem, especially when a Vac-Lok is being used, because the marking was already completed at the radiotherapy department, when it was being prepared, and the isocenter will be lost if adaptations are necessary. So, often the height has to be altered and the marking has to be redone in order for the scanner to start acquiring and correctly perform the examination.

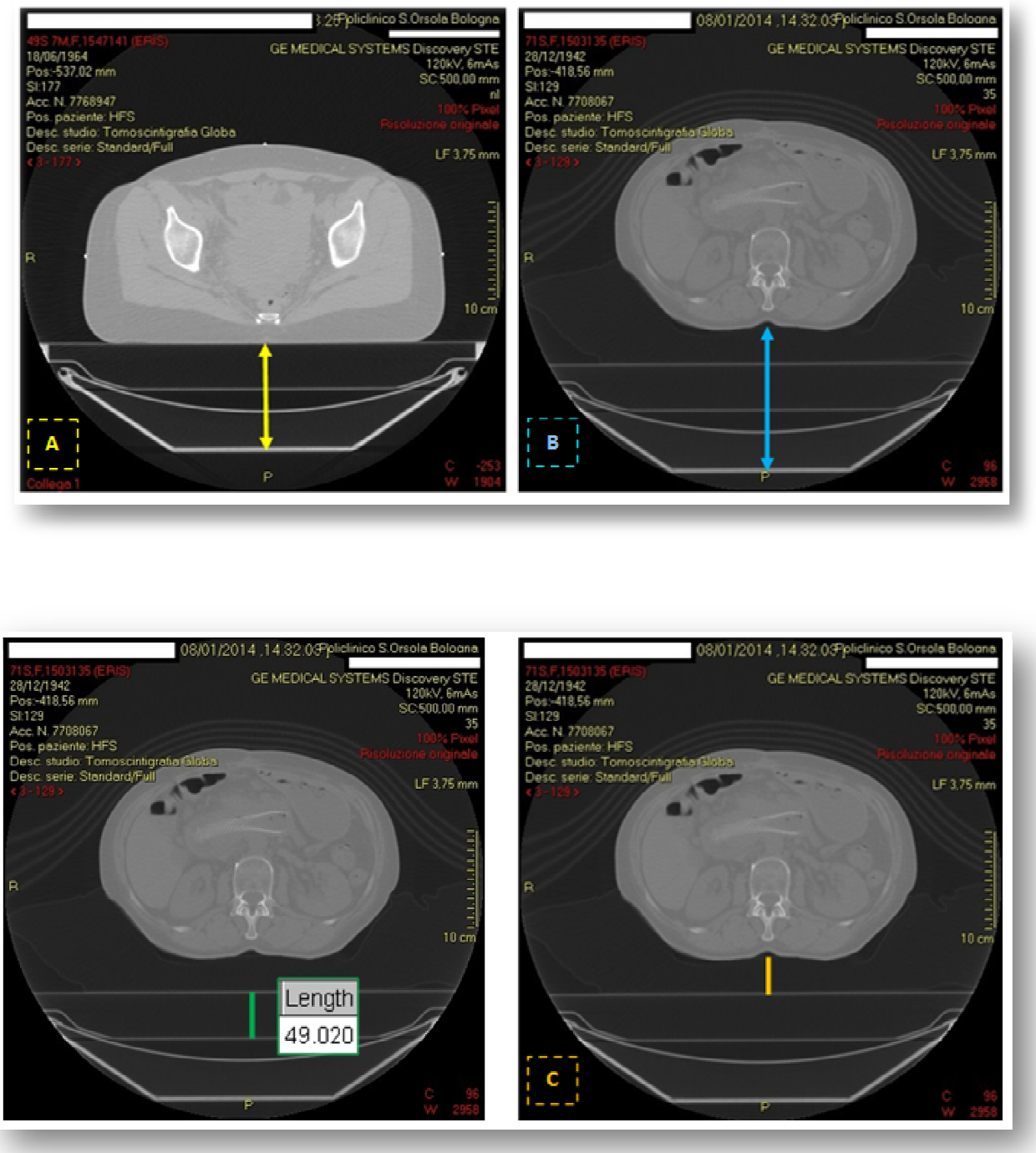


Figure 53 – Images acquired in examinations for RTP where a Vac-Lok was being used (B, C, D) and without this immobilization device (A) for comparison.

In order to verify alterations in terms of height, two images from two different examinations were compared. As confirmed previously, the carbon fiber couchtop used for radiotherapy

planning is much thicker (approximately 49 mm) than the one used regularly for diagnostic PET/CT scans; but normally this isn't a problem, unless the patient is obese.

Using *ImageJ*, different distances were calculated with the purpose of showing the changes in height. The obtained results are shown below (Figure 54).

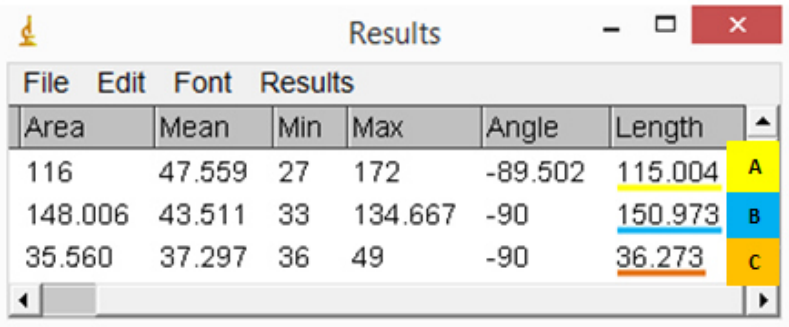


Figure 54 – Results obtained using *ImageJ*, regarding the indicated distances on Figure 53.

When a Vac-Lok is being used these extra millimetres of height can have a big impact on the examination, because we have to consider the thickness of the device together with the thickness of our patient. Images **(A)** and **(B)** clearly show the difference that is confirmed by the results.

For this comparison, the slice chosen from patient **(B)** was the thickest part of this particular Vac-Lok. This case was one perfect example of what problems can occur when the height of the couchtop can't be set at the 140 cm mark, in order to match the external laser lights with the marks already drawn on the device in the radiotherapy department. All the preparations for the scan were done, when the PET/CT wouldn´t start the acquisition. After discovering that the height of the table was the cause for this malfunction, the radiotherapy technicians had to erase the marks and re-do them, which increased the time of the examination and the exposure of the technician to the radioactive patient.

Adjustments on the length of the scan

As explained, a standard PET/CT examination includes the area between the orbits (if the head is not the target region, if it is, the complete skull is studied) to the mid-thigh region. But when a thermoplastic mask is being used, pared with a base plate and a headrest, the first fixation slot in the carbon fiber couchtop is 31 cm (310 mm) away from its extremity (Figure 55). So, because of that gap, in taller patients the length acquisition may need to be shortened, excluding possible areas of interest.

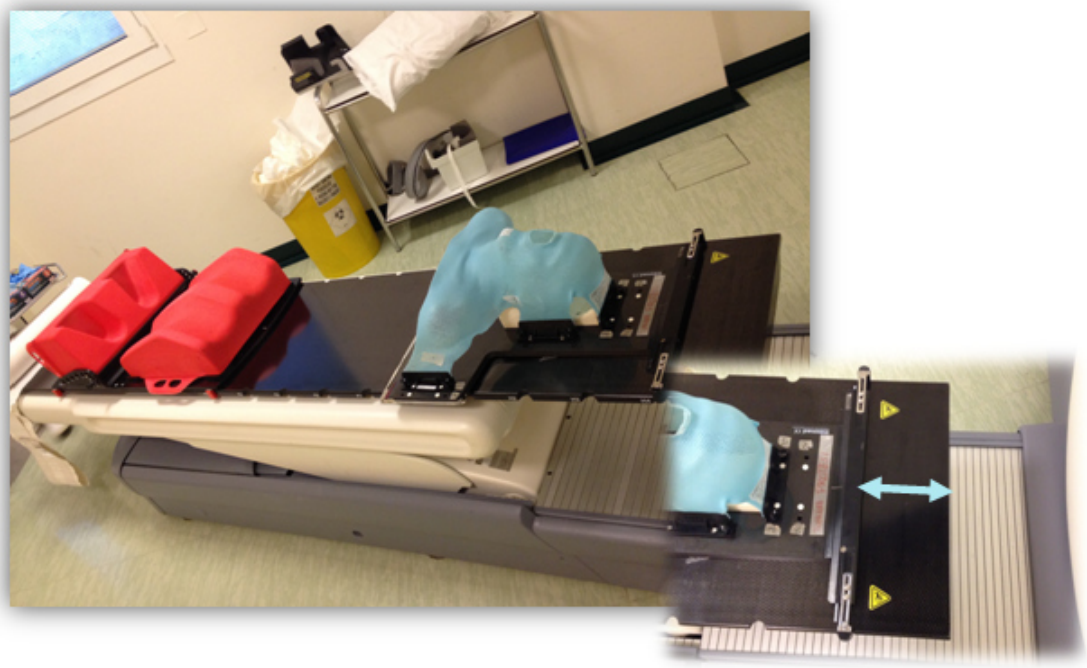


Figure 55 – Pictures taken at the Nuclear Medicine Department of the Sant'Orsola-Malpighi Polyclinic, when the PET/CT scanner was being prepared for a treatment planning examination, where the patient was going to be immobilized with a mask and the Combifix. The blue arrow identifies the distance that cannot be utilized because of where the base plate insertion is located.

