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FORNITURA, POSA IN OPERA, MESSA IN FUNZIONE, OPERAZIONE, GARANZIA BIENNALE FULL RISK E MANUTENZIONE DI UN ACCELERATORE CON TESTATA ISOCENTRICA PER IL TRATTAMENTO CON PROTONI DEI TUMORI PROFONDI

Autori (CNAO se non diversamente indicato)

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Riassunto

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1 GENERAL DESCRIPTION

The National Oncological Hadrontherapy Center, CNAO, was originally designed with five treatment rooms and one experimental room. However, a limitation of the initial investment was decided, and therefore a reduction of the therapeutic potential of the CNAO was accepted and thus in its initial phase the Center was built with only three treatment rooms. Also, in 2004, an isocentric gantry able to rotate the carbon ion beams around the patient was evaluated as technologically premature. Then, the main technical limitations to treatment at CNAO are represented by the lack of a gantry and by the limited field size of 20 cm x 20 cm.

In order to improve in the future the technical capabilities of CNAO, space was reserved next to the actual building to allow the addition of novel treatment solutions able to improve the clinical activities.

Recently the possibilities of expansion of the Center have been re-evaluated and the following options were considered:

a) commercial single room facilities for protons equipped with gantry;

b) a gantry for carbon ions;

c) a facility for BNCT (Boron Neutron Capture Therapy);

d) a facility for the production of radioisotopes;

e) a new experimental room.

The present technical specification refers to the acquisition and installation of a state-of-the-art single room facility for protons, equipped with an isocentric gantry, fully independent of the existing CNAO accelerator facility, to be installed in a new building which will be realized close and integrated with the existing one. The services object of this Bid refer to the expansion of CNAO. The installation of the technology for proton therapy in the available area shall take into account, besides other aspects, the possibility of installing the options b) to e) at a later time.

The new single room for protons shall include a gantry equipped with an active pencil beam scanning system capable of Intensity Modulated Proton Therapy (IMPT) and state-of-the-art IGRT (Image Guided Radiotherapy) technologies. Organ motion management functionality shall also be provided.

To date, various commercial solutions are available on the market for this type of device, for each of them an *ad hoc* design of the building is required. In addition, for each of them a detailed study of the shielding and of all the other safety and radiation protection issues are needed as well as a proper design of the plants to be implemented to support the technology.

The single room facility shall be integrated within the existing CNAO infrastructure and consequently the control and management system of the new treatment room shall be connected with the OIS (Oncological Information System) and patient management systems already operative in CNAO. Also the treatment plans performed with the existing Treatment Planning System (TPS) in use at CNAO shall be transferable to the new accelerator.

Besides the proton accelerator with the isocentric gantry, this tender includes the treatment room equipment and all what is needed for its proper operation and shall be in the state-of-the-art of available technology.

The Supply shall include (non-exhaustive list):

- proton accelerator;
- transport line up to the gantry (if needed);

- Bragg Peak depth in water of the proton beam selectable at least in the interval 50 mm to 300 mm;
- isocentric gantry with sufficient clearance to allow lateral and vertex irradiation (90° rotation and 270° isocentric couch rotation according to IEC 61217, for head&neck treatments) with easy access to the patient in any geometry;
- active dose distribution system (Pencil Beam Scanning, PBS) with the possibility of placing collimators and passive elements, such as ripple filters and range shifters, at different distances from the isocenter (e.g. for eye treatments and stereotactic setup);
- control system, diagnostics, vacuum, source, power supplies and all the necessary systems for the proper operation and full functionality of the technology;
- radiological safety and access control systems able to communicate with CNAO systems;
- a robotic patient positioning system with 6 degrees of freedom;
- an in-room alignment and verification system of the patient's position including isocentric lasers, 2D IGRT system and CBCT (Cone Beam Computed Tomography);
- systems for local and remote management and control of all treatment-related movements, respectively located in the treatment room and in the treatment control room;
- patient video surveillance and audio communication systems;
- evidence (show examples, photos….) that the gantry, the CBCT and the Patient Positioning System are compatible with the treatment of anaesthetized patients;
- interface compatible with Mosaiq OIS and Raystation TPS;
- interface with external gating / tracking / motion management systems;
- proposal of acceptance tests of the system and of all sub-systems, including an estimation of the time required to perform them. The proposal of acceptance tests will be discussed and integrated with CNAO;
- transport, assembly and commissioning until the acceptance;
- a minimum of 24 months full risk guarantee, starting from the positive acceptance test signature;
- operation during the full risk guarantee period;
- 24 months full risks maintenance starting from the end of the guarantee;
- 24 months of operation during the full risk maintenance period;
- CNAO staff training for the operation and maintenance of the technology;
- Uptime minimum 98% (as detailed in section 9.1).

The devices supplied shall comply with all applicable laws and shall have obtained, at the time of acceptance, the CE marking as medical device. If within the supply other devices are individually CE marked as medical devices, the list of individual certifications must be provided.

Any omissions in this document shall not relieve the seller of his obligation to furnish a system that be inherently complete and can be treated as a stand-alone turnkey entity. It must perform satisfactorily in accordance with this Specification.

The Supplier will carry the full responsibility for the design, construction and testing of the technology. He shall provide all the necessary equipment, materials, tools, instruments, facilities and labour to manufacture and test the technology and demonstrate that this Specification and the offered performance are met.

The offer shall include full technical details on each section of this Specification and describe how the Bidder intends to meet the Specification requirements and the offered performance.

The Bidder shall provide a technical report describing the proposed solution, illustrating all the details useful to evaluate the proposed machine. The report shall describe the performances and the needs of the offered device, highlighting the requirements on the building and plants needed to operate it.

The Bidder shall include a description of the accelerator and treatment room and their needs in terms of areas, heights, volumes, structural needs, air conditioning needs and temperature stability and any other requirement that must then be implemented in the building and plant design. All the relevant information shall be provided also for other rooms with special requirements.

