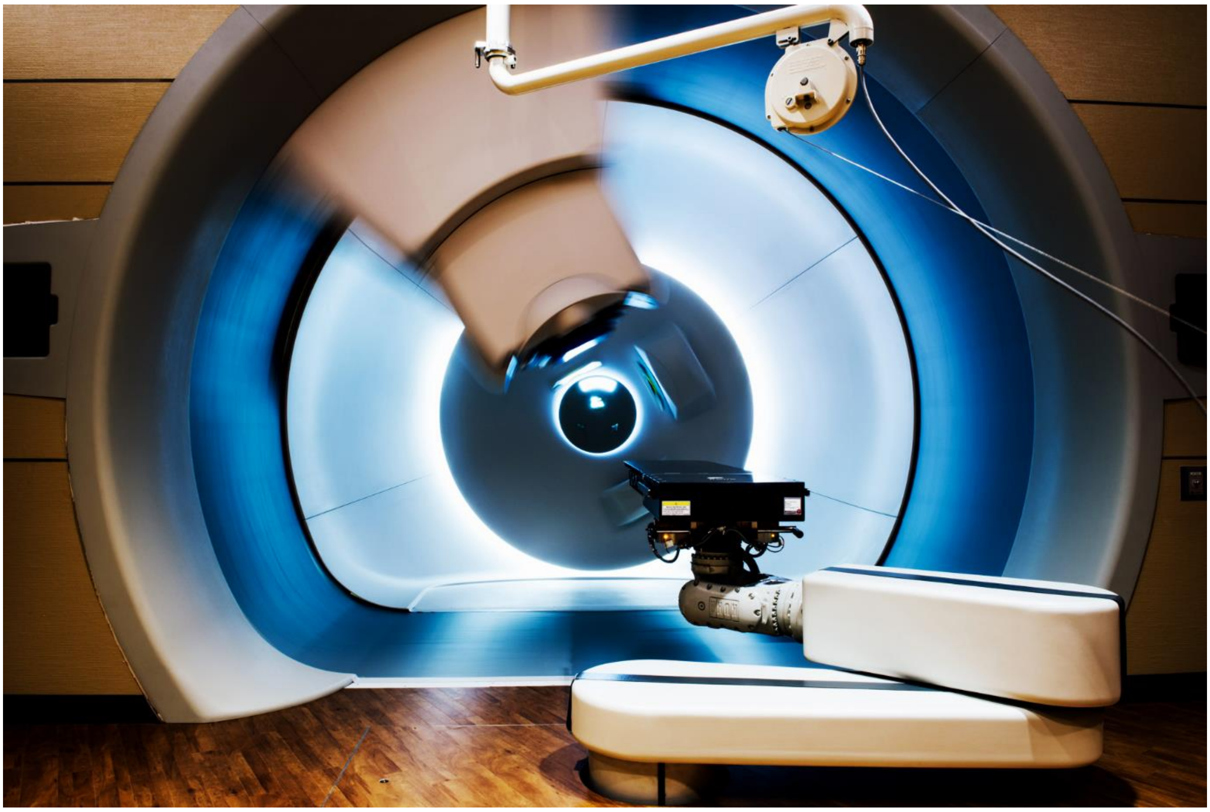
PROTON-THERAPY MANUAL



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OUTLINE

1. FUNDAMENTALS OF OPERATION

Proton-therapy is a type of invasive treatment equipment, which uses ionizing radiation to destroy tumoral cells in patients, to induce apoptosis in them.

First, with a cone beam CT, which is integrated in the proton-therapy complex, the tumor is located, and the irradiated volume is defined.
Once the irradiated volume is set, the treatment phase can start.

For that, it has a particle accelerator, in this case a LINAC, which accelerates, using magnetic fields, the H^+ protons injected, carrying up to 235 MeV of energy. Then, there is a long set of electromagnets which guide the protons towards the gantry.
The gantry can rotate 360º around the patient to irradiate the patient in the most efficient / optimal direction, which was previously set.
Finally, the nozzle will guide the proton particles, which due to their high mass compared to electrons or photons [1], will strike the tumor while preserving healthy tissue **[Figure 1]**.

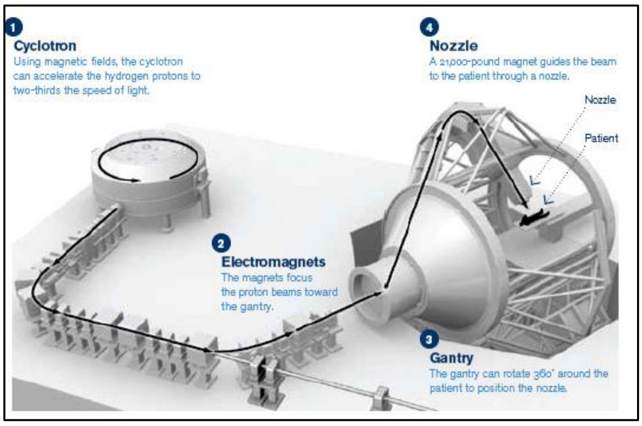

Figure 1. Schema of Proton Therapy System [2]

The depth of the tissue where energy is released, affecting the tumor directly, is called Bragg Peak. This would constitute the main advantage compared to conventional radiotherapy, as it can be observed in **[Figure 2]** almost all the energy is released in the tumor, and after the tumor, there is a strong steep descent in the dose absorbed, and is no energy released, so there is a non-negligible difference in the amount of irradiated tissue [3]

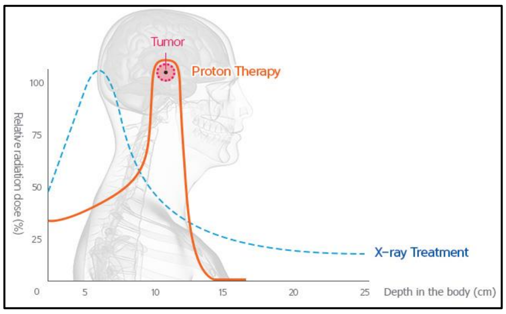

Figure 2. Energy Delivered Based on Depth of Tissue [4] .

2. COMPONENTS OF THE SYSTEM

The main components of the proton therapy system are **simulation procedure**, an **accelerator**, **an energy selection system**, **a beam transport system**, **a treatment nozzle,** and **imaging equipment**.

The **simulation procedure** consists of taking multiple CT x-rays images of the patient in the treatment positioning, and several marks are made on the patient's skin so that they can later be repositioned in front of the proton beam. When all the treatment planning has been done, the patient has to lie on the computer-controlled couch and its positioning is adjusted to align the marks that were made before, thus not losing the reference treatment position.

All the proton therapy equipment is linked together and controlled by several computers to ensure that the treatment can be delivered in a safe way and with extremely high precision.