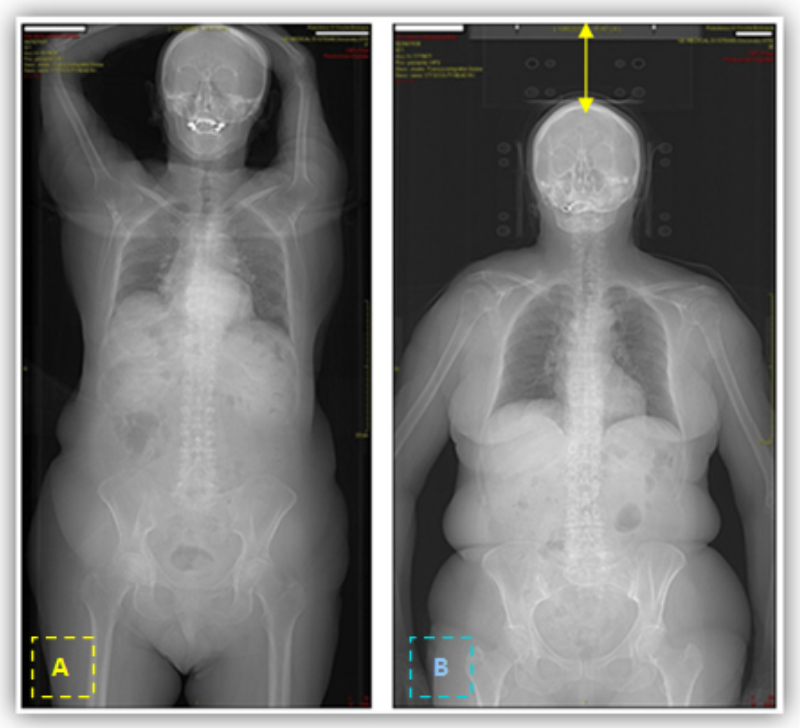


Figure 56 – Scout images from different examinations including the skull. On image (A) the head was not immobilized and on image (B) was used a thermoplastic mask.

On figure 56, images **(A)** and **(B)** are scouts from a diagnostic PET/CT scan and a scan for radiotherapy planning, respectively, both including the skull. Comparing the images, it's understandable what difference it makes, in terms of length, when the patient has to be immobilized with a thermoplastic mask. Despite the 310 mm that are lost because of where the base plate is inserted on the couchtop (Figure 55), more scan length is lost between the beginning of the base plate and the headrest (Image **B**). Using the analysis function on *ImageJ*, that distance was measured.

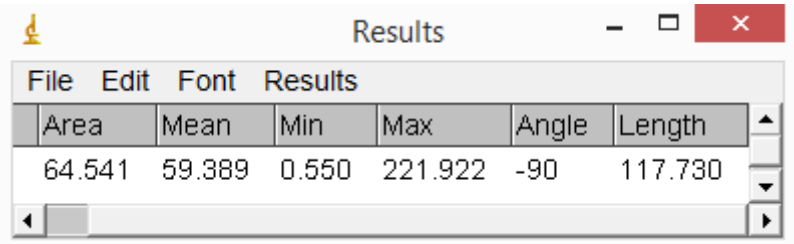


Figure 57 – Distance lost between the beginning of the base plate and the headrest when a thermoplastic mask is being used.

It was concluded that besides the 310 mm, another 117 mm are lost (427 mm in total). Because of this gap, in taller patients the scan length may have to be shortened. This happened on patient's **(B)** examination, where the last step could not be acquired and the scan had to finish before reaching the mid-thigh area.

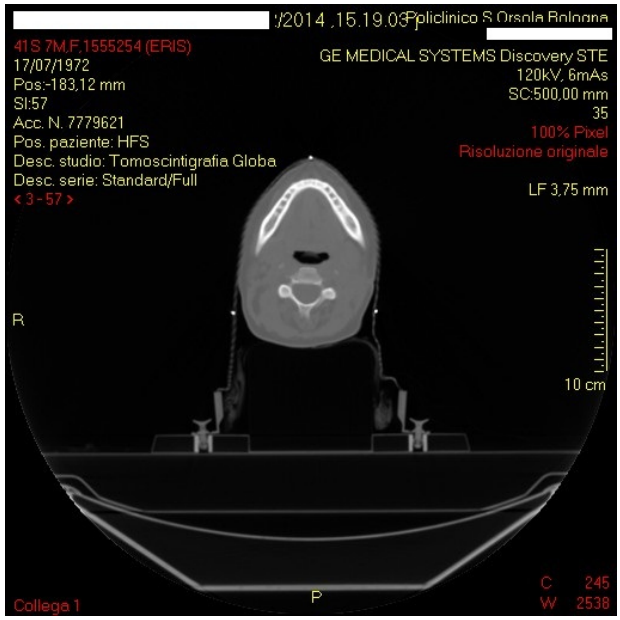


Figure 58 – Slice of a PET/CT examination for radiotherapy planning, where the metal pins placed before the scan are visible as well as the structure of the base plate and the contour of the mask and headrest. This patient was diagnosed with thyroid cancer.

Weight limit of the PET/CT scanner

Positioning an obese patient for a PET/CT scan may be very challenging, but prepare him/her for a radiotherapy planning examination is very problematic because all of the problems explained above are worsened.

First of all, the couch of the PET/CT equipment can only carry a maximum of 160 Kg, with a 5 to 10% tolerance; which may exclude the possibility of some patients to perform diagnostic PET/CT scans. This problem is even more serious when it is a scan for radiotherapy planning that requires the patient to fit in a standard immobilization device (adding up on weight) and being specifically positioned for a certain type of scan.

Usually, when a heavier patient has to perform a diagnostic PET/CT examination, the technicians first do a trial, positioning the patient on the couch and experimenting if the scanner works properly.

The external laser system

The external laser system is a key component for a PET/CT examination for radiotherapy planning. However, various problems can occur compromising its accuracy. For instance, the laser light can be out of alignment or can vary between the scanner and the treatment equipment; causing errors in the establishment of the isocenter (5).

3.3.2. PATIENT-RELATED PROBLEMS

Problems related to the general health

Although when working with machinery problems are expected, the status of the patient cannot be forgotten; especially oncologic patients, that are debilitated physically and mentally. Some challenging situations when performing the exam may be caused by difficulties in lying down because of pain, dyspnoea, coughing, nausea, agitation, anxiety or claustrophobia. Patients with dementia or mentally disabled also require extra-care (5).

Age

Besides the patient's health condition, just based on the person's age potential problems can be predicted. The patient may be a small child or a toddler needing anaesthesia, or an elderly person with reduced mobility (5).

Patients under anaesthesia or sedation need to be monitored throughout the scan, which brings several problems, due to the presence of several cables and equipment

to which the patient needs to be connected during the exam, increasing the time spent preparing the patient, as well as affecting the quality of the scan, since some materials are not adapted for this type of examination.

Because throughout the scan the table moves, the staff needs to pay extra attention to the patient and equipments, guaranteeing that the patient is never at risk.

PRACTICAL EXAMPLE

During the internship, there was one remarkable examination that due to its long preparation and difficulty, made me more aware of the real challenges professionals face when performing these types of examinations, especially on children.

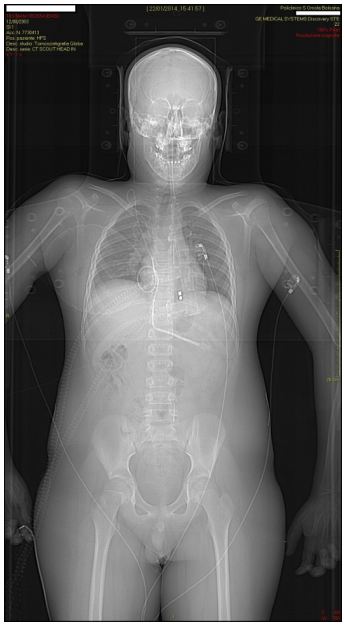


Figure 59 - Scout image from a paediatric patient where cables and intubation materials are visible.

Figure 59 is the CT scout of a paediatric patient that was immobilized using a head, neck and shoulder thermoplastic mask and the Combifix. The patient was sedated in order to stay completely still during the scan and because, as it is understandable, he was very agitated when he entered the room.

This examination required the presence of many professionals: an Anaesthesiologist, a nurse, two radiotherapy technicians, the patient's Oncologist and a nuclear medicine technician.

Preparing the patient for the scan was very time consuming because of the anaesthesia, connecting the patient to all of the equipment, position and immobilize him on the table and proceeding to all of the necessary adjustments throughout this phase.

As seen on figure 59, cables and intubation materials are visible on the scout. This was a very challenging examination due to the fact that the patient was a child and was sedated, but also because he was at risk during the exam, since he was connected to equipment outside of the scanner and there are risks associated with this fact since the table was moving. Also, another factor that motivates the professionals to be more careful and fast, is the fact that in children the anaesthetic dose administrated is light; so, if the preparation takes too long, the Anaesthesiologist may have to reinforce the dose, increasing the risk for the child, or there is a possibility that the child will wake up while the procedure is not yet completed.

In this case, it was definitely a great advantage that the all staff was well prepared and aware of all the risks and ready to handle any unexpected situations; which contributed for the success of this examination.