The beam production, transport, measurement, control and delivery shall be exhaustively illustrated providing all the details needed to CNAO to perform calculations and verification of the expected performances. Accelerator, sources, lines, gantry and all their equipment like vacuum system, beam diagnostics, power supplies, support and alignment system shall be clearly described and illustrated with all the documentation and drawings needed. In particular the dose distribution system, including both the beam monitoring and the beam scanning, shall be described illustrating the performances of the system and of its elements. The minimum number of delivered particles in each spot, the beam current, the rescanning philosophy, the beam positioning precision, the beam scanning speed, the beam monitoring velocity and all the relevant parameters, also when not explicitly mentioned in this specification, that influence the dose distribution shall be provided.

2 TREATMENT ROOM

The treatment room must include a gantry with an integrated floor solution, a patient positioning system and an imaging system. Furthermore, the necessary safety and communication systems must be included.

The Bidder shall include a description of the room and its needs in terms of areas, heights, volumes, structural needs, air conditioning needs and temperature stability and any other requirement that must then be implemented in the building and plant design.

Any limitation regarding the displacement of connections and monitoring equipment mounted on walls, in particular for general and/or paediatric anaesthesia has to be specified.

2.1 AUXILIARY SYSTEMS AND GENERALITIES

The description of the features of the offered system shall include the following, non-exhaustive, list of items.

General room geometry: provide a description of the room illustrating the various systems present and their relative positions and motion possibilities. Limitations on the gantry-couch-imaging system relative positions shall be highlighted and the space for additional third party instrumentation shall be described. The Bidder shall highlight any limitations in the possibilities for the personnel to work and move around the patient couch during both set-up and in the treatment positions.

Possibility of treatments in anaesthesia: the layout of the treatment room must be such that it includes the space needed for the installation of the equipment for deep anaesthesia of general or paediatric treatments. A layout that includes the space needed for the installation of the equipment for anaesthesia and paediatric treatments is required.

Anti-collision hardware and software system: inside the treatment room there are several movable devices: gantry including nozzle and passive elements, patient positioning system, imaging system. A possibly redundant system is required to avoid collisions between these systems. The Bidder must describe the anti-collision strategy and characteristics of the offered system.

Isocentric lasers: the treatment room must be equipped with a 3D system of precision laser lines aligned to the isocenter, for patient positioning and QA purposes. It shall feature at least 3 perpendicular laser planes: vertical, longitudinal and lateral. The lasers light shall preferentially be red or green. Describe the laser system included in your offer.

Laser alignment accuracy and tuning: the lasers shall be clearly visible with normal room illumination; the fine-tuning and adjustment of the lasers shall be done manually or with a remote control, specify the offered solution. The alignment accuracy shall be ±1mm or better.

Laser line width: the laser line width shall be less than 1 mm FWHM at the isocenter.

Patient surveillance system: the treatment room must be equipped with a video camera system to monitor the patient from the treatment control room during treatment with any orientation of gantry, couch and imaging system. The images shall be recorded and saved for at least 24 hours. At least 2 cameras shall be included in the offer. Describe the proposed solution.

Audio communication system: the treatment room must be connected to the treatment control room via an intercom system that allows to communicate with the patient during the setup and treatment phases.

Connection between fixed floor and mobile floor: the Bidder shall describe, also with the help of drawings and photographs, the transition area between the fixed and the rolling floor, highlighting

movement limitations, obstacles to the passage of trolleys, holes and risks of tripping and any other relevant information for easy access to the patient.

Maximum load on the rolling floor: specify the load capacity of the floor in the gantry aperture.

Noise Level: specify the maximum and average noise level in dBA in the treatment room measured at the isocenter (if other, please specify). The measure shall be done and reported during treatment, during start and stop of gantry rotation, during 360° gantry rotation, during the patient setup operations, including deployment and operation of in-room imaging equipment and during movement of the couch.

2.2 GANTRY

The system offered must allow irradiating the patient from all directions, including head&neck vertex treatments (90 ° gantry angle and 270 ° couch rotation, according to IEC 61217).

The Bidder must include a complete description of the geometry of the gantry and of its technical properties. The description must also illustrate the space around the patient and the possibilities of access to the patient when immobilized on the couch.

The description of the offered gantry must include at least the following items.

Gantry rotation angle: a gantry that offers 360 degrees of rotation is preferred as it reduces the number of couch movements during treatments. Alternatively, it is possible to offer a gantry with a rotation greater than 180° which allows the patient to be treated from all directions by rotating the patient table by 180°. In any case, the offer must demonstrate that the combined Gantry + Couch system allows treatment in all directions with a supine patient. A gantry with rotation less than 180° is not acceptable.

Gantry rotation speed: the maximum rotation speed desired is not less than 1 rpm; a maximum rotation speed between 0.5 and 1 rpm is considered acceptable, even though not desirable.

Multiple selection of the gantry rotation speed: in many cases it is useful to have the possibility of moving the gantry at speeds lower than the maximum. An offer that allows two or more rotation speeds will be preferred.

Gantry angle accuracy: the angular positioning accuracy of the gantry is preferred to be $\leq 0.25°$.

Gantry residual rotation after an emergency stop at maximum speed: the gantry residual rotation during emergency stop at maximum speed shall not exceed 5°; a rotation below 3° is preferred.

Isocentricity of the beam: specify the minimum radius of the sphere crossed by the center of the beam for each angle of the gantry and for each energy of the beam.

Fringe field around isocenter: specify the magnetic field around the isocenter, where patient and workers can be.

2.3 IN ROOM PATIENT POSITIONING SYSTEM

Patient positioning shall be performed with a dedicated robotic system. Swift, easily operated and precise equipment for patient positioning and verification of the desired treatment position is needed in clinical routine.