Regarding the **proton accelerator**, there are mainly two types [5] used:

- Cyclotron: Its main components are a large electromagnet, a source of protons at the middle of the magnet, and two semicircular hollow copper electrodes ("DEES") between the magnet pole pieces. The electrodes are inside a vacuum compound. A representation of the cyclotron can be seen in **[Figure 3]** and **[Figure 4].**

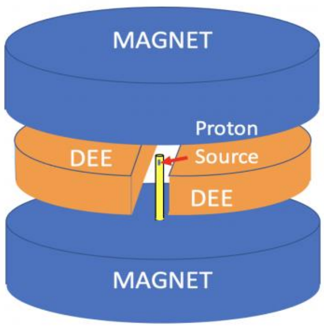

Figure 4. Cyclotron Scheme [5]

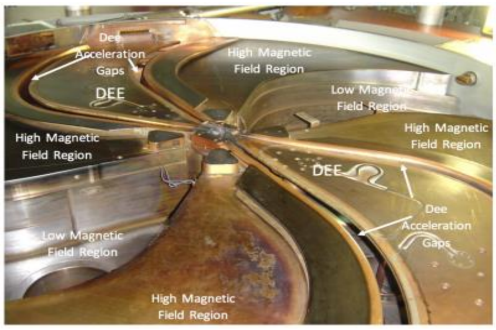

Figure 3. Magnetic Poles and DEES [5]

- Synchrotron: The big magnet of the cyclotron is replaced by a ring of smaller magnets that surround the vacuum tube, with the radius of the ring that is constant. The magnets produce a low magnetic field, and low energy protons are inserted from a small accelerator into the ring. It also includes a radiofrequency source in the ring. A scheme of the synchrotron is seen in **[Figure 5].**

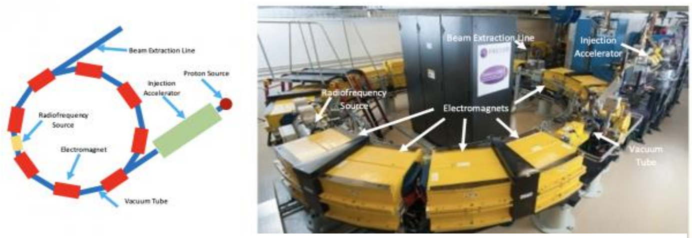

Figure 5. Synchrotron [5]

The main advantage of synchrotron over the cyclotron is that it produces a pulse of protons each 1-2 seconds, hence producing less ionizing radiation in comparison with cyclotron, which produces a continuous stream of protons [6]. The efficacy of the proton beam is not affected by the exact type of accelerator used to produce the proton beam.

Once the proton beam has been generated, it will go through an Energy Selection System (ESS) to degrade the beam energy with respect to the appropriate depth of the tumor and a Beam Transport System (BTS) that will direct the beam towards the gantry. There will be a Treatment Control System (TRCS) that interfaces with the Energy Selection and Beam Transport System to achieve said goals [7].

The energy selector can vary the proton energy between approximately 70 and 250 MeV. The degrader is made of beryllium, for energies lower than 120 MeV, and graphite, for higher energies [8]. When passing through the graphite the energy spread of the beam is increased, spoiling the sharpness of the Bragg peak. To restore the sharpness, the beam is passed through dipole magnets, bending low energy protons, and causing the beam to fan out. Then highest and lowest energy protons are stopped by placing a slit in the path of the beam, only allowing a limited range of proton energies to arrive at the treatment room [5]. The described process is seen in **[Figure 6].**

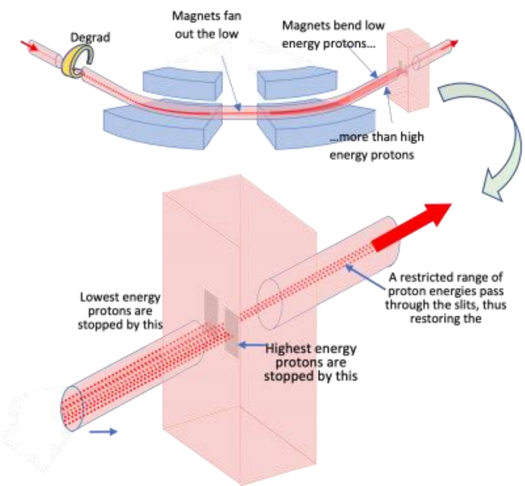

Figure 6. Schematic showing how magnets are used to restore the energy spread of the beam. [5]

The synchrotron does not require an energy selector as the beam energy can be modified during the process of acceleration.

After the beam leaves the ESS, it is transported to the gantry through a vacuum tube with quadrupole magnets (2 pairs of diametrically opposed pole pieces) that keep the beam focused throughout the path. Then dipole magnets steer the beam into the treatment room.

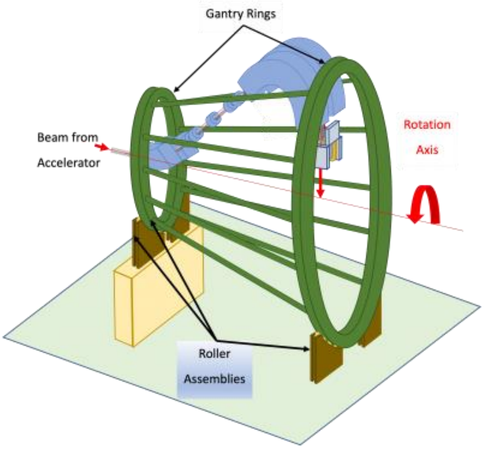

Figure 7. Schematic of gantry structure [5]

At the gantry **[Figure 7],** protons are focused into a thin beam and aimed at the tumor. The ideal way to deliver the beam is to rotate it 360 degrees around the tumor. Bending and focusing magnets are mounted in the gantry to do this. What allows the gantry to rotate are four roller assemblies on which the rings of the gantry sit on. The Treatment Control System (TRCS) interfaces with the gantry motor drives to orient the gantry at the appropriate angle. The TRCS includes high level software that coordinates and supervises the complete treatment session [9].

Finally, the nozzle, which contains scanning magnets and instrumentation for monitoring the dose and beam position. The TRCS also interfaces with the nozzle, to direct the beam at the treatment area and control the irradiation [7].

3. CONDITIONS OF ACCESS TO THE SYSTEM

It is clear that proton-therapy equipment is not a type of biomedical equipment that can be easily purchased. In fact, nowadays in Spain there are only two places where proton-therapy is performed ("Quirón Salud" and "Clínica Universitaria de Navarra"). This is because, firstly, of the enormous cost of the equipment, and secondly, because of all the facilities, adaptation, staff training and hospital configurations that this equipment requires.

Therefore, how can this equipment be acquired? Focusing on Spain, the acquisition of this equipment is by the method of **direct purchase.** In this case a total investment of around 40.000.000 euros [10] (based on previous cases in Spain and in the world) will be necessary. The distribution of the costs will be explained in chapter 11 **"COSTS"**

The final price is approximated and will depend on the business in charge of the project. Companies that have been working in this sector are IBA or HITACHI [11]

Because of the great amount of money needed to adapt the hospital to the requirements of this technology, renting or leasing are not a sustainable solution. The most common way to access technology is, therefore, direct purchase, especially a direct purchase divided in multiple pays. Moreover, apart from the investment of the equipment, it is also important to think about all the other aspects that should be taken into account when trying to access the technology **[Figure 8**Error! Reference source not found.**]** .