Respiration and organ motion

Lesions located on the thoracic or abdominal region, like tumours in the lungs, liver, pancreas and kidneys, as well as breast tumours, are the most affected by respiratory motion and represent a major challenge in radiotherapy. Also, varying amounts of content in the stomach, the intestines or the bladder contribute to the movement of internal organs and thus the target (5).

Respiratory movements cause the target area to move which creates uncertainty when defining an isocenter, as well as during treatment. What is likely to happen is that the tumour will receive a lower dose than what was intended and the surrounding healthy tissue will be exposed to an unwanted dose of radiation (5). So, in the treatment of tumours affected by respiration, their motion must be taken into account, during imaging as well as during treatment delivery.

During treatment planning, respiratory motion will also affect the quality of the examination. In a CT scan, respiratory movements can cause motion artefacts, translating in a smeared or heavily distorted image of the tumour, for example during an extreme breathing phase such as end-inspiration or end-expiration (5).

PET examinations can also be affected by motion artefacts in the form of blurring effects. The consequences are an underestimation of quantitative parameters, such as the maximum standardised uptake value (SUV_{max}), as well as an overestimation of the apparent tumour volume (5).

In PET/CT scans another problem that can occur, for example with patients that have an irregular respiration pattern, is that the lesion will appear in slightly different positions between the PET and CT images (Figure 60). For smaller lung lesions, this could cause problems during attenuation correction, causing the tumour to mistakenly appear PET negative (5).

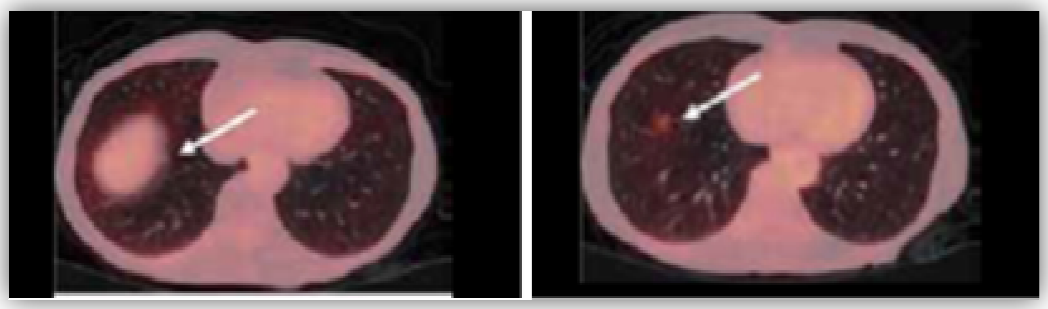


Figure 60 – Images from a PET/CT examination of a patient that experienced an irregular respiration pattern, resulting in a mismatch between the CT and PET images. The lesion is seen close to the liver during the CT scan (image on the left), but later the PET positive focus appears to have moved in the cranial direction (image on the right) (5).

To minimize the effects of respiration and organ motion some strategies can be applied. In conventional radiotherapy, movement is usually compensated by adding large margins to the treatment volume to guaranty that the tumour will always move inside a high dose volume, but healthy tissue will still be irradiated inevitably (5).

In order to reduce the probability of cardiac and pulmonary side-effects, when the tumour is located in especially problematic areas, the radiotherapy treatment can be performed with the patient at deep inspiration breath hold (Figure 61). If this approach is chosen, it can be of great advantage to also perform the planning PET/CT examination in breath hold (5).

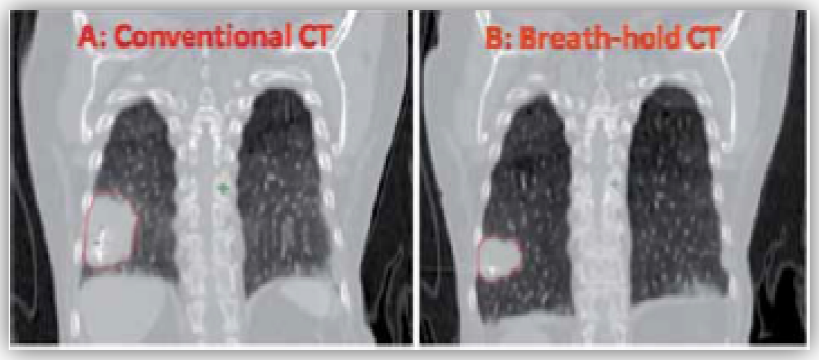


Figure 61 – Coronal reconstructions of a conventional (A) and a deep inspiration breath-hold CT scan (B), performed in a patient with a non-small cell lung cancer. Comparing the two images it's noticeable a distortion of the tumour in the conventional CT scan due to motion artefacts (5).

3.3.3. OTHER

Disease progression after the therapy PET/CT scan

In patients with a fast-growing tumour or progression of lymph node disease, a long interval between the therapy PET/CT scan and the first treatment session may entail changes in the shape of the tumour and the skin surface and the fixation device may no longer fit (5).

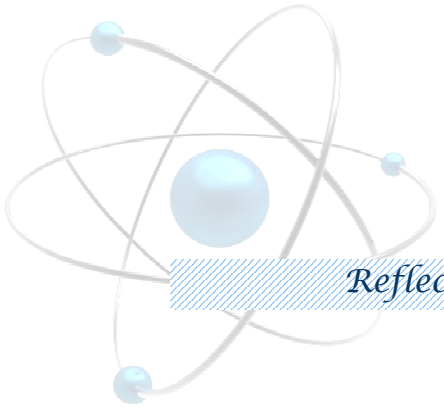
A recurrent problem is that in some cases this planning examination is the only PET/CT scan the patient does and many times it completely changes the treatment intentions, if metastases are found or secondary tumours. The exam is then useless and the time the technicians spent preparing the immobilization devices, positioning the patient,

marking, etc., was in vain. Approximately 40 minutes were spent preparing a planning PET/CT scan, when a diagnostic scan would only take 15 minutes.

Professionals exposed to radiation

Although the security of the patient and the wish to perform a high-quality planning examination are the main concerns for the health professionals, it cannot be forgotten that the all staff faces risks during this type of examinations, unlike when the treatment is planned using a CT scan. Since in this type of planning examination the professionals are exposed to radiation during the all preparation process, the longer it takes to position the patient and solve problems, the higher will be the dose received by the professionals. This is much more worrying if in the end this examination was inadequate for that specific case.

To save time preparing for the scan, it's very important to think about potential problems beforehand and act more efficiently, if necessary.



Reflection about the future of PET/CT for RTP

PET/CT for radiotherapy dose planning will most likely in the future substitute planning CT scans for several treatment techniques (such as IMRT, stereotactic radiation therapy and proton therapy). The fact is that PET/CT often leads to alterations in the previously defined tumour size and staging (regional and distant metastases are in some cases detected during the exam, as well as other synchronous malignancies) often leading to changes in the treatment modality, which can be the addition of concomitant chemotherapy or surgery, cancellation of radiotherapy or even a switch to other treatment strategies (5). Therefore, if the PET/CT examination is performed earlier on, less time will be wasted preparing for a treatment that may not be adequate for the patient's condition.

Instrumentation

Besides a necessary modification in the physician's way of thinking when planning a patients' course until the start of a treatment (as discussed in the previous chapter), an improvement of the PET/CT imaging techniques for radiotherapy planning must also take place. Currently, PET/CT scans are being performed with low-dose CT, but this type of scan cannot be used for planning since it does not allow precise tumour delineation or the definition of organs at risk. An effort to improve PET/CT examinations for radiotherapy planning would include a high quality CT scan with intravenous and oral contrast media, if relevant, and a slice thickness of 2 mm (5). Also, the acquisition of scanners with larger gantry openings would facilitate the immobilization and positioning of the patients, as mentioned previously.

Being respiratory motion a true challenge in radiotherapy dose planning, it's excellent that imaging strategies able to correct or account for respiratory movements are becoming more widespread and have shown considerable potential for radiotherapy applications, given that motion management can improve the accuracy of tumour volume definition, in both CT and PET, or of quantification in PET images (Figure 62).

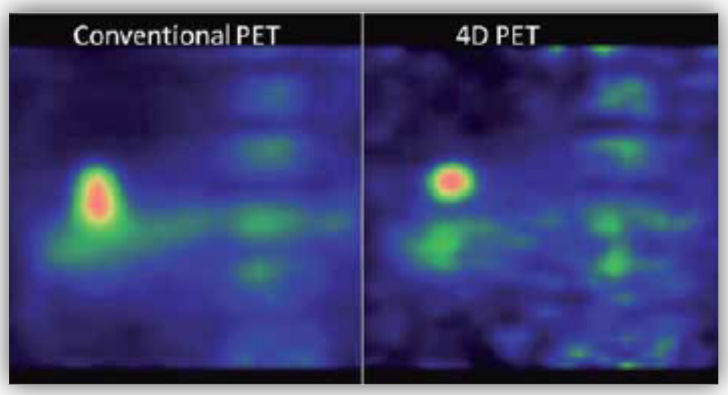


Figure 62 – Images of the same lung tumour studied in a conventional PET examination (on the left) and a 4DPET (on the right). The uptake area is noticeably blurred in the conventional image due to breathing artefacts (5).