General criteria are some summarized in the following:

- patient positioning system shall be intended as a robotic system featuring adequate accuracy and resolution in motion and/or steady state, with 6 DoF;
- the system shall ensure repeatability in reaching a target position;
- the system shall include a rigid, and reasonably comfortable couch top to prepare and immobilize the patient. In particular, it has to be designed for proton therapy and must be CBCT compatible;

- the system shall be adequately safe for patients during clinical operations, both in motion and or steady state;
- the system shall be adequately safe for trained operators during motion and\or steady state;
- system controls shall be available with appropriate interfaces, both close to the patient positioning system and remotely. In addition, clinical users shall interact with a more intuitive interface than service users;
- in case of emergency, operators shall intervene and operate as quickly as possible ;
- emergency buttons shall be easily detectable, and eventually activated, at any time;

Provide a description of the offered system and of patient table top in detail. Table top shall have well defined properties with respect to the possibility for CBCT acquisitions and irradiation through the table top.

Patient positioning system shall be defined in details, with particular attention to the mechanical properties of the couch system for movements in x, y, z, pitch, roll and yaw and isocentric rotation. Define specifications for position and angle:

- absolute positioning accuracy; an accuracy equal to 0.5 mm or lower is preferred;
- relative positioning accuracy;
- motion range;
- motion speed;
- the accuracy of isocentric setup corrections.

Specify the maximum patient load (table top weight not included) and if the load can be anywhere or if there are limitations on the load distribution. A patient load equal to 150 kg or higher is preferred.

Specify and describe the automatic procedures and manual operations of the couch.

Describe, if applicable, any areas of the table top where treatment through the table top is prohibited or not recommended.

Specify the working volume with particular attention to minimum height from the floor in the treatment room to the upper surface of the table top while the table is in the patient loading position. If relevant, please describe any additional solution to help during clinical operations. A minimum height equal to 75 cm or lower is preferred.

Specify and describe if the couch enables isocentric rotations: i.e., rotations while a fixed point above the couch is kept at the isocenter. If so, please specify the tolerances on any deviations between this fixed point and the isocenter for the three orientations of rotation (roll, pitch, and yaw). An absolute rotation accuracy of the couch at the isocenter equal to 0.5° or lower is preferred.

Specify the freedom of patient table top movement as a function of gantry and imaging system position by specifying the range of movement in the x, y and z directions of the table when the gantry is at 90°, at 180° and at 270°.

Specify the freedom of gantry movement as a function of patient table top position by specifying the range of movement for the gantry, when the table is rotated to 90° and 270° in yaw direction with and without eventual nozzle accessories mounted.

Provide specifications of speed and acceleration/ deceleration of the couch motion. Specify also the average time required when the couch is moved ±20 cm vertically, ±20 cm longitudinally, and ±20 cm laterally around a fixed point.

Describe the material composition of the table top, and provide details about its physical properties, in terms of Water Equivalent Thickness (WET) and the WET homogeneity.

In addition, the description of the features of the offered system shall include the following items.

Standard table tops indexing compatibility: specify the table top geometry and in particular clarify if a standard indexing system is present.

Patient weight compensation system: clarify if the patient positioning system can record and compensate for different patients' weight or loads during treatment procedures. Specify, if possible, how different distributions of weight may affect the accuracy in reaching a desired position.

Treatment volume: specify the parallelepiped above the couch top in which the clinical isocenter can be moved for treatment at any gantry angle; calibrated for absolute position accuracy within ±1 mm: a volume of at least 100 cm (length) x 50 cm (width) x 40 cm (height) is expected;

Distance between center of treatment volume and couch rotation axis: specify the distance between the center of treatment volume and the couch rotation axis; a distance equal to 80 cm or higher is preferred;

Imaging volume: specify the parallelepiped above the couch top in which the clinical isocenter can be moved to acquire a CBCT; calibrated for absolute position accuracy within ±1 mm: a volume of at least 100 cm (length) x 50 cm (width) x 40 cm (height) is expected;

Couch operation: the couch shall be possible to be operated both from inside the treatment room and remotely from the treatment control room.

Table top rotation in treatment mode: specify the rotation angle of the table top around the vertical axis in treatment mode. Rotation angle equal to 180° or higher is preferred.

Roll and pitch angles: specify the roll and pitch angles of the table top. Roll and pitch angles equal to ±5° or higher are preferred.

2.4 IN ROOM IMAGING

X-ray based verification systems are necessary in radiotherapy to minimize inter- and intra- fraction misalignments that occur between daily patients' position and nominal setup defined in the treatment planning system. State of the art imaging system shall be included in the offer.

The possibility of acquiring images in the treatment position, particularly with a CBCT, is highly appreciated.

The imaging system shall ensure precise irradiation of the patient accurately immobilized in a verified treatment position and its usage could also be foreseen for monitoring of anatomical changes and displacements during a patient's treatment series. Specify all imaging systems included in the offer and give a detailed description of their application.

The imaging systems shall be integrated with the control system of the patient positioning and of the gantry. Control systems shall be interconnected for a univocal and safe use of the systems.

The technical proposal must include both kV Orthogonal images (2D) and kV volumetric imaging (3D, CBCT) for patients' imaging verification. The orthogonal kV and kV CBCT imaging systems shall support and enable online-guided patient positioning and re-positioning based upon image registration with respect to reference images (planning CT).

Field of view in both modalities shall be adequate for a precise clinical evaluation of setup uncertainties.

Specify the required steps and the workflow during online image-guided patient re-positioning based upon automatic image registration with reference images from the planning-CT.

For calibration and QA, a smooth and intuitive workflow is important. Calibration and QA software which is integrated into the imaging software system is preferred. Less time-consuming calibration and QA procedures are preferred.

Describe the system and workflow for calibration and QA of both the orthogonal kV imaging system and kV CBCT system.

The description of the offered system shall include at least the following items.