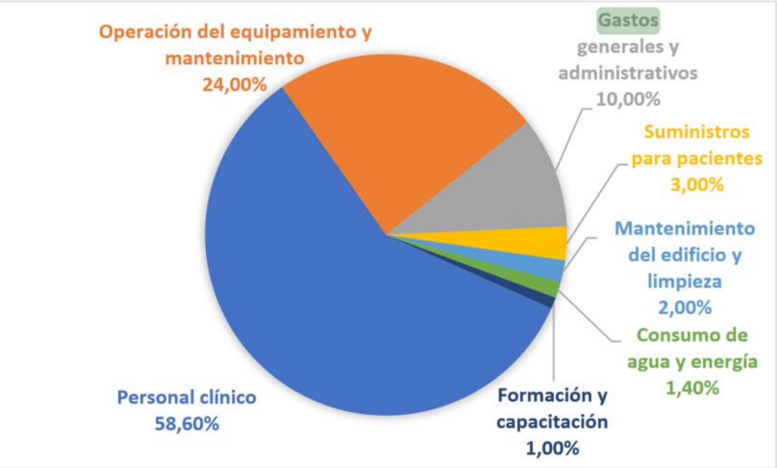

Figure 8. Distribution of Costs [10]

Another possibility to access this system would be the **total cost of ownership (TCO)**. In this case the health establishment should do an analysis aimed at discovering all lifecycle costs (acquisition costs, operating costs and personnel costs). TCO is a common alternative in case of purchasing large medical equipment such as proton-therapy equipment.

Another final option to take into account would be **innovative public purchase**.

In this case, since very innovative equipment is used, future new equipment installations (for instance, new devices installed in the equipment for a more accurate treatment in areas in movement such as the heart) could be acquired thanks to the innovative public purchase. [10]

4. GENERAL RULES OF SYSTEM USE.

Proton therapy is a technique that works with radiation, a fact that implies some risk for the patient. It's an expensive technique and requires maximum accuracy and efficiency to improve a patient's health [12]. Here is developed a summary of the main rules or considerations that should be considered when performing proton-therapy by the technician, the doctor and the patient.

- *In relation to the treatment dose:*

The user should follow the guidelines in Report 78 of the International Commission on Radiation Units (ICRU) and Measurements ICRU, which recommends the protocol for dose calibration contained in Technical Report Series No. 398, published by the International Atomic Energy Agency (IAEA).

- *In relation to the immobilization device:*

Every patient should have a treatment site–specific proton-compatible immobilization and protection devices if it is required e.g.: eye-thermoplastic mask, brain- plastic mesh, chest-vacuum bag…

- *In relation to the patient motion management:*

A motion management program must be established for patients for whom motion may be an issue.

- *In relation to the possible uncertainties:*

Depending on the mode of treatment, each facility should investigate the specific uncertainties (e.g., CT image noise and geometric uncertainties in proton beams) at their facility to prevent possible problems in the system outcome.

- *In relation to the simulation and treatment planning:*

Depending on the organ treated there will be applied a specific procedure of simulation and treatment planning. All the personnel involved in the treatment should know the steps of the procedure and their implication in it before starting.

- *In relation to the Machine Quality Assurance:*

Scattered and Uniform Scanning Beams Treatment site–specific and vendor-specific QA recommendations should be adopted.

- *In relation to the Medical Physics Chart Review:*

Every chart (physical or electronic) should be reviewed through a checklist by the Qualified Medical Physicist before the treatment starts. The checklist should include prescription, disease site, specific beam line, range (energy), gantry treatment angles and site setup coordinates…

- *In relation to the patient's position:*

During simulation, patients are typically seated upright, and this position must be reproducible and comfortable enough for the patient to remain in this position throughout the treatment [13].

5. SYSTEM INSTALLATION

5.1 PHYSICAL INSTALLATION

Although depending on the specific proton therapy equipment installed the installation of it might vary, there are some common characteristics and general procedures that can be applied to any of them.

The complete installation will be around 3600-3800 m² and it will need the authorization and supervision of the Ministry of Industry among other corporations.

The installation of all the proton therapy units will be divided into different areas, each of them with a specific purpose. In general terms, these will be the units [14] [15]:

- Treatment area: In this part of the installation, it will take place the proton therapy per se. It will have among others the gantry zone, anesthesia room and a control room for the equipment and its use. The synchrotron is included.
- Simulation area: It has a virtual simulation zone and the installation (TAC or PCT) for obtaining the images of the tumor.
- Office's area: Counts with secretariat, medical archive, waiting room among others.
- Medical area: Physician's offices, warehouse and coworking room.
- Administrative, teaching and support area: Counts with secretariat, kitchen, office, library, changing rooms and other spaces for providing the services aforementioned.
- Waste management warehouse: Area for placing radioactive wastes of minimum 30 m². There will be until ENRESA, or other waste management enterprise collects them.

Some technical aspects that should be pointed out is that the treatment area will vary its size depending on the synchrotron model. The more compact models will occupy an area varying between 100 and 250 m². Normally the proton therapy unit is built underground and with 5 meters thick concrete walls, as it can be observed in **[Figure 9]**, for preventing the radiation from going to the exterior. Another radiation prevention design action is the compartmentalization of the spaces and a 'labyrinthic' disposition of them.

To conclude this physical installation section, it's worth mentioning that this installation requires a big plan and involves many technicians for transporting and preparing the equipment for its use due to the big size of the components and the care that they must be treated.

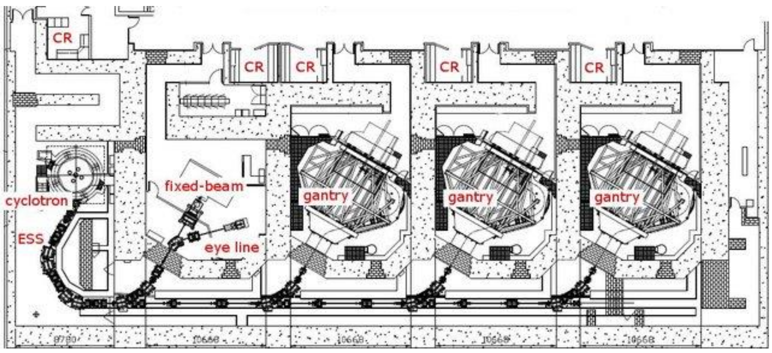

Figure 9. Project Plan of PT Center [16]

5.2 AIR CONDITIONING INSTALLATION

Air conditioning regulation does not only provide comfortable environments for patients and staff, but it also prevents overheating from cyclotron, and limits occurrence of safety hazards.