Four-dimensional CT (4DCT) is an imaging technique that combines CT information in the three spatial dimensions with time as the fourth dimension, visualising the tumour as a function of time during a respiration cycle. An advantage of using a 4DCT scan for respiratory gated RTP is that the tumour motion pattern can be used to select the most optimal gating phase. However, despite the notorious advantages, the dose delivered during a 4DCT acquisition is significantly high (5).

As mentioned in the previous chapter, a breath-hold CT scan used for planning of breath-hold RT is a good option to minimize the effects of respiratory motion, with a much lower dose to the patient (Figure 63). For this reason, 4DCT is normally not preferable for patient groups where the optimal gating phase is predictable (5).

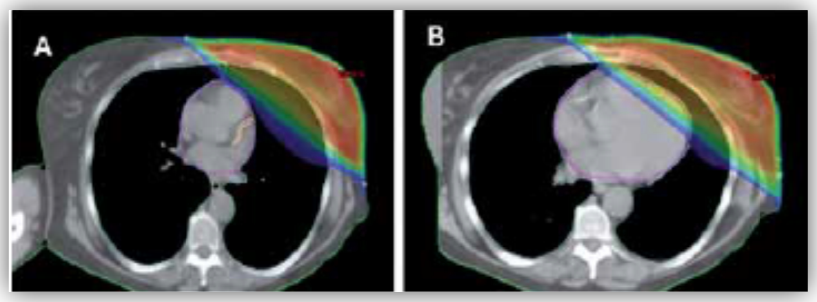


Figure 63 – Transverse reconstructions at mid-breast position from the same breast cancer patient. (A) Image from a deep inspiration breath-hold CT and (B) from a conventional CT scan. The cardiac structures are moved away from the chest wall, being pushed in the caudal direction, when the lungs are inflated. The coloured region represents the areas covered by the radiotherapy fields (5).

Although 4DCT provides information about the tumour over the whole breathing cycle, single-phase (gated or breath-hold) approaches may be preferred depending on the treatment strategy for an individual patient (5). Still, respiratory motion management during a PET/CT examination will likely have a prominent role in the adoption of new treatment paradigms, such as tumour tracking and "dose painting".

This new paradigm, called "dose painting" is gaining interest in radiotherapy. Using the metabolic information provided by the PET images, the tumour can be "painted" so that volumes showing a high tracer uptake (and containing aggressive cancerous cells) receive a higher dose of radiation (Figure 64) (5).

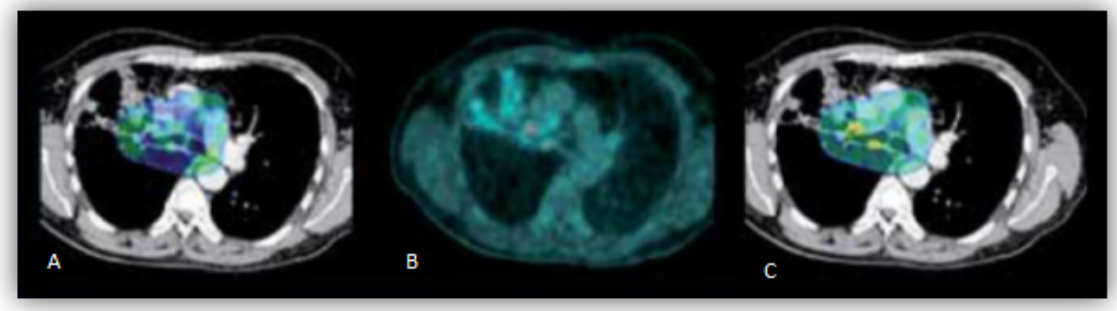


Figure 64 – Example of a simple dose painting strategy. (A) Standard treatment where the target volume receives a uniform dose. The dose distribution is represented by the blue-green colour wash. (B) Selection of high dose volumes. (C) The sub-volumes of the tumour where the tracer uptake is higher (yellow-red colour wash) receive an extra dose of radiation (5).

The greatest benefit of breathing-adapted PET/CT imaging, for radiotherapy planning, is without a doubt better target definition. It has been proved that PET/CT can reduce delineation variation by, for example, differentiating between malignant lesions and atelectasis. So, it is predictable that breathing-adapted PET/CT will further increase delineation accuracy and thereby reduce the uncertainty margin applied to treatment fields for lesions located on the thoracic or abdominal region (5).

Development of radionuclides and biomarkers

Apart from advances in instrumentation, the continued development of radionuclides and biomarkers, designed to target specific characteristics of a tissue or disease, will improve the detection, treatment and monitoring of the course of therapy.

The ability to non-invasively image cellular characteristics (membrane receptor expression, cellular processes, such as proliferative activity; protein synthesis, apoptosis and hypoxia) may serve as a platform to personalise a treatment. This personalised approach is often named **'Theragnostic' imaging**, as it combines the diagnostic and tumour characteristics to yield important information that permits optimisation and individualisation of therapy (5).

Even though FDG PET holds an important position in the study of many cancers, which will probably continue in the future, there are cases where the use of alternative radiotracers would be more advantageous. For example, physiological accumulation of FDG in brain tissue (especially grey matter) makes the distinction between normal physiological and pathological uptake difficult; the same in circumstances where imaging is complicated by inflammatory and infectious conditions, recent treatment with chemotherapy and radiotherapy, metabolic disorders and co-existing diseases. Besides, glucose metabolism varies significantly between different malignancies and for some the uptake of FDG may be similar to that in surrounding tissues (5).

PET/CT Imaging of Brain Tumours

Since PET is of limited use in brain tumours, used only in special cases (for example, cerebral lymphomas), radiolabelled amino acids have shown great promise in the evaluation of brain and head and neck malignancies, seeing that they are not avidly taken up by tumour-surrounding tissues. Early studies of ^{11}C-methionine, for imaging cancers of the head and neck as well as brain tumours, reported a high sensitivity and specificity (25). However, the relatively short half-lives of ^{11}C-labelled isotopes (approximately 20 minutes) make them unsuitable for widespread distribution and routine clinical use.

Recent studies have shown that 3',4'-dihydroxy-6'-[^{18}F]fluoro-L-phenylalaline (DOPA), an amino acid-based tracer, mostly used in the imaging of phaeochromocytoma (a neuroendocrine tumour of the adrenal gland), is more accurate than ^{18}F-FDG in the imaging of low-grade brain tumours and can better distinguish recurrence from radiation necrosis, being comparable to ^{11}C-MET in diagnostic accuracy (Figure 65). L-DOPA is a precursor of catecholamines, such as dopamine and adrenaline, and the abundant production of these hormones is a characteristic of neuroendocrine tumours.

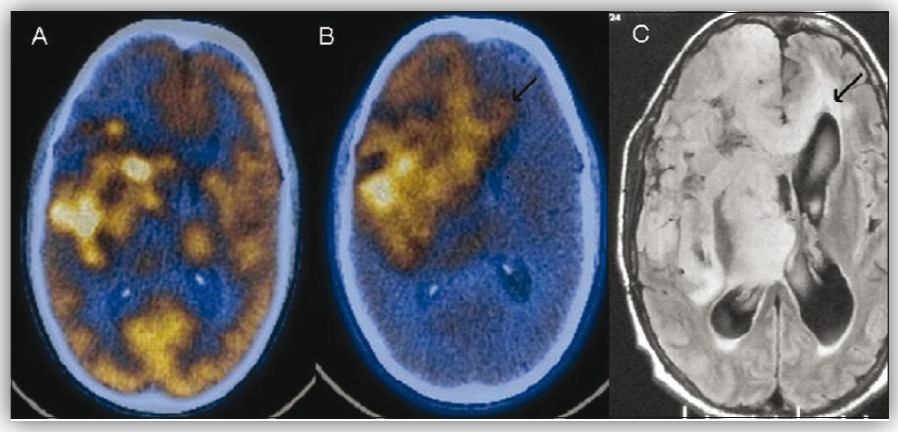


Figure 65 – Post-operative study of a low-grade right frontal astrocytoma. Image (A) corresponds to a FDG PET/CT scan, showing residual tumour in the right fronto-parietal region. Image (B) from a PET/CT scan with F-DOPA, facilitates the delineation of the actual extent of the lesion (arrow), which appears to cross the midline, as proven by the FLAIR axial MRI image (C) (46).

The clinical use of radiolabelled amino acids has recently been improved by the introduction of ^{18}F-labelled analogues such as ^{18}F-tyrosine. Studies comparing FDG with ^{18}F-tyrosine have shown that FDG may exhibit greater sensitivity, but ^{18}F-tyrosine can offer increased sensitivity, particularly when distinguishing between inflammatory and malignant lesions (Figure 66). This may be especially important when evaluating patients after radiation therapy (5).

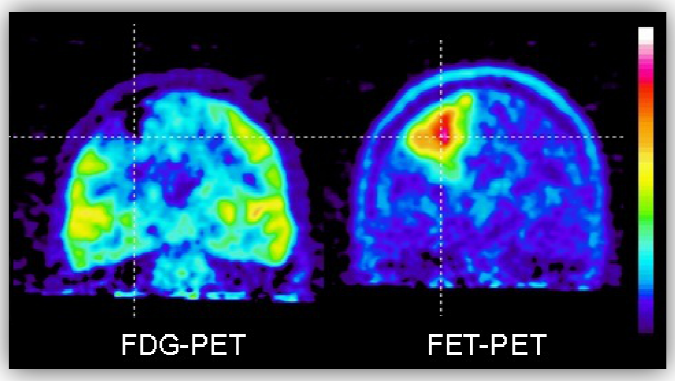


Figure 66 – Anaplastic astrocytoma grade III studied by PET/CT with two different tracers: FDG, on the left, and ^{18}F-Fluoro-Ethyl-Tyrosine (FET) on the right. FET PET allows a precise definition of the cancerous tissue (47).