CBCT at the isocenter: specify if the system allows acquisition of CBCT at the isocenter. An isocentric CBCT is preferred.

Imaging limitations: specify for kV CBCT imaging system any limitation with reference to situations where imaging cannot be performed (e.g. at any specific combination of couch rotation and gantry angle).

Stereoscopic X-ray isocentricity: specify the distance between the X-ray isocenter and the reference isocenter; isocentricity equal to 1 mm or lower is preferred.

Stereoscopic X-ray Flat panel sensitive area: specify the maximum rectangular field size at isocenter of the orthogonal kV imaging system. A sensitive area equal to 30 x 30 cm^2 or higher at the isocenter is preferred.

Stereoscopic X-ray high and low contrast resolution: specify for the orthogonal kV imaging system high and low contrast spatial resolution in lp/mm; an high contrast spatial resolution at 70 kVp equal to 2 lp/mm or higher is preferred.

Imaging limitations: specify for the orthogonal kV imaging system any limitation of the imaging system with reference to situations where imaging cannot be performed (e.g. at any specific combination of couch rotation and gantry angle).

Stereoscopic X-ray Field of view: specify the maximum rectangular field size at isocenter of the orthogonal kV imaging system.

Gating for image acquisition: specify if the X-ray imaging system can be synchronized with respiratory signal using third parties gating signal.

Fluoroscopy mode of the Stereoscopic X-ray imaging system: clarify if fluoroscopy mode is available for image acquisition and volume reconstruction.

Imaging recovery: specify, for the orthogonal kV and kV CBCT imaging systems, whether the kV CBCT imaging system is able to resume imaging after an interruption without having to restart the imaging at the original imaging start position.

CBCT transversal field of view: specify the maximum transverse diameter of the CBCT volume (Field-Of-View, FOV – Imaged cylinder diameter). A CBCT transversal FOV equal to 45 cm or higher is preferred.

CBCT inferior-superior field of view: specify the maximum size in inferior-superior direction of the CBCT volume (Field-Of-View, FOV - Imaged cylinder height). A CBCT inferior-superior FOV equal to 20 cm or higher is preferred.

CBCT frame rate: specify the maximum frame rate for the CBCT acquisition; a CBCT frame rate equal to 7 fps or higher is preferred.

Maximum gantry speed for CBCT acquisition: specify the maximum rotation speed for the CBCT gantry; a maximum speed equal to 1 rpm or higher is preferred.

CBCT image typical reconstruction time at the end of acquisition: specify the time needed to reconstruct the 3D image set after the end of acquisition for a set of standard clinical acquisition protocols (H&N, pelvis and thorax); a reconstruction time equal to 15 s or lower is preferred.

Multiple resolution capability: specify if the system allows acquisition of images with multiple resolutions (e.g. voxel size, high/low contrast spatial resolution) and their values; such a feature is preferred.

Typical image registration time: explain and specify, for the orthogonal kV and kV CBCT imaging systems, the automatic 2D/3D and 3D/3D matching time (consider CBCT volume with 90 slices of 2 mm). A typical registration time equal to 30 s or lower is preferred.

Typical dose for imaging: specify preset exposure parameters for the orthogonal kV and kV CBCT imaging systems;

Deployment time: specify for the orthogonal kV and kV CBCT imaging systems the deployment time of the imaging systems from fully parked position to imaging position, given that the gantry angle is in the required treatment position.

Quality Assurance: the delivery shall include all the phantoms and software systems necessary for Quality Assurance (QA), calibration and maintenance of the complete imaging system. Provide the list and their specifications.

2.5 GATING

Respiratory gated treatments can be regarded as a pre-requisite for proton treatment for some indications, especially when organ motion is not negligible.

Gated beam delivery usually requires the use of additional tools to record and synchronize external signals as a surrogate, in order to estimate physiological organs motion. Techniques applied to counteract the effects of intra-fractional anatomical changes and interplay effects such as application of 4D planning, rescanning and/or use of enlarged and overlapping spots are of relevant importance in particle therapy. Given these premises, a minimum of one interface to a respiratory gating system and/or a surface guidance system shall be included in the offer.

The system for verification and monitoring of patient motion and position during irradiation shall be delivered as an integrated functionality of the proton therapy system. This system shall include and imply possibilities for gated irradiation through automatic beam control based upon input from an online system.

Provide a description of the offered equipment and systems for gating and management of organ motion and interplay effects, including the possible application of fiducial markers and the possibility for marker free techniques if applicable. Explain the integration with the proton beam delivery system.

The description of the features of the offered system shall include at least the following items.

General strategy: describe the general strategy to cope with organ motion (rescanning, gating, tracking, …).

Rescanning strategies: specify the rescanning strategies foreseen for organ motion effect mitigation (layer, volumetric, combined, no rescanning).

Hardware description: specify the offered solution, if any, to generate the gating signal.

Interface for third parties motion management sources: the system shall provide at least an interface to third parties motion management sources, e.g. a respiratory gating system (describe its logic/technology , TTL or similar). Describe the available interfaces (e.g. Anzai belt, Polaris, vision RT…). A number of interfaces higher than one is preferred.

3 TREATMENT DELIVERY

The proton therapy system shall allow treatments by Intensity Modulated Proton Therapy with Pencil Beam Scanning. Among the pathologies treated at CNAO are paediatric tumors for which a large treatment field is highly desirable to ease cranio-spinal irradiations reducing to a minimum the required field patching. A treatment field of 30 cm x 40 cm is strongly desired.

In particular the dose distribution system, including both the beam monitoring and the beam scanning, shall be described illustrating the performances of the system and of its elements. The minimum number of delivered particles in each spot, the beam current, the rescanning philosophy, the beam positioning precision, the beam scanning speed, the beam monitoring velocity and all the relevant parameters, also when not explicitly mentioned in this specification, that influence the dose distribution shall be provided.