- Temperature and humidity control: Fluctuations in temperature and/or pressure have an impact on beam measurement performed by the ionization chamber in the nozzle. Internal heat loads generated by the cyclotron must be dissipated. Heat dissipation of the entire facility is estimated to reach 280 kW [17]. To ensure manufacturer recommended operation conditions and a stable environment that ensures optimal operating efficiency and patient comfort, water cooling plants will be used to cool down the cyclotron, gantries, transport system and vacuum pumps. General air conditioning outlets should not be placed directly over partially undressed patients on beds or trolleys. The temperature of the different areas should be maintained within a comfortable range: Cyclotron, energy selection system and beam transport system between 25ºC and 30ºC, treatment room between 22ºC and 26ºC, patient areas a 23ºC and control rooms and offices 19ºC to 26ºC. Regarding humidity all areas must have less than 65% RH, non-condensing, additionally electrical rooms must not condense at 18ºC. [18]

- Pressure and airflow: room pressure must be kept at a lower level than the surrounding areas to prevent the escape of radioactive particles. Proper airflow prevents the buildup of gas and other contaminants in the treatment room [19]. For air exhaust in the cyclotron area pressure relief is necessary to allow gasified helium to escape without causing damage in the event of unplanned heating of superconductor. In radiation-controlled areas a pressure of 6 bar, relative to the surrounding atmosphere must be kept. [18]

- Air quality and ventilation: Appropriate air exchanges and exhaust for chemicals and dust is necessary. The proton beam will not only radiate a desired material, but it will also cause the neutronic activation of the air, free neutrons in the air form a neutronic field which. These neutrons interact with the nucleus of stable molecules to form radioactive isotopes (concentrations of ^{3}H, ^{11}C, ^{13}N, ^{15}O y ^{41}Ar) that can become sources of internal radiation if inhaled [8]. Ventilation and frequent air renewal is required to limit the risk of inhalation of radioisotopes. A renewal rate of 500 liters/min is required in radiation-controlled areas. Filtered air, free of dust, particles, moisture, oil, and other contaminants that might interfere with the proton beam is supplied by redundant compressors. This compressed air is essential for the operation of machinery and cleaning, it has a flow operation of 250 liters/min per outlet and a storage tank with more than 500 liters is recommended [18]. Regarding filtration levels, these will follow the specifications of the manufacturer and the legislation of the hospital (in Spain it will follow the RITE and UNE legislation).

5.3 ELECTRICAL INSTALLATION

The electric requirements for the installation of a cyclotron depend on the specific type of cyclotron and its energy output, but in general, the following electrical requirements should be considered:

1. **Power supply**: A cyclotron requires a high-power electrical supply to accelerate charged particles. The power supply should be capable of providing a stable and continuous supply of high voltage and high current.
2. **Voltage regulation**: The power supply should be able to regulate the voltage to maintain a stable beam of charged particles.
3. **Grounding**: Proper grounding is essential to ensure safe operation of the cyclotron. A dedicated grounding system should be installed to prevent electrical shocks and damage to the equipment.
4. **Cooling system**: The cyclotron generates a significant amount of heat, which must be dissipated to prevent damage to the equipment. A cooling system, such as water cooling, should be installed to keep the equipment within a safe temperature range.
5. **Backup power supply**: A backup power supply, such as an uninterruptible power supply (UPS), should be installed to ensure continuous operation of the cyclotron in the event of a power outage.
6. **Electrical safety equipment**: Electrical safety equipment, such as circuit breakers, surge protectors, and ground fault circuit interrupters (GFCIs), should be installed to prevent electrical hazards.

It is important to consult with a qualified electrical engineer and follow all applicable safety guidelines and regulations when installing a cyclotron [8] .

Moreover, there are other needs where special attention must be paid:

- **Transfer elements**: Installations must have reliable electrical transfer switches. That is, all emergency areas or zones, for example, should have individual switches for each piece of equipment to ensure an electrical transfer that allows healthcare personnel to work without problems.
- **Safety cabling**: Essential in all facilities where any kind of patient care is carried out. In these cases, safety cables must be independent in each equipment and connection. In addition, they must be on different channels and remain isolated. In other words, the cables that provide electrical power must not remain in contact with each other. In this area, hospital ground panels and electrical outlets should be highlighted, which helps to prevent contact voltages within the critical medical area.
- **Emergency systems**: It is vitally important for hospitals to be prepared for any type of emergency. There is equipment and elements of our equipment that must continue to function even in the event of power outages. In this sense, it is important to have, for example, exit signs, power for alarm and warning systems, power for blood banks, lighting for generator locations, etc. [20].

5.4 LIGHTING INSTALLATION

For this installation it is important to keep in mind at all times, the two variables by which the decisions will be based on:

- Patient
- Energetic efficiency

Regarding the patient, it must be considered the stressful psychological situation that they might be in, due to the procedure and all the facts related to suffering from cancer. Therefore, we want to use warm ambient lights (2000 - 4000 K), as we can see in **[Figure 10]**. In the bunker and simulation rooms for the patient to feel comfortable, relaxed and to create a welcoming environment, and accent lights could also be added using LED with cold colors (RGB scale), such as blue, for the same reason. An example is shown in **[Figure 11].**

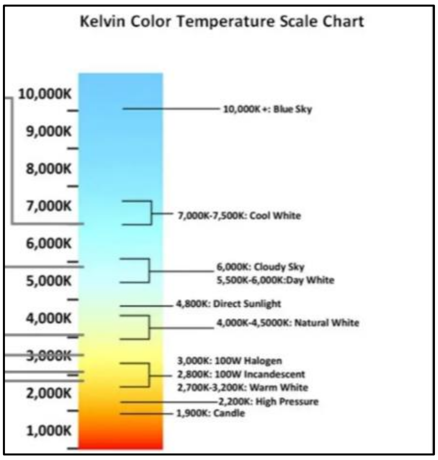

Figure 10. Kelvin Color Temperature Scale [56]

In the control room, where the radio physicists and oncologists will be at, it is preferred the use of colder color temperatures, such as cool white (5000 K) and an average of 500 lux to keep them focused.

Also, it is worth to denote that for kids, the use of proton therapy rather than radiotherapy is indicated. Some kids might be woken up during the procedure, thus, it is also recommended the use of projectors displaying cartoons or images of nature.

Figure 11. Example of lighting in a proton therapy room [57]

Then, in terms of energetic efficiency, the best option is the use of LEDs in all the rooms including the control rooms, simulation rooms and the bunker.
They provide the best illuminance, for the lowest power consumption and have the highest life expectancy.
Also, using LEDs we could even change the color of them or let the patient set the color he/she feels comfortable with.