Another tracer, ^{68}Ga-DOTATOC can be used as a PET tracer for the diagnosis of meningiomas. DOTATOC is very helpful for the detection of infiltration of bone structures (5).

Hypoxia

Tumour hypoxia is a negative prognostic factor, since hypoxic tumour cells are more resistant to radiotherapy and certain chemotherapeutic agents than identical normoxic tumour cells. Tumour hypoxia has been shown to increase the risk of both local recurrence and metastasis. The ability to identify tumour hypoxia may allow adjustments in the selected treatment, including modification of radiotherapy to increase doses to hypoxic regions, or chemotherapy to potentially improve therapeutic outcomes, or even the use of radiosensitizers (5).

Cu-ATSM is among the most promising tracers for non-invasive hypoxia imaging. Cu-ATSM PET studies have reported high intratumoral contrast, high membrane permeability and rapid blood clearance. It has been suggested that hypoxia-guided IMRT, based on PET images using hypoxia radiotracers, can serve as a basis for dose escalation of radiation to the hypoxic tumour sub-volumes (Figure 67) (5).

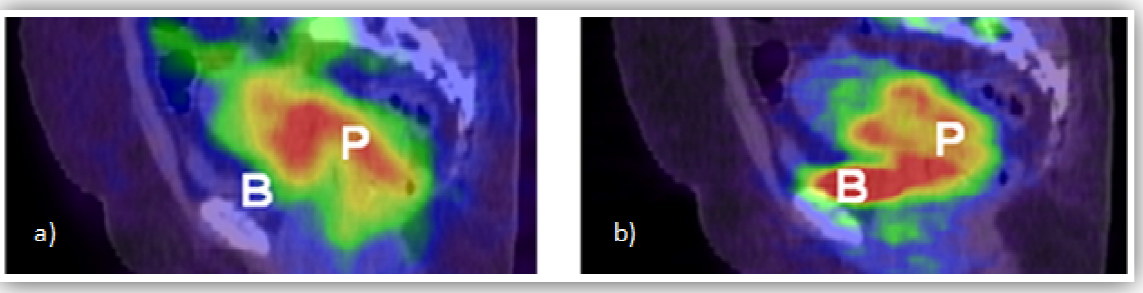


Figure 67 – Sagittal reconstructions from the same hypoxic tumour. a) ^{18}F-FDG PET/CT image, showing an intense ^{18}F-FDG uptake in the known primary cervical tumour (P). b) CU-ATSM PET/CT image, at the same level, also shows an increased tracer uptake. Note that there are different uptake patterns between the two tracers. B = Urinary bladder (48).

Other

^{18}F-fluoroestradiol is an example of a PET imaging agent which can provide important quantitative non-invasive biological information on breast carcinoma cell's oestrogen receptor status (5).

Another ^{18}F-labelled analogue, ^{18}F-fluorocyclobutyl-1-carboxylic acid (ACBC), has shown effectiveness in imaging prostate cancer. It is believed that ^{18}F-ACBC is transported intracellularly via a Na^+ amino acid transporter that is over-expressed in prostate cancer tissue (5).

Tracers like ^{18}F-3'-deoxy-3'-fluorothymidine (FLT) that visualise cell proliferation are currently under research and might prove to be a valuable tool in response assessment, but are not yet used in clinical practice. FLT enters the exogenous DNA pathway as a specific substrate for a principal enzyme in the salvage pathway of DNA synthesis (thymidine kinase 1,TK1) and reflects cellular proliferation (46). Recent studies have demonstrated the potential of ^{18}F-Fluorothymidine (FLT) imaging in

conjunction with radiotherapy in the evaluation of therapy, in addition to the detection and evaluation of tumours. Because FLT is accumulated in proliferating cells, it has been used to detect radiation-induced repopulation of cancer cells. It is possible that FLT PET could permit early evaluation of therapy, being used during the course of radiotherapy, and thereby allow for alterations and optimisation of treatments and protocols (Figure 68) (5).

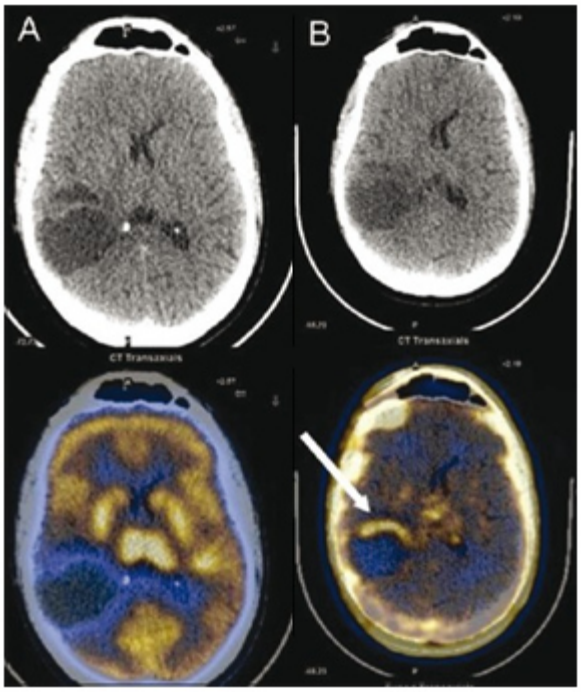


Figure 68 – Patient suffering with a grade III glioma, postoperative examinations. (A) FDG PET/CT image showing no abnormal tracer uptake at the operative site. (B) FLT PET/CT image shows evidence of tumour recurrence anteriorly at the periphery of the lesion (arrow) (46).

More disease-specific tracers are emerging and their roles as radiotracers are constantly increasing. These new radiotracers can be put into categories according to those that optimize tumour detection, that are used for tumour delineation and staging and those that provide information for evaluation, optimisation and individualisation of therapy (5).

New tracers, for example for prostate and brain cancer, will undoubtedly increase the use of PET/CT for radiotherapy planning in the future; as well as the ability of new tracers to deliver information on prognostic parameters such as hypoxia and tumour

cell proliferation. Additionally, it is of great importance to find new tracers for inherent tumour radiosensitivity, which seems to be a significant prognostic factor for local control of carcinoma of the cervix and head and neck malignant tumours (5).

As predicted by the International Atomic Energy Agency (IAEA) expert report 2006-2007, whole-body FDG PET/CT scanning is revolutionizing radiotherapy planning and becoming the examination of choice for many different tumours (43).

In my opinion, it is the close collaboration among nuclear medicine physicians, radiologists, radiation oncologists and physicists that can dictate the success of a radiotherapy treatment, planning and concretization, and mostly, innovate in this field. By sharing knowledge, experiences and difficulties, solutions can be found; by working together, these experts can grandiosely improve radiation therapy.

Conclusion

Integrating PET/CT into the planning of radiation therapy is readily achievable. Upfront, PET/CT impacts the treatment goal of radiotherapy through improved staging. Next, it optimizes the treatment plan to increase the radiation dose to the tumour and decrease the dose to sensitive organs (improving the therapeutic ratio). After the treatment, PET/CT can be used to monitor the response to therapy and assess for recurrence.

However, the introduction of PET images into the treatment planning procedure remains a challenging issue. The use of ^{18}F-FDG PET for target volume selection should be considered within the framework of its sensitivity and specificity for various tumour types. Given the considerable ranges of accuracy of FDG PET across different tumours, its role will not be identical in different tumour locations.

Although it is now widely accepted and acknowledged that PET/CT significantly impacts treatment planning, a new modality such as PET must be integrated into this knowledge base, with decisions on treatment modification, based upon probabilities of false positive and negative data within particular structures and locations. Before proper validation of the use of various PET/CT tracers has been performed and all of the methodological aspects have been fully optimized, it is reasonable to state that the use of PET for treatment planning should not be routine for every oncologic patient but used on specific cases, selected by the radiation oncologists.

'Theragnostic' imaging with various molecular imaging probes is an emerging and exciting area of research that has the potential to revolutionize the practice of radiation oncology in the future and the nuclear medicine technicians are a key-element in this process, since they have an exclusive knowledge about their current difficulties when adapting PET/CT scanners and protocols for radiotherapy planning examinations.

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Appendix

This appendix includes images of different immobilizers and information regarding their dimensions to allow a better understanding about some devices used in radiotherapy planning. It is particularly interesting in order to attest some affirmations made during this dissertation regarding the difficulties faced when adapting PET/CT scanners for radiation therapy planning.

It is divided in seven sections:

Section A includes the measurements of different couchtops of a few brands;

Section B shows different types of thermoplastic masks for adults and children and includes descriptions, as well as their thicknesses;

Section C contains information regarding different types of Vac-Lok cushions, including their dimensions, different finishes and pictures;

Section D displays some support cushions and wedges that can be used in conjunction with other immobilization devices;

Section E shows different types of Wingboards, referring their dimensions and explaining their differences;

Section F includes information regarding a specific type of immobilization device, a carbon fiber Bellyboard, and shows a new type called Contoura Bellyboard. It also shows support equipment for patients that have to be positioned in prone, named Prone Thorax Support;

Section G is about the Combifix and includes its components and measurements.