The complete list and detailed description of beam interlocks which can be activated by the beam monitoring system shall be reported. The management strategy for any interlock at the level of the treatment console shall also be specified.

The full description of the treatment console, including irradiation start/interrupt/terminate buttons shall be provided.

The proton accelerator, the possible energy selection system and the active beam delivery system must meet the requirements set by the clinical need of treating a broad variety of tumours; it must be possible to treat superficial as well as deep target volumes.

The use of passive range shifters when treating targets located at superficial depths is accepted. Detail the offered system and clarify which passive elements, if any, are inserted by an actuator and which ones have to be inserted manually.

The offer must provide a complete description of the accelerator system, of the properties of the beam, of their stability and reproducibility and of the beam delivery system offered. Devices and interfaces included in the offer for the management of organ motion shall be described.

The description of the features of the offered system shall include at least the following items.

Maximum treatment field size at the isocenter: a treatment field equal to 25 cm x 40 cm, or larger, is preferred for cranio-spinal treatments with minimum field patching. Specify the treatment field size offered. Minimum accepted field size is 20 cm x 20 cm.

Adjustment of the Bragg Peak depth in water: specify the depth adjustment step size, measured in water. A depth adjustment step size equal to 1 mm or lower is desirable.

Accuracy of the Bragg Peak depth in water: specify the absolute depth error in water. A depth accuracy equal to 1 mm or lower is desirable.

Minimum spot size: specify the 1-σ spot size in air at the isocenter, as a function of energy, for all treatment energies. Beam sizes at the minimum energy without range shifter equal to 8 mm or lower are preferred.

Variable spot size: specify the number of available spot sizes selectable for each energy and their values, measured in air at the isocenter.

Spot symmetry (difference between X and Y spot sizes): specify the spot symmetry for all angles of the gantry and for all energies. The specification of the spot symmetry must be valid for all lateral positions within the whole (maximum) treatment field; spot symmetry should be equal to 10% or lower.

Spot position accuracy: spot position accuracy shall be equal to 1 mm or lower at any beam energy and at any gantry angle.

Resolution of the dose monitoring system (MU): an intrinsic resolution of the dose monitoring system equal to 0.01 MU or lower is preferred.

Dose monitoring system short term (1d) reproducibility: short term (1 day) reproducibility of the monitoring system shall be within ±0.5% (1-σ).

Dose monitoring system medium term (1w) reproducibility: medium term (1 week) reproducibility of the monitoring system within ±0.5% (1-σ) is preferred.

Linearity of the dose monitoring system: linearity of the dose monitoring system within ±1% is preferred.

Redundancy of the beam monitoring system: the offered monitoring system shall measure in real time beam fluence as well as spot position and size in a redundant way.

Treatment recovery: the beam monitoring system shall be able to save all the relevant information to build a recovery plan in case of abnormal termination and even in case of electrical blackout, according to the relevant standards.

Typical treatment time: for 10x10x10 cm^3, 2Gy, uniformity +/- 3%, 30 to 20 cm depth; provide the calculation of the expected time needed describing the various contributions (beam current, time for each slice, number of slices, time to change energy, etc). A typical treatment time equal to 60 s or lower is preferred.

Typical treatment time: for 10x10x10 cm^3, 2Gy, uniformity +/- 3%, 15 to 5 cm depth; provide the calculation of the expected time needed describing the various contributions (beam current, time for each slice, number of slices, time to change energy, etc). A typical treatment time equal to 60 s or lower is preferred.

Delay between beam-on request and beam in room: describe the beam request procedure and the time needed to physically start a treatment. A delay equal to 10 s or lower is preferred.

Time to switch off the beam in emergency: describe how the beam is stopped in emergency and provide the maximum delay between the alarm and the beam off. Evaluate the maximum delivered unwanted dose and comment on the efficacy of the proposed switch off performance. A delay equal to 150 microseconds or lower is preferred.

Snout: describe the characteristics of the nozzle. A motorized adjustable snout for passive elements is desirable to minimize the air gap and thus beam scattering.

Motorized passive elements: describe the available nozzle accessories that can automatically be deployed for treatment purposes.

Manually applied passive elements: describe all required manual operations performed by the treatment staff in order to mount and apply nozzle accessories that cannot be deployed automatically.

Collimators: describe the possibility to apply a collimator to the nozzle and if a multileaf collimator is included in the offer: describe its features.

Pencil beam scanning: specify the scan speed as a function of beam energy in both directions and the minimum spot duration, if any.

4 TREATMENT CONTROL SYSTEM

It is crucial that the data transfer between the Oncology Information System (OIS) and the Treatment Control System is efficient, safe and seamless. The system shall be compliant with DICOM RT ION.

Describe the offered system including at least the following points.

Partial treatments: the Treatment Control System must include a functionality that allows recovery of the treatment session (starting from data such as delivered fields, spot pattern, monitor units values, etc.) for all available treatment techniques (such as IMPT, Single Beam Optimization, etc.) even after a sudden interruption like a power failure, and the possibility to complete treatment of a patient.

Control system description: give a full description of the treatment control system and the relevant applications of use.

Record and verify information: the control system shall produce and provide all the necessary information for enabling Mosaiq to verify the correct execution of the plan.

Redundancy and back up: describe the redundancy and back up method for the Treatment Control System.

Control system usage modes: the control system shall allow operation in different operation modes including at least clinical, medical physics (QA) and service modes.

External interface: the control system shall be able to accept plans (in service and QA mode) built by means of other platforms. A communication protocol for this information exchange shall be made available to CNAO to implement this type of solution.

QA software tools: QA software tools to test the machine and to perform experiments shall be provided. Describe the QA tools offered, their performances and their options.

TCS-OIS interface: describe the interface between the Treatment Control System and the Oncology Information System (Mosaiq); the data transfer protocol shall support all transfer of information between the Treatment control System and the OIS and between the in-room image acquisition system and the OIS.