5.5 WATER /SANITARY HOT WATER INSTALLATION

Proton therapy requires some water facilities to be performed without any danger and in an accurate way. Among the different water-based installations required for proton therapy the following are the most significant [21] [22] [23]:

- Toilets: In a proton therapy treatment room we find different types of toilets, different mainly by the type of user that will utilize them. We can find patients toilet, staff toilet and general toilets also called public/staff toilet. It is worth mentioning that all toilets should have hot water installation and that in some cases the patient's toilet will incorporate a shower. Furthermore, in each area of the proton therapy complex (planning zone, appliance area, radiation treatment ...) there will place all the aforementioned kind of toilets. In the radiation area toilets will be placed near the concrete walls to avoid possible spread of radiation
- Water cooling systems: The cooling system in proton therapy treatment plays a key role in its success. The quadrupole magnets, that focus the proton beam into pencil width shapes and prevent the beam spreading outwards, heat during the process. If this thermal energy is not diminished, the magnets would change size physically and the focus of the beam would be sub-optimal. The cooling system basically consists of pipelines carrying the water around the quadrupole magnets. The number of quadrupole magnets used is dependent on the length of the beam line, so this also affects the length of the pipelines.
- Sinks and handwash basins: To ensure hygienic and aseptic conditions in every moment during the planning and the development of the treatment, sinks and handwash basins will be placed around the different areas of the complex providing hot water installation.

5.6 MEDICAL GAS INSTALLATION

For the correct functioning of the installation, supply of several gasses will be needed [8]:

- Reservoir for pneumatic actuators (valves, gantry brakes...).
- Dry nitrogen is needed for accelerator venting. Nitrogen is also needed for the ventilation of evacuated devices. For this, nitrogen tanks must be installed at fixed locations of the building.
- Hydrogen in the cyclotron's ion source and provides the necessary protons.
- Helium for superconducting magnet and vacuum leak detector.
- Oxygen for electrostatic baffle conditioning in the extraction of the beam from the Cyclotron. Oxygen is also needed continually during operation for the conditioning of the deflectors in the cyclotron. The pressure tanks must be operated in an area separate from the cyclotron in order to prevent their activation.
- Medicinal gases.

Distribution of medical gases in proton therapy installations typically involves a central gas distribution system that supplies medical gases to the treatment rooms, patient care areas, and equipment rooms. This system consists of pipelines, valves, regulators, and pressure gauges that are designed to deliver medical gases safely and reliably to where they are needed.
The storage of medical gases in proton therapy installations is also an important consideration. Medical gases must be stored in accordance with strict regulations to ensure their safety and efficacy. This includes the following guidelines for maximum storage capacity, pressure levels, and temperature control.

Medical gasses should be stored in dedicated storage areas that are designed to minimize the risk of contamination and ensure proper ventilation. Storage areas should be kept clean and dry and should be free from sources of heat and ignition.
It is also important to ensure that medical gases are properly labeled and that their contents are clearly identified. This helps to prevent confusion and ensure that the right gas is being used for the intended purpose.

In addition to these considerations, proton therapy installations must also comply with local and national regulations governing the use, storage, and distribution of medical gasses. This includes the following guidelines for installation, inspection, and maintenance of gas distribution systems and storage facilities [24].

5.7 COMMUNICATION INSTALLATION

Effective communication systems are essential to ensure patient safety, efficient treatment delivery and storage of data. The following are some of the key requirements for this type of installation [25] [26]:

- Emergency communication: In the event of an emergency, the communication system should enable staff to quickly call for assistance. This may include a dedicated emergency phone line or intercom system that connects directly to the hospital's emergency response team.
- Security: implement technical measures so that unauthorized access to sources can be detected. These technical measures should be independent of any interlocks that terminate the radiation beam during normal operation. Such measures could include a video camera and motion sensors for continuous surveillance. In the presence of an unauthorized person, an alarm should indicate this locally and remotely.
- Intercom system: to enable communication between staff in different areas of the bunker, such as the control room and treatment rooms. This, along with a camera system in the treatment room will enable staff to monitor the procedure and communicate with the patient during treatment if they experience anxiety or discomfort.
- Network connectivity: The communication system should be connected to the hospital's network infrastructure to enable staff to access patient records and treatment plans.
- Redundancy: is essential to ensure the integrity and availability of patient and treatment data. This could involve the use of multiple servers and regular data backups (ACS).

Images taken by the CT scans, MRI scans, PET scans and or X-rays and calculations made during the simulation phase and planning studies need to be stored along with the planning data. Typically, these images are stored electronically in a Picture Archiving and Communication System (PACS), following the DICOM RT (Radio Therapy) standard which contains the entire treatment plan as well as beam delivery information from the treatment. [27]

The immobilization position of each patient is also documented during the planning phase. It is recorded using specialized devices such as masks, headrests, and body molds. The position of each device is also stored electronically in the patient's medical record, which is accessible through the hospital's electronic medical record (EMR) system.

An ethernet network allows connectivity from the equipment control level to the user interface level and the database system [28]. Cabling and passive components will be provided in CAT 7, and the cabling should be routed through radiation-shielded conduits to minimize risk of radiation exposure to staff and patients. Additionally, all areas where proton therapy equipment is installed must be equipped with several RJ45 outlets connected to a patch panel in the server rooms, which must be interconnected [18].

5.8 FIRE PROTECTION

In a proton-therapy room it is extremely important the correct sectorization of the different rooms, since it uses highly flammable chemical compounds (H^+) for the generation of the proton beam, therefore everything must be sectorized to avoid the spread of any possible fire, which could be devastating, but most importantly the cyclotron room, since the H^+ protons are stored there.
The delimitation of the fire sectors must be fulfilled by fire-resistant materials that can keep the fire isolated for a certain time given by the country's regulatory framework, which depends on the height of the rooms.

In terms of fire detection, the use of automatic optic detectors must be considered, as well as alarm pushbuttons, at a height with respect to ground of between 80 and 120 cm.

Regarding portable extinguishing systems, the use of a dust fire extinguisher is recommended, in this case multipurpose powder, strategically placed in the farthest point of the room to the exit doors in case someone is trapped at the end of the room.

In the different rooms as well, having fixed extinguishing systems might be needed. Sprinklers are the best option for installing, but for these rooms, it is recommended the use of dry-pipe sprinklers with closed head [19] since we want the sprinklers to have water just when the alarm is activated, because the incorrect activation of water-based sprinklers could cause high damages to the system. These sprinklers should also be connected to a sensor system so that they are activated automatically.

It is important to highlight the fact that we are dealing with ionizing radiation systems, which alter the correct functioning of our fire protection devices, therefore we will specify in the maintenance section how to deal with them.

6. MAINTENANCE AND REPAIR OF THE SYSTEM

6.1 WARRANTY AND SERVICES CONTRACTS

Proton therapy systems are usually well covered in terms of warranties due to the high investment they represent, but also because of the vast complexity behind them.
On the line of this last cause, the system's warranties are given by the own provider, since highly specialized personnel is needed to fix any issue that comes up.

Manufacturing companies cover any defect, present or that appears, in materials of the system and/or workmanship for between 1 and 5 years. This coverage includes the repairing or replacing the defective equipment.
In the case the damage is caused by misuse or negligence, the manufacturing company does not cover it.

Regarding services contracts, manufacturing companies offer 3 types of services [29].