All of the information and images are from the **CIVCO Medical Solutions catalog:** Solutions Guide Volume 2.0 (available online) (17).

A. Couchtops

CT Overlays

Carbon fiber overlays securely lock onto a cradle, providing a surface consistent with treatment couchtops. They are lightweight and durable, allowing them to be easily removed or reinserted for use on non-dedicated imaging machines.

Indexable carbon fiber couchtops and overlays provide a radiation-friendly base, creating fewer image artefacts and more treatment plan options.

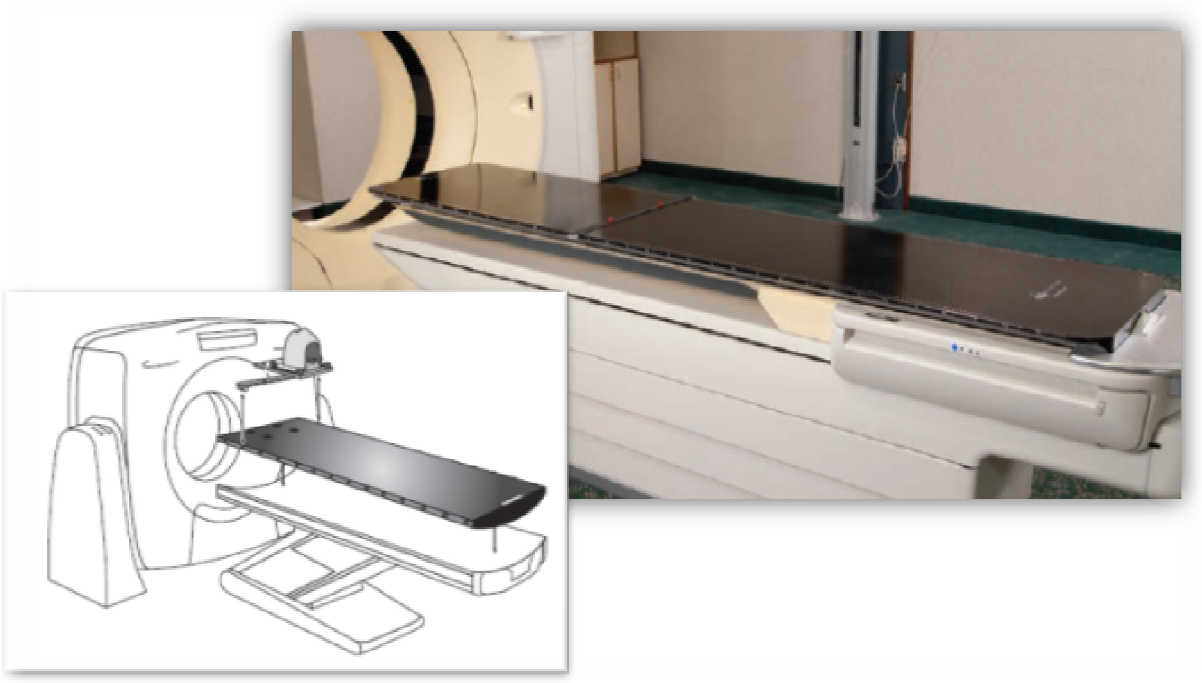


Figure A.1 – Image of a carbon fiber couchtop and illustration of how it is placed on the equipment and how immobilization devices can be attached to it.

Description	Dimensions
Overlay Siemens	200 x 49.5 x 2.9cm
Couchtop Siemens	200 x 53 x 2.2cm or 193 x 53 x 5.4cm
Nucletron Simullx Couchtop Siemens	252.6 x 53 x 7cm
Nucletron Simullx Couch Insert Siemens	90 x 53 x 2.1cm
Siemens Biograph	239 x 53 x 2.7cm
GE HiSpeed Advantage, HiSpeed CT/i & LightSpeed QX/i	229 x 53 x 5.1cm
GE Discovery LS	266 x 48 x 4.8cm
GE Discovery ST (H-Power Base)	266 x 53 x 4.8cm
GE LightSpeed VCT & Discovery ST (Global Base)	217 x 53 x 5.1cm
Philips / Marconi MX8000	245 x 53 x 3.2cm
Philips Gemini PET/CT	253 x 48 x 3.7cm or 253 x 53 x 3.7
Toshiba Aquilion (Short)	201 x 53 x 4.2cm
Toshiba Aquilion (Long)	231 x 53 x 4.2cm
Toshiba Aquilion One	252 x 53 x 2.6cm

Table A.1 – Different types of couchtops from several brands and their dimensions.

- ***Tranquillity Series Thermoplastic Masks*** were designed with patient comfort and 3D tracking in mind. These masks feature a unique open pattern, balanced with a traditional rigid mask design.

Image	Description	Thickness
	**FreedomView** IMRT Style 18, Head Only: Pre-cut eye and mouth holes, increasing patient comfort and setup efficiency	3.2 mm
	**FreedomView** IMRT Style 27, Head Neck & Shoulders	3.2 mm
	**ClearVision**, Head Only: Open face mask designed to use with vision/camera system	3.2 mm
	**PureVision**, Reloadable, Head Only: Open face mask designed to use with vision/camera system; separate reinforcing thermoplastic strips included.	3.2 mm

Table B.1 – Different types of thermoplastic masks and their thickness.

- ***ZENTEC*** thermoplastics require less heating time and produce a mask that more closely captures the contours of the patient, resulting in a comfortable cast of the patient.

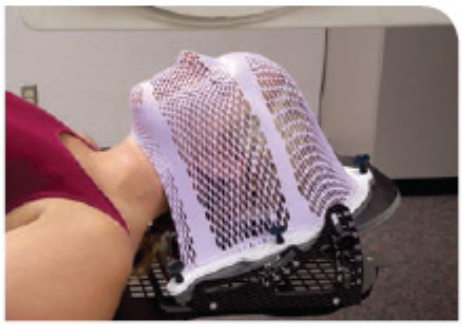


Image	Description	Thickness
	**ZENTEC** IMRT Style 18, Head Only	2.4 mm or 3.2 mm
	**ZENTEC** IMRT Style 27, Head Neck & Shoulders	2.4 mm or 3.2 mm

Table B.2 - Different types of thermoplastic masks and their thickness.

In the 2.4 mm thickness, these masks provide a lighter feeling, which offers a more pleasant experience for anxious patients. ZENTEC thermoplastic in 3.2 mm provides a highly conforming mask with increased rigidity.

- ***IMRT Reinforced Thermoplastics*** feature a combination of perforated and solid thermoplastics to provide rigidity and secure immobilization for IMRT treatments.

Image	Description	Thickness
	**IMRT** Style 18, Head Only	2.4 mm or 3.2 mm
	**IMRT** Style 27, Head Neck & Shoulders	2.4 mm or 3.2 mm
	IMRT Style 27, Head Neck & Shoulders with Neck Relief	2.4 mm or 3.2 mm

Table B.3 - Different types of thermoplastic masks and their thickness.

- Standard Perforation Thermoplastic Masks feature standard perforation and are available in a variety of lengths and thicknesses.

Image	Description	Thickness
	Standard Perforation, Head Only	2.4 mm or 3.2 mm
	Standard Perforation, Head Neck & Shoulders	2.4 mm or 3.2 mm

Table B.4 - Different types of thermoplastic masks and their thickness.

***- Solid (non-perforated) Masks*:** A solid sheet of thermoplastic with a perforated nose region for a rigid mask with breathability.

Image	Description	Thickness
	Solid with Perforated Nose, Head Only Solid with Perforated Nose, Head Neck & Shoulders	2.4 mm

Table B.5 - Different types of thermoplastic masks and their thickness.

- Pediatric Masks - Narrower, reloadable thermoplastic frame and sheets are available to accommodate pediatric patients.

Image	Description	Thickness
	Reloadable Frame for Pediatric Masks	Non available
	Solid with Perforated Nose, Head Neck & Shoulders	2.4 mm

Table B.6 - Different types of thermoplastic masks and their thickness.

- Mastercast Pro and Posicast thermoplastics provide excellent positioning and reproducibility during treatment and do not stick to the skin or hair. Posicast is a drapestyle material requiring less stretching, therefore resulting in minimal shrinkage after cooling.

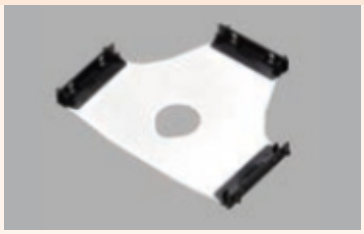
Image	Description	Thickness
	**Mastercast Pro** PR3 Head-Only	2.3 mm
	**Mastercast Pro** PR31 SRS	2.3 mm
	**Mastercast Pro** PR5 Head, Neck & Shoulder	2.3 mm

Table B.7 - Different types of thermoplastic masks and their thickness.

- Posicast-Lite: Posicast-Lite feels like a traditional thermoplastic with a smooth spray coating on both sides of the mask.

Image	Description	Thickness
	**Posicast-Lite** PR3 Head-Only	2.3 mm
	**Posicast-Lite** PR31 SRS	2.3 mm
	**Posicast-Lite** PR44 Larynx Extension	2.3 mm
	**Posicast-Lite** PR5 Head, Neck & Shoulder	2.3 mm
	**Posicast-Plus** PR33 Pediatric Head-Only	2.3 mm
	**Posicast-Plus** PR55 Pediatric Head, Neck & Shoulder	2.3 mm

Table B.8 - Different types of thermoplastic masks and their thickness.