Treatment time log: the Bidder is required to offer a treatment log reporting all the details of the machine usage, including at least the beam-on time, the room occupation time for the field under consideration, the room occupancy time for the patient under consideration, the beam occupancy time for the measurement under consideration when the machine is used for QA or experimental activities, the control system modality and, in case of fault, the fault duration.

Irradiation log: a log file shall be produced for every irradiation and must allow the tracking of all the particles transported to the treatment room. Each log shall contain at least particles number for each energy and gantry angle. These data are naturally contained in the treatment plan, but they may not be immediately available when in service or QA mode.

Error log: the Bidder is asked to offer an error logging system to allow identification of weaknesses. The logging system shall be available for inspection both to the Supplier and the Customer and the customer shall be warned by meaningful messages as soon as the problem arises. The Supplier is invited to set up an automatic mechanism (mail, messages, ….) to be immediately warned about any malfunction that can affect the machine, so that the intervention, if necessary, can be executed in the fastest possible way.

Italian and English keyboard: all the provided software and applications must accept Italian and English keyboards.

5 WORKFLOW AND SYSTEM INTEGRATION

The Supplier shall take responsibility for, and be in charge of, integration of the data communication between the systems in the treatment room and the systems in the treatment control room. The workflow shall be highly automated and time-efficient.

Workflow for patient positioning and verification: the Supplier shall be responsible for the system integration and the seamless data flow between the Treatment Control System and the imaging systems to be used for positioning and treatment purposes; e. g. kV CBCT imaging system and orthogonal kV imaging system and the robotic couch system.

Verification images saving: the image acquisition system shall have the functionality that images acquired in a treatment session shall be saved and stored in the OIS, where these can be reviewed and evaluated independently. This functionality will allow physicians and other personnel to evaluate treatment images from locations outside the treatment control room.

Image guided adaptive treatment: describe the Bidder's strategy for integration of all systems required for image guided adaptive treatment; i.e. integration of the data communication between the OIS and the Treatment Control System (including the Beam Delivery System) and with all in-room imaging and positioning control systems.

Verification and registration: describe the possibilities and workflow for image acquisition and evaluation of verification images during patient setup. Describe the workflow when repositioning the patient after verification by orthogonal kV imaging or kV CBCT acquisition.

Local and remote repositioning: describe which of the required re-positioning operations can be performed from the treatment control room. Describe which of the required re-positioning operations can only be performed from the treatment room.

6 RADIATION SAFETY ISSUES

In order to possess, to deploy and to operate an accelerator suitable for proton therapy, CNAO will have to obtain a license according to Italian regulations for ionizing radiations (D.Lgs 230/95, as amended and supplemented).

During this process, a close cooperation is necessary between CNAO and the Supplier. The latter shall take all the necessary steps to ensure the effectiveness of that cooperation, and shall provide all the information required by CNAO, in order to apply to, obtain, manage and keep the requirements for the due radiation safety license.

Since several radiation emitting machines and sources, owned and managed by CNAO, are already hosted in the CNAO property, the radiation safety evaluation of the proton therapy machine requires an ad hoc study, that takes these peculiar conditions into proper consideration.

For these reasons, the Bidder is asked to meet the following requirements.

A) **RADIATION SAFETY REPORT**

a.1) The Bidder shall provide, as a part of the technical report included in the offer, a radiation safety report, that includes all the information that are necessary to fully evaluate the proposal. The contents of the report are described in sect. E. After the contract signature, the Supplier shall appropriately update it. Ways and times of the update are stated in sect. F.

a.2) The Supplier shall appoint a person with a suitable qualification and knowledge about radiation safety (preferably the author of the submitted radiation safety report, described in a.1), to act as an interface between the Supplier and CNAO for the related matter during the design, the commissioning and the operation and maintenance of the machine.

B) **SAFETY INTERLOCK SYSTEM**

b.1) The machine shall come with a safety interlock system (SIS), designed in order to prevent any unclear access to the areas where the beam, or where radiation emitting devices can be on, and to provide all the due ancillary features, as foreseen by the applicable international guidelines and by the Italian law.

b.2) The SIS shall provide at least all the features described in sect. G, unless the Bidder can prove that the requested features are not applicable to the provided machine and/or that a different technology has been adopted that can provide the same safety standards.

b.3) The SIS shall be designed in order to be possibly updated and/or modified accordingly to CNAO needs, as arisen during the design, the validation, the licensing and the commissioning process.

b.4) At the end of the SIS deployment, and at any update of the system, its wiring diagrams, the user manual, the source code (if FPGA or equivalent system is used) shall be provided to CNAO.

C) **CONTROL SYSTEM**

The control/diagnostics system:

c.1) shall measure and log the number of particles accelerated to the extraction energy in the machine and their extraction energy;

c.2) shall measure and log the number of particles transported to the isocenter and their energy;

c.3) shall be able to limit (e.g. to the typical clinical values) the beam current transported at the isocenter to intensities (set by the user), in terms of instantaneous current or integrated current over a given (user defined) time span.

D) **FURTHER RADIATION SAFETY REQUIREMENTS**

During the commissioning, operation and maintenance, the areas where the machines are located will be under CNAO control, and the radiation safety will be carried out according to CNAO radiation safety license and CNAO internal radiation safety procedures. For these reasons:

d.1) the Supplier's personnel shall comply, at any moment during the commissioning, the operation and the maintenance of the plant to the Italian applicable laws and internal radiation safety procedures;

d.2) during the commissioning and the "full risk" guarantee and maintenance period, the Supplier shall bear the costs to transport, detain and dispose of the activated machine parts according to the Italian applicable laws and the CNAO radiation safety license.