- **Corrective Maintenance Contracts**. Support is provided 24/7 in case any emergency maintenance is needed. Online and onsite support services are facilitated to diagnose issues.
- **Preventive Maintenance Contracts**. It is provided to avoid errors or malfunctions. These contracts include calibration procedures, performance verifications, mechanical reliability, or, in the case parts are exposed to high stress constantly, they are also checked periodically.
- **Update Coverage**. Manufacturing companies provide systems with constant updates to keep them at constant peak performance. These types of updates include software updates or improvements in protocols.

6.2 TOOLS

Correct maintenance of the complete proton-therapy equipment is key in order to ensure an optimal and secure performance of it.
In this sense, there are several tools that may be helpful for this task. [30] [31]

1- Digital Multimeter: Useful tool to make sure that the electrical installations are properly working.
2- Torque wrench: A torque wrench is used to tighten bolts and screws to a specific torque value. This is very useful in order to prevent over or under-tightening which can cause problems with the equipment.
3- Thermal imaging camera: A thermal imaging camera can detect heat signatures in proton therapy equipment, which can help identify hotspots or areas that are overheating. This can be useful in preventing equipment damage and safety hazards.
4- Laser alignment tools: these kinds of tools are used to ensure that the proton beam is properly aligned with the patient`s tumor.
5- Vacuum gauge: This is used to measure the level of vacuum in a system. It is very useful in order to correctly detect leaks or blockages that may affect the performance of the equipment.
6- Cooling system test equipment: This is implemented to analyze how well the cooling systems of the cyclotron are working. This includes temperature, pressure and flow rate of the cooling system [32].
7- Oscilloscopes and Megohmmeters: Being able to correctly measure the insulation resistance of the components and the behavior of the electronic circuits is very important to prevent equipment damage. These tools may be helpful for that.
8- Radiation survey meter: This tool is used to measure the level of radiation in that area, for instance near the cyclotron. This can be helpful in order to detect any leaks or spills of radioactive material which can be harmful to both patients and workers.
9- Calibration tools: It is very important to make sure that the system is correctly calibrated. Some examples of these tools may be phantoms or dosimeters.

Going in detail with the calibration tools, there are several different types of phantoms that are useful tools to calibrate the machinery in different aspects in order to make sure there are not accidents such as the one occurred in the Clinic Radiological Hospital of Zaragoza: Dosimetry phantoms (measure radiation which is useful for dosimetry analysis) such as the Water phantom, image quality phantoms (to evaluate the image quality, spatial resolution, contrast, noise...) or motion phantoms (to simulate the movement of organs and tissues to asses a more secure radiation therapy). [33]
Moreover, it is always recommended to follow the manufacturer's rules and recommendations as well as the local regulations. The correct use of these tools must be done by qualified technicians to ensure the effective operation of the equipment.

6.3 MAINTENANCE AND LOGS

Proton therapy is a high-risk procedure due to the dangerous adverse effects that any failure or bug in the system could cause. That is why it is extremely important to ensure the correct, safe and effective functioning of the system.

For that, here are some steps involved in the system maintenance and repairing of the system.

- **Preventive Maintenance**. Preventive maintenance is done first, daily, or weekly, involving tasks such as inspection of system components, calibration, quality control or even cleaning.
  Then, monthly, there are deeper inspections, such as adjustments of the beamline components, adjustments in the vacuum system, and the same for other key parts of the proton therapy system.
  Finally, yearly preventive maintenance may include replacement of obsolete parts of the system, some calibrations or software updates.

- **Corrective Maintenance**. This type of maintenance is not scheduled, it is a sudden breakdown of any part of the system. It includes all sorts of fixings, such as replacement of damaged parts, repairing of electrical systems.

- **Calibration**. It is extremely important to have the correct calibration of the system, as a treatment with millimetric margins of error due to the high risk of irradiating healthy tissue is being delivered, in terms of depth and dosage. That is why it is recommended to do calibrations every day or week.

- **Software Updates**. The continuous and exponential growth of the artificial intelligence field makes it even more interesting to look for software updates that will optimize the functioning of the system. Also, regarding corrective maintenance, the system might return some bugs in the software, which will need to be fixed.

Regarding the planning CTs used in the process, the correct calibration of it is key for two main reasons.

- The radio physician must be able to discriminate correctly between tissues for the correct planning of the treatment.
- The exact same positioning of the patient is crucial to provide the planned treatment.

6.4 OBSOLESCENCE

Proton therapy is a fairly new technology, so it is constantly evolving. Therefore, as new equipment becomes available, the oldest ones become obsolete.

One of the main reasons why proton therapy might become obsolete is because of the technology it uses, which is constantly emerging. This might lead to devices becoming outdated or obsolete.

Moving on to the life expectancy of a proton therapy device, it must be considered that it usually depends on the quality and the frequency of maintenance, the manufacturer's specifications, and the level of usage. However, there are some estimations:

- **Proton therapy device:** The life expectancy of a proton therapy device is typically around 10-15 years, although some devices can endure up to 20 years [34].
- **Cyclotron:** The life expectancy of a cyclotron is typically around 20-25 years [35].
- **Synchrotron:** Synchrotron's life expectancy is usually around 25 years, although some of them can operate for up to 40 years or longer with proper maintenance and upgrades. However, some synchrotrons might also have shorter lifespan due to the high intensity and frequency of usage [36].

Overall, proton therapy devices must follow the European Cocir Golden rules, which state that at least 60% of the total devices must be less than 5 years old, a maximum of 30% of the total devices should be between 6 and 10 years old, and a maximum of 10% of the total devices older than 10 years old.
Moreover, these rules also focus on some other points [37]:

1. Plan for obsolescence from the beginning of the device lifecycle.
2. Ensure frequent updates to its software and hardware.
3. Make sure that you can replace the components of the device in case something breaks or there is any issue.
4. Contingency plans in case the device fails at some point.
5. Proper documentation and record-keeping to make the replacement or upgrade of the device easier.

7. SAFETY OF THE SYSTEM

7.1 INSTALLATION

Proton therapy is a type of radiation therapy that uses high-energy proton beams to target and destroy cancer cells in the body. Proton therapy facilities require a range of safety installations and measures to ensure the safe and effective delivery of the treatment, but they are not just applied to the use of the equipment itself, they should also be regarded when building, preparing and installing the proton-therapy area.