C. Immobilization Devices - Vac-Lok Cushions

Vac-Lok cushions form a custom mold of a patient's anatomical contours and can easily be reinflated and remolded. Cushions are available in two durable finishes: urethane and nylon. Nylon cushions are reinforced and can be ordered with indexing bars attached. It's recommended to locate the valve away from the region of interest to prevent image artefacts.

Rectangular Cushions

Dimensions	Fill	Finish
25 x 50cm	2.25 Liters	Urethane or Nylon
50 x 70cm	15 Liters	Urethane, Nylon or Nylon with indexing
70 x 70cm	20 Liters	Urethane, Nylon or Nylon with indexing
70 x 100cm	35 Liters or 40 Liters	Urethane, Nylon or Nylon with indexing
75 x 100cm	28 Liters	Urethane, Nylon or Nylon with indexing
75 x 120cm	34 Liters	Urethane, Nylon or Nylon with indexing
75 x 150cm	50 Liters	Urethane, Nylon or Nylon with indexing
75 x 180cm	62 Liters	Nylon with indexing
100 x 100cm	40 Liters	Urethane, Nylon or Nylon with indexing
100 x 150cm	80 Liters	Nylon
100 x 200cm	120 Liters	Nylon

Table C.1 – Some available Rectangular Vac-Lok cushions and their characteristics.

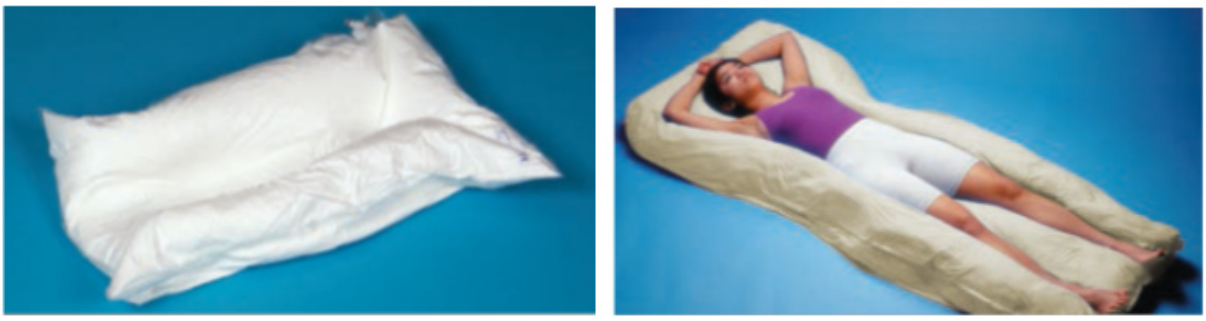


Figure C.1 - 25x50cm cushion useful for extremity positioning (on the left) and 100x200cm cushion useful for full body positioning (on the right).

Non-Rectangular Cushions

Description	Dimensions	Fill	Finish
Prone Cushion (Vac-Lok Cushion only)	15 x 26cm	0.5 Liters	Urethane
Head & Shoulders "T" Cushion	50 x 70cm	6 Liters	Urethane
"T" Cushion	87.5 x 140cm	25 Liters	Nylon or Nylon with indexing
	108 x 125cm	44 Liters	Nylon with indexing
Type-S™ Cushion	61 x 65cm	8 Liters	Nylon
"L" Cushion	140 x 65cm	27 Liters	Nylon with indexing
	74 x 80cm	18 Liters	Urethane
	80 x 90cm	28 Liters	
Hourglass Cushion	80 x 100cm	28 Liters	Nylon
Split Leg Cushion	60 x 100cm	15 Liters	Nylon with indexing

Table C.2 - Some available Non-Rectangular Vac-Lok cushions and their characteristics.

Breast and Thorax Vac-Lok Cushions

Figure C.2 – Breast and thorax Vac-Lok cushions

Arms up made out of Urethane, Nylon or Nylon with indexing (75cm long)

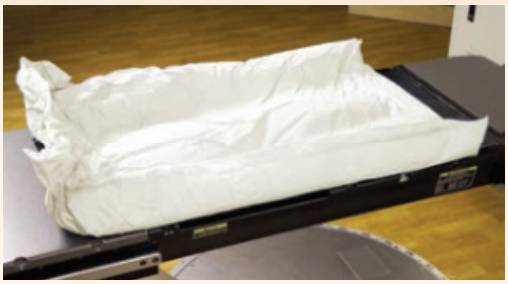
Arms up made out of Urethane, Nylon or Nylon with indexing (105cm long)

Wing Board Cushion made out of Urethane, Nylon

T-Shape Cushion - Nylon

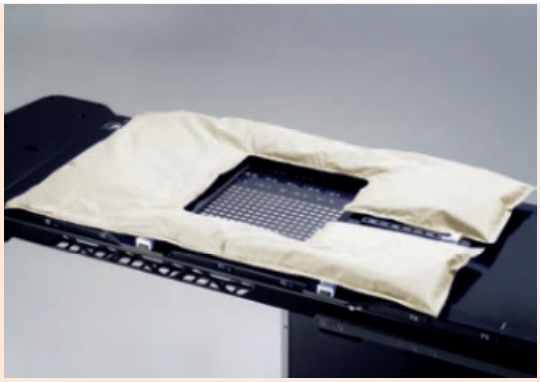
Hip and Pelvic Vac-Lok Cushions

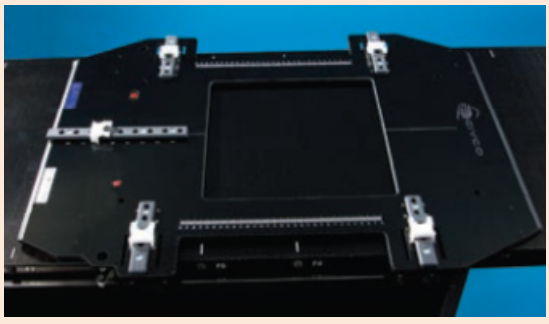
Table C.3 – Hip and pelvic Vac-Lok cushions and their dimensions



75 x 100cm – Urethane	75 x 120cm – Urethane
75 x 100cm – Nylon	75 x 120cm – Nylon
75 x 100cm - Nylon with indexing	75 x 120cm - Nylon with indexing

Figure C.3 – Other Hip and Pelvic Vac-Lok Cushions





80 x 100cm Hourglass - Nylon

Split Leg Cushion - Nylon with indexing (To be used with the HipFix System)

Diagnostic Vac-Lok Cushion

The Diagnostic Vac-Lok Cushion provides a quick and easy method for creating a custom patient positioning cradle. This comfortable cushion makes it easy for a patient to relax during lengthy imaging procedures. An optional head cushion provides additional stabilization of the head and neck. Reduced patient movement results in clearer images, maximizing the benefits of today's advanced imaging technologies.

Figure C.4 – Representation of a person immobilized using a Diagnostic Vac-Lok Cushion.

	Shape	Dimensions
	**Rectangle**	27.9 x 17.8 x 5cm 25.4 x 17.8 x 2.5cm 25.4 x 17.8 x 5cm 25.4 x 17.8 x 7.6cm 25.4 x 17.8 x 10.1cm 50.8 x 17.8 x 10.1cm
	Rectangle - Chest Positioner	35.6 x 60.9 x 5cm 35.6 x 63.5 x 10.1cm
	Circle	15.2 x 3.8cm

Table D.1 – Various foam cushions and wedges and their dimensions.

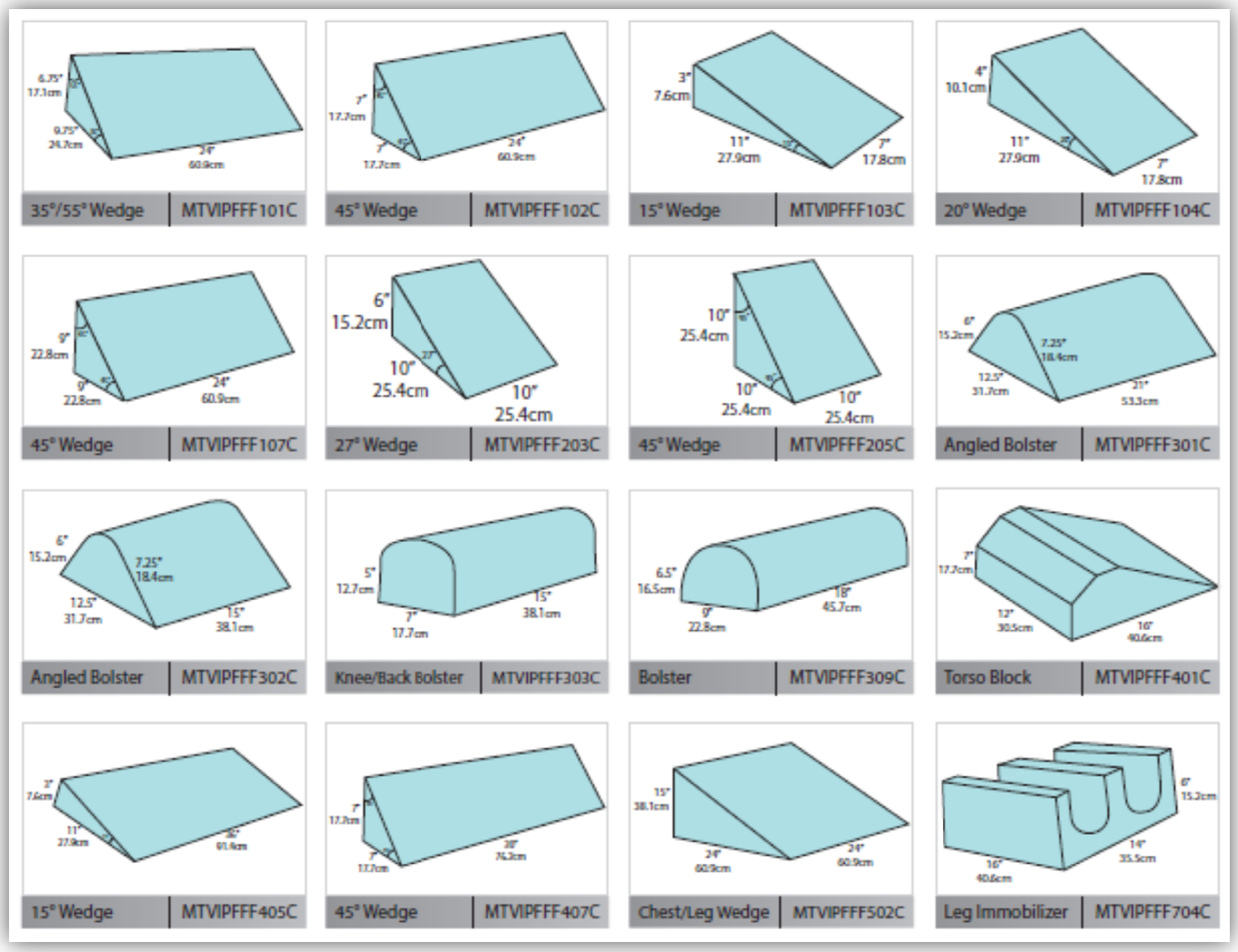


Figure D.1 – Different foam cushions and wedges and their dimensions.

Multi Purpose Support Cushions

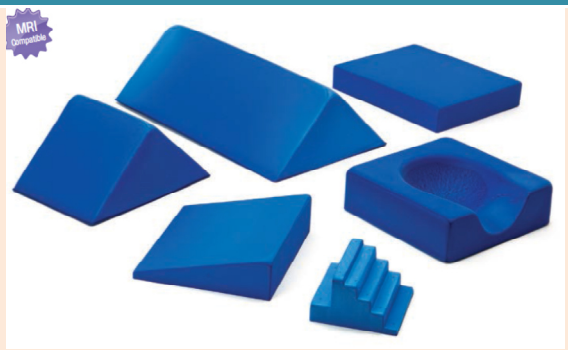
Image	Shape	Dimensions
	**Rectangle**	30 x 24 x 5cm
	15° Wedge	24 x 22 x 7cm
	45° Wedge	28 x 48 x 14cm or 28 x 20 x 14cm
	Head Support	25 x 25 x 8cm

Table D.2 – Some available support cushions and their dimensions.

E. Immobilization Devices – Wing Boards

Image	Description	Dimensions
	**Standard Wing Board -** The Standard Wing Board is constructed of durable, lightweight ABS and features Delrin post hand grips. It is CT compatible and indexable for enhanced reproducibility from imaging through treatment.	57cm wide
	**Tapered Wing Board -** The Tapered Wing Board has angled wings providing patient comfort and support. Its narrow profile is ideal for CT and PET bores. It is available with a T- or U-Grip Handle.	55.9cm wide
	**Extended Wing Board -** The Extended Wing Board is constructed of durable, lightweight ABS and can be used with a T- or U-Grip handle. Its extended length allows for additional arm positioning flexibility. It is CT compatible and indexable for enhanced reproducibility from imaging through treatment.	57cm wide

Table E.1 – Different types of Wingboards and their dimensions.

F. Immobilization Devices – Carbon Fiber Bellyboard

The Carbon Fiber Bellyboard has been developed in order to reduce the irradiated small bowel volume of patients undergoing treatment in the pelvic region. The contoured opening allows for displacement of the small bowel, as the central support structure assists in compressing the small bowel forward into the opening. For patient comfort, the lower part of the Bellyboard has been adapted to support the upper legs. A soft polyethylene padding on the cranial side ensures a comfortable position for the head.

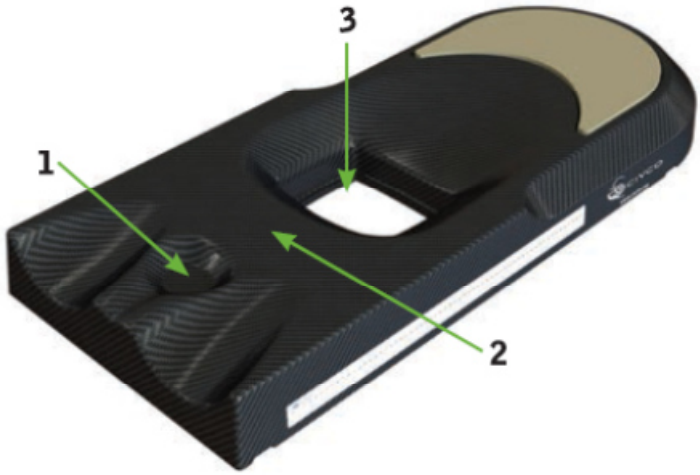


Figure F.1 – The Bellyboard and its different apertures.

The Bellyboard has two apertures: The caudal aperture (1) is to relieve pressure in the genital area. The central part (2) of the device is for the compression of the small bowel in order to push it cranially towards the major aperture (3).

Contoura™ Bellyboard

This device is made out of carbon fiber to provide maximum treatment versatility. Customized bowel displacement achieved with the use of three interchangeable

padded inserts. Shorter board allows for additional setup flexibility for various patient lengths.

Figure F.2 – Picture of a Contoura Bellyboard.

Prone Thorax Support

The Prone Thorax Support is designed to relieve chest compression during treatments in the prone position. It can be used as a stand-alone patient support or as an option on the Bellyboard to allow large patients to be treated in the prone position in order to decrease the volume of irradiated small bowel.

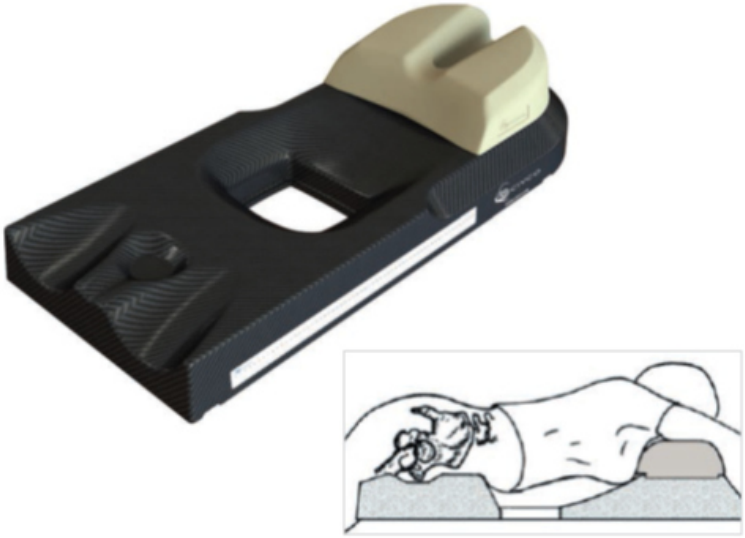


Figure F.3 – Picture of a Prone Thorax Support and illustration of a patient positioned on the device.

G. Immobilization Devices – Combifix

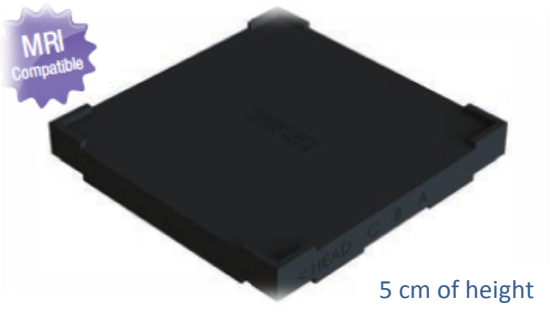
The Combifix is a baseplate that indexes to the couchtop and combines the Feetfix and Kneefix. It is recommended that both cushions are used in combination, as each cushion enhances the performance of the other, especially when treating the pelvic region.

Figures G.1,2, 3 & 4 – Picture of a Combifix and its different components.

Kneefix

The Kneefix cushion contributes to better stability and reproducibility in the supine position, regardless of the target area. It promotes patient comfort and is therefore ideal for use during lengthy procedures on rigid surfaces. The Kneefix is 16cm tall and is made of lightweight, closed cell foam that is easy to clean and is both two and three-pin indexable.

Kneefix 3 Elevation Blocks can elevate either the Kneefix 3 or Low Kneefix 3 by 5cm. The Kneefix fits in the topside of the elevation block and will not slide off. Elevation Blocks may be stacked to raise the legs even higher.



Feetfix 3

The Feetfix 3 is a universal patient support cushion for radiotherapy and diagnostic procedures and has been designed to provide comfortable positioning with enhanced immobilization. The Feetfix 3 is 16cm tall and is made of lightweight, closed cell foam.