E) **RADIATION SAFETY REPORT CONTENTS**

The radiation safety report stated in sect. A, as included in the offer, shall contain:

e.1) beam data (beam losses and description of the beam lifetime)

The Bidder shall provide a full description of the beam generation and transport, and all the necessary information that can be used to perform the necessary radiation safety evaluations. It is anyway in the right of CNAO to ask for more information about these data.

The report shall include at least:

e.1.1) nominal beam data: typical average over an hour of operation and maximum accelerated beam current (at injection, extraction, isocenter), maximum energy, time structure of the accelerated beam;

e.1.2) beam losses description and magnitude, provided as a table, where the beam loss locations and direction, the lost particle energy, the target material are provided. In the same table, the beam losses magnitude should be stated, as a yearly average in standard conditions (i.e. defined by the Bidder), and as an hourly maximum, in all the possible given operation modes;

e.1.3) in the report, a full description of the machine functioning modes, also stating how the beam losses of the table cited in sect. e.1.2 have been obtained, shall be included. A description of the machine parts where the most relevant losses take place shall be provided, including (if the case) dumps, septa, collimators, beam stoppers etc…;

e.1.4) the suppliers shall also describe how the beam not transported to the isocenter is dumped (if any);

e.1.5) all the data cited in sect. e.1.1 – e.1.4 shall also be provided for pre-acceleration machines (e.g. sources, LINAC etc..) if applicable.

e.2) radiation fields, dose rates and particle spectra

e.2.1) the report shall include all the relevant information about the radiation field generated by the unshielded machine, including isodose curves and produced particle spectra;

e.2.2) the information stated in sect. e.2.1 shall be provided for any radiation emitting device in the accelerator assembly (e.g. linacs, radiofrequency generators, klystrons, HV vacuum tubes etc…).

e.3) radiation safety evaluations

The report shall include a detailed evaluation about the radiation safety issues of the proposed machine, that shall include all the relevant issues for the radiation safety of the workers, the public and the environment.

It shall include at least:

e.3.1) a radiation shielding design for standard (i.e. Bidder defined) conditions, comprising a typical operation workload (including treatments, maintenance, machine setting and tuning, clinical QA) shall be provided. The proposed shielding shall keep the dose rate below 1 mSv/y - H*(10) at any point outside the shielding (including the bunker roof). The calculation method used for these evaluation shall be clearly and explicitly stated and described, so to make it possible to perform the required validation process by the CNAO RSO. If Monte Carlo evaluations have been carried out, the input files should be provided;

e.3.2) a statement (for any room where the beam is produced and transported) about the minimum ventilation (air exchange rate) that is needed inside the machine vault for technological needs. An evaluation of the total activation of air (i.e. production of radioactive gas) should be carried out, including:

- activity produced for any nuclide produced in air in typical conditions and at full current;

- maximum specific activity (Bq/g) and volume (m^3/h) of released exhaust air in typical conditions.

The calculation method used for these evaluations shall be clearly and explicitly stated and described, so to make it possible to perform the required validation process by the CNAO RSO; if Monte Carlo evaluations have been carried out, the input files should be provided;

e.3.3) a description of the activation issues on the machine parts, on the related structures, on the materials placed in the room shall be provided. Where appropriate, data can be provided based on previous experiences on the already installed facilities. The following data are required:

- activation issues on machine parts (magnets, septa, etc..). Cooling time (in typical conditions) required to perform the routine maintenance operations;
- typical cooling times required to access the accelerator bunker (dose rate <10 μSv/h), or (where applicable) to other areas.

The report shall also include:

e.3.4) an estimate of the production of radioactive waste (and typical procedures for their management) during commissioning, operation, ordinary maintenance;

e.3.5) the evaluations of the relevant activation issues (and typical radionuclide inventory and specific activity) for the accelerator cooling water;

e.3.6) a description of the radiation safety issues (activations, beam intensities, procedures) during transport, assembly, and the different commissioning phases of the accelerator and its ancillary systems;

e.3.7) it shall also include a description of any peculiar problem, e.g. the interaction with the SIS of the single machine parts, the machine activation related with the fact that the machine is under commissioning (i.e. different from the typical situation during operation) shall be appropriately stated;

e.3.8) a description of the typical doses received by the technical and the sanitary personnel during the commissioning, the ordinary operation (treatments and QA) and the ordinary maintenance activities.

F) **UPDATE OF THE RADIATION SAFETY REPORT**

Thirty days (30) after the contract signature, unless a different timing is agreed with CNAO, an updated radiations safety report shall be produced, in which the Supplier provides the information that should have been provided in the first radiation safety report, as described in sect. E.

If requested by CNAO, the Supplier shall anyway integrate the report with further information, if necessary to the evaluations needed to apply to, obtain, manage and keep the requirements for the due radiation safety license.

G) RADIOLOGICAL SAFETY INTERLOCK SYSTEM (SIS): GENERAL FEATURES

A complete description of the built-in radiological safety interlock system (SIS in the following) shall be a part of the technical report.

The SIS shall:

g.1) prevent any access to areas where the beam, or any radiation-emitting device, is on;

g.2) shut down (i.e. inhibit radiation emission) any radiation emitting device in a room within a negligible time, so to prevent it from emitting further radiation, in the case of access;

g.3) shut down the beam in the room within a negligible time, in case of access;

g.4) keep the beam down, and any radiation emitting device off, in the rooms where access is permitted;

g.5) manage a set of signaling devices (lamps, sirens, tv screens) that can inform the operators about the machine and treatment room status;

g.6) be built in order to properly interface (both input/output) with the ventilation system. It shall be aware of the ventilation status and be able to inhibit the ventilation system when necessary;

g.7) be built in order to have a proper interface (both input/output) with third party radiation monitoring system, chosen by CNAO. It must be thought in order to receive radiation alarms, and to provide the monitoring stations an individual alarm enable/inhibit signal;

g.8) receive alarm signals from an adequate number of emergency buttons, that inhibit the beam and any radiation emitting device that can have any influence on the area where the button is hosted. These buttons shall be placed in the control rooms and in the radiation areas (where the beam, or any radiation emitting device, can be on);

g.9) enable access to radiation areas only after a delay time set by the user or, at the user's choice, when the dose rate is below a certain threshold, as measured by a radiation monitor (by the monitor mentioned in sect. g.7 as well);

g.10) be conceived so that its intervention is based on hardware technologies (so that no alarm or intervention solely depends on a software);

g.11) check every access to rooms where radiation emitting devices or the beam may be present, with redundant microswitch system (two independent microswitches, with AND condition, connected to two independent cables);

g.12) be conceived so that all the alarm signals are redundant;

g.13) stop the beam, or switch off radiation emitting devices, via two independent systems. The cited systems should be fail safe;

g.14) be conceived so that, if the beamlines passes through different rooms, beam stoppers shall be placed on the beamline between a room and another, that are fully able to completely stop the primary beam, so that the beam cannot be transported to accessible areas;

g.15) require a patrol procedure (with buttons pressed in the right sequence and within a given time) to effectively verify the clearance of the areas where the beam will be transported, or where a radiation emitting device is going to be switched on;

g.16) force the operator to perform a patrol procedure in the area where an emergency button has been pressed, before being allowed to switch on the beam or any radiation emitting device;

g.17) provide an overview system for the SIS, preferably in the accelerator control room (if any), so that the system status and the input/output signals can be individually seen by the operators;

g.18) provide enable/disable keyframes, that enable/disable radiation emitting machines and/or beam transport to the treatment room.

7 EQUIPMENT BUILDING INTERFACES

In this chapter the main principles for some major technical interfaces are given.

The details of all interfaces and their specifications shall be supplied by the Bidder in form of a preliminary Equipment to Building Interface (EBI) document.

After the award of the tender, the Supplier shall prepare the final EBI document (*Documento Definitivo di interfaccia macchina ed edificio*); the Supplier shall also commit to collaborate with the civil engineering company designing the building providing the necessary information and requirements of the technology and with periodic meetings to discuss the design in progress.

Interface descriptions.

Cooling systems: a centralized cooling system will be installed by CNAO according to the requirements of the accelerator in terms of pressure and flow. The delivery will be in the form of demineralized water, to be sent directly to the various devices, or primary cooled water to feed the cool side of an heat exchanger, depending on the requirements of the accelerator.

HVAC: according to the EBI document the central air handling units, humidifiers, driers, ductwork, dampers, grilles etc. will be installed by CNAO. The Supplier shall supply complete drawings of ductwork as well as air flows in areas where the Supplier has installations.

Compressed air: compressed air system will be installed by CNAO terminated on outlets specified by the Supplier. Connection to the Supplier's equipment from the outlet shall be done by the Supplier. Available pressure is 0.8 MPa; available flow depends on the regime of the supply (continuous or pulsed) and shall be verified after the detailed requirements are included in the EBI document.

Lifting devices for maintenance and handling of components: CNAO will provide overhead cranes, monorails, hooks, hoists and other lifting devices indicated by the Supplier in the EBI document for the technical rooms (accelerator room, gantry room, power supply room, etc). The Supplier shall specify transport gates, hatches and associated solutions for temporary and permanent situations.

Power supply: CNAO will provide all the required power supply to the accelerator and ancillary systems/devices. The power supply network will be organized in three levels:

- a main power supply, directly derived from the grid. This is intended for the normal operation of the accelerator. The instantaneous power shall be limited to 3 MVA;
- an emergency power supply, fed by a diesel generator, that will start within 2 minutes after a blackout. This power supply is not intended to allow the full operation of the accelerator, but only to maintain it in a condition which allows a quick restart as soon as the main supply is restored. The instantaneous power shall be limited to 200 kVA;
- an Uninterruptible Power Supply for critical systems/devices or systems/devices that ensure the patient's safety. The instantaneous power shall be limited to 150 kVA for a maximum time of 5 minutes.

The supply voltage shall be in the Low Voltage range, typically but not limited to 400 V three phase.
All the required transformers, switchgear, switchboards, panels up to the interface point indicated by the Supplier in the EBI document, shall be provided by CNAO. CNAO will also provide all the necessary cable tray and floor and wall openings.

Information Technology: the CNAO facility is equipped with a complete IT infrastructure, including a Data Centre, centralized storage, physical and virtual servers, firewalls, wired and wireless connectivity, Internet access and so on.

CNAO will provide all the connectivity required by the Supplier and specified in the EBI document. Servers and other IT equipment supplied by the Supplier for the operation of the accelerator can be housed in CNAO's Data Centre.

Firefighting systems: CNAO will install a firefighting system according to the EBI document and legal regulations.

Lighting system: CNAO will install a permanent lighting system according to the EBI document and legal regulations.

Other requirements: any other requirement indicated in the EBI document shall be discussed with CNAO.

8 STRATEGIC PROPOSAL OF RESEARCH AND DEVELOPMENT ACTIVITIES

The presentation of future research programmes performed by the Bidder using the technology, or related to it, is required. The number as well the quality of the programmes proposed will be evaluated. The conditions, priority and the exclusivity to involve CNAO shall be declared and will be evaluated.

CNAO is a research institution and R&D programmes are ongoing also in collaboration with many national and international, research and industrial partners. The Bidder shall declare the interest and the intention to participate to R&D programmes, calls, EU projects etc. proposed by CNAO, specifying the resources and the facilities that will be put at disposal (detailed in terms of skills, FTEs, experience, time, costs) for research projects in the next 3+3 years.

9 MAINTENANCE AND OPERATION

9.1 WARRANTY AND MAINTENANCE FULL RISK

The new Proton Therapy Center in Pavia aims to treat a total of 350 patients per year at full capacity. The planned clinical operation hours (including patients treatments and clinical