Some of these safety measures taken into account in the installation of the system would be [38] [39]:

- *Site Selection*: Evaluation of seismic activity, soil conditions, and proximity to populated areas. The location should be chosen in a low-risk seismic zone and the soil should be stable and resistant to erosion.
- *Shielding:* Proton therapy installations require a significant amount of shielding to protect the surrounding area from radiation exposure. Typically, the proton therapy vault is constructed with several feet of concrete or other dense materials, such as steel or lead, to absorb any stray radiation that may escape the treatment room.
- *Facility Design:* The design of a proton therapy facility should incorporate many safety features to protect patients, staff, and the public such as at controlled access area, designed to keep the general public and non-essential personnel outside of the treatment zone.
- *Redundancy:* Proton therapy installations should be designed with redundant safety systems to minimize the risk of equipment failure or other safety hazards. Backup generators, redundant cooling systems and other installations as fire prevention can help maintain a safe environment in the event of a power outage or equipment malfunction.
- *Compliance:* It is critical that all safety measures and procedures be in compliance with national and international regulations and guidelines, such as those issued by the International Atomic Energy Agency (IAEA). Proton therapy installations must also adhere to local building codes and safety regulations.
- *Safety Training:* All staff members involved in the proton therapy installation should receive proper safety training to ensure that they understand the safety protocols and procedures.
- *Transport*: The transport of the needed materials for proton-therapy installation should also be subjected to safety measures. Among these measures we can find the selection of a reputable transportation company, the compliance with regulatory requirements (following IAEA guidelines), the packaging and labeling of materials and an emergency response planning.

7.2 USE

Before undergoing proton, therapy patients must be informed and must follow some rules for their own safety preservation [40]:

- **Clothing and jewelry**: Patients should wear loose-fitting clothing without metal buttons, zippers, or snaps. Jewelry should be removed before treatment.
- **Communication:** Patients should communicate any discomfort or concerns to the radiation therapists during treatment. After the treatment patients should report any malaise or side effect for them to be properly assessed by a professional
- **Immobility**: Patients must lie still during treatment to ensure accurate delivery of the radiation dose.
- **Hydration:** Patients should drink plenty of fluids before and after treatment to stay hydrated.
- **Radiation safety:** Patients should follow radiation safety instructions provided by their physician, including avoiding close contact with pregnant women and young children after treatment.

Regarding the technicians, they also must follow a set of rules with respect to patient safety and overall safety of the installation [25]:

- **Emergency preparedness:** The physician should have a plan in place for responding to emergencies, including power outages, equipment malfunctions, and patient reactions to treatment. Emergency stop buttons should be conveniently placed in the treatment and control room. **[Figure 12]**
- **Patient Instructions:** thoroughly and clearly explain to the patients the rules they must follow and make sure they are properly understood before proceeding with the treatment. Also explain possible side effects that the patient might experience.
- **Verify patient identity and treatment plan:** the physician should verify the patient's identity and ensure that the correct treatment plan is being used. Verification of patient positioning and target localization should also be performed, along with a check of the dose calculation.
- **Perform safety checks on the machine:** The physician should perform safety checks on the radiotherapy machine before each treatment session. This includes checking the machine's settings, calibration, and radiation safety protocols.

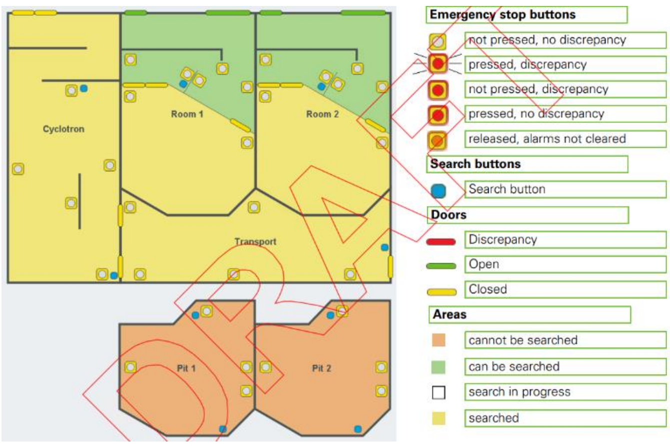

Figure 12. Location of Emergency Devices [7]

8. USAGE PROBLEMS AND ARTIFACTS

Although proton therapy equipment is known for its high precision in radiating the tumor without radiating the healthy tissues, it still produces some artifacts and usage problems:

- **Range uncertainty artifacts:** Caused by the uncertainty in the range of protons in tissue. It can be a consequence of patient setup errors, anatomical changes, or beam delivery uncertainties. The main problem is the dose distortion caused by this issue [41].
- **CT artifacts:** Proton therapy planning mainly relies on computerized tomography to determine the location of the tumor and the surrounding tissue volumes. CT images can cause artifacts in proton therapy treatment plan, such as streaking or metal artifacts, which can lead to errors in dose calculation [42].
- **Beam angle-dependent artifacts:** Proton therapy treatment planning usually uses multiple beam angles to deliver the dose to the desired tumor. However, beam angle-dependent artifacts can appear due to the interaction of the beam with different materials along its path. Consequently, dose deviations can occur, as well as affecting the overall treatment plan quality [43].
- **Image registration artifacts:** Proton therapy treatment planning uses multiple image modalities to determine the tumor and the surrounding tissue volumes. Therefore, image registration artifacts can occur while aligning images from different modalities, which might lead to errors in dose calculations.
- **Patient motion artifacts:** Patient movement during the treatment with proton therapy can lead to dose distortion and reduction in the accuracy of the overall treatment plan. For instance, some movements may be coughing, swallowing, or breathing [44].
- **Bragg peak artifacts:** The Bragg peak is the point at which the proton beam's energy deposition peaks in the tissue, so it is a crucial stage in the proton therapy treatment. This type of artifact can be caused by range uncertainties and dose delivery errors [41].
- **Proton beam delivery artifacts:** Caused by factors such as beam scattering, beam steering errors and hardware errors. As a consequence, there can be dose deviations and affect the quality of the treatment plan.
- **Hounsfield unit conversion artifacts:** Hounsfield unit conversion artifacts can be caused due to the variability of Hounsfield unit values across different imaging devices and types of tissue [45].
- **Shielding artifact:** Shielding is sometimes used in radiation techniques to protect healthy tissues from the radiation. The main issue with shielding is that some artifacts can appear due to the shielding material, thickness, and design, which can deviate the dose [46].

9. WASTE MANAGEMENT

Waste management in radiotherapy is a crucial aspect of radiation safety that involves the proper handling, storage, and disposal of radioactive materials generated during treatment. Radioactive waste is a type of hazardous waste that requires special handling to ensure that it does not pose a risk to human health or the environment [47] [48]

The first step in waste management in radiotherapy is to minimize the amount of waste generated. This can be performed by calibrating and preparing the linear accelerator to generate exactly the necessary amount of radiation for the treatment with the help of phantoms and other kinds of devices. It will also be important to have a highly qualified and prepared team to prevent unnecessary radioactive waste generation and to develop an accurate record of waste generation to continuously monitor and improve its handling and treatment.

If waste has already been generated, it is worth mentioning that there are different types of radioactive waste generated in radiotherapy, depending on the amount of radiation.

- **Low-level (LLW)**: Gloves, gowns, and other disposable materials that have been contaminated with radioactive material but have a low level of radioactivity. The storage of low-level radioactive waste is usually located within the radiotherapy facility or in a separate building on the same site and should meet some regulatory requirements such as proper shielding, ventilation and labeling of containers. These containers are typically made of a strong and durable material such as steel, concrete or lead, which helps to shield the radioactive material inside. The containers may also be lined with radiation-shielding materials such as lead or concrete and their size might vary depending on the generated waste and its storage time.
- **Intermediate level (ILW)**: Waste includes items such as used sources and contaminated equipment and clothing that have a higher level of radioactivity. It's worth mentioning that as well as low-level radioactive waste, intermediate-level waste will be placed in an independent area inside or outside the facility in labeled special containers (steel, lead...) like the ones used in LLW.

After its storage, radioactive waste can remain for a different period depending on its characteristics and the legal regulations and guidelines. In general terms, LLW can remain stored in the containers from several months to several years and ILW from several years to several decades.
Once the storage period has passed, a Waste-Management company will take the waste and carry it to end its handling and treatment. In Spain there are public enterprises like ENRESA and private companies like Tecnatom.

10. ENERGY EFFICIENCY

Energy efficiency protocols in proton therapy refer to techniques and technologies that optimize the use of energy in the proton therapy process to provide the highest level of cancer treatment and minimize the environmental impact. This does not only involve the efficiency regarding energy consumption of equipment but also the HVAC, plumbing, power, and lighting systems, which should also be designed for overall energy efficiency and lowest life-cycle environmental cost in order to achieve sustainable centers [49]. To conceptualize the importance of efficiency protocols, the emissions from a proton therapy center can be estimated to be 34.5 kg of CO_2 from the proton therapy machine itself, per day [50], plus 15 MW total power consumption from the cyclotron [51], plus the consumption from other installations. Efficiency protocols include:

- **Beamline design**: The design of the beamline can also have a significant impact on energy efficiency. Optimization of the beamline design can help to reduce energy loss and improve the overall efficiency of the treatment.

- **Energy management systems**: Implementing energy management systems such as Building Management System (BMS) can help monitor and control energy usage through software. Allows controlling the different systems and, with data analysis, take decisions and actions to improve the efficiency and well-being of occupants, as well as implementing strategies to reduce energy consumption during non-treatment periods. [52]

- **Optimization of facilities & energy-efficient equipment**: Designing proton therapy facilities with good insulation, using natural lighting, and implementing efficient heating, cooling systems and power supply systems. Replacement of technology for more efficient systems that waste less energy in the form of heat, reduce carbon emissions and minimize overall energy consumption. [53]

- **Energy efficiency programs:** following guidelines from energy policies, e.g., Green Papers from the European Commission, or Sustainable Building Certificates (BREEAM) [52]. Moreover, COCIR establishes that by using low power mode during night hours the daily energy consumption can be reduced by 30% and an off mode for most equipment can save up to 48% of the daily energy consumption. [54]

- **Sustainable energy:** energy is the main contributor to climate change, accounting for about 60% of all global greenhouse gas emissions. Therefore, following UN's guidelines is a great way to obtain affordable, safe and sustainable energy [55]. Implementing renewal energy sources for production of hot sanitary water greatly contributes to this objective, since it constitutes 20% of the energy consumption.

11. COSTS

Costs need to be divided in those that are part of the proper proton-therapy equipment (cyclotron costs, gantry etc.) and the ones that involves the installation of an equipment such as this one: [10]

CENTER	QuirónSalud	Clínica Universitaria Navarra
Construction costs (NO VAT)	6.100.000 euros	7.500.000 euros
PEC (NO VAT)	7.100.000 euros	9.000.000 euros
Facultative direction	1.200.000 euros	6000.000 euros
Equipment	35.000.000 euros	Not available data
TOTAL EQUIPMENT INVESTEMENT	**43.300.000 EUROS**	**40.000.000 EUROS** (according to media)

TABLE 1: EQUIPMENT DISTRIBUTION OF COSTS [6]

These costs are from two proton-therapy centers in Spain. In the first case the company in charge of providing the equipment was IBA and the installed equipment was the Proteus One. In the second column the company in charge was Hitachi.
However, these costs can vary depending on the localization, the equipment acquired, the number of treatment rooms, the energy generator etc...

On the other side it must also need to take into account all the costs related to other parts of the installation such as the site acquisition, training and education, research and development, infrastructure, facility design and construction...:

- **Facility design**: This includes the costs of design and site preparation. The range of costs of this part can vary between 5 to 50 million. The high variance in this part comes because it depends on several aspects such as size, location, equipment, number of rooms, expected number of patients...etc.
- **Installation and commissioning**: Installing and commissioning proton therapy equipment can cost between $5 million to $20 million. This includes the cost of transporting the equipment to the facility, installing it, and testing and commissioning it to ensure it is working correctly.
- **Operating Costs**: Operating a proton therapy facility is expensive due to the high costs associated with staffing, maintenance, and ongoing equipment upgrades. The ongoing operating costs can range from $15 million to $40 million per year, depending on the size of the facility and the number of patients treated.
- **Site selection and preparation**: Before starting with the construction there are many requirements that need to be fulfilled: land acquisition, utility connections, soil testing... In this sense these costs may range between 1-10 million euros.
- **Workers costs**: A proton-therapy center requires from a lot of highly specialized and skilled staff (radiation oncologists, medical physicists, dosimeters, maintenance staff, doctors...). Moreover, since the equipment is highly new there can be some added

costs related to the training of the staff in some areas of proton-therapy. All of this makes an approximate cost of around 1-15 million euros per year.

- **Equipment maintenance and improvements**: Proton-therapy equipment is a highly state-of-the-art technology. Because of this, new improvements in the technology are going to appear in the following years so the equipment acquired may be outdated. To prevent this, the acquisition of equipment upgrades is necessary. This cost may range from 1-5 million euros per year depending on the age and the complexity of the equipment. In this range it is also added the costs of equipment maintenance
- **Insurance and regulatory costs**: Operating proton-therapy equipment requires a lot of insurance and regulatory compliance (medical insurance, state and federal regulations, liability insurance...). All of this may give a total cost of around 1-5 million euros per year.

It is again important to highlight that all these costs vary depending on multiple factors. Therefore, giving concrete costs is almost impossible. [10] [8]

Here is a table of the total approximated costs of building a complete proton-therapy center, with all the above costs included:

EQUIPMENT INVESTEMENT	40.000.000-50.000.000 EUROS
FACILITY DESIGN	5.000.000-50.000.000 EUROS
INSTALLATION AND COMISSIONING	5.000.000-20.000.000 EUROS
OPERATING COSTS	15.000.000-40.000.000 EUROS/ YEAR
SITE SELECTION AND PREPARATION	1.000.000-10.000.000 EUROS
WORKERS COSTS	1.000.000-15.000.000 EUROS/YEAR
EQUIPMENT MAINTENANCE AND IMPROVEMENTS	1.000.000-5.000.000 EUROS/YEAR
INSURANCE AND REGULATORY COSTS	1.000.000-5.000.000 EUROS/YEAR
TOTAL COSTS	**69.000.000-200.000.000 EUROS**

TABLE 2: TOTAL COSTS DISTIBUTION

This is approximately the cost of building and setting in motion a proton-therapy center. The cost may be lower through the years since the equipment investment was already performed. Moreover, other costs such as marketing costs may rise over the years.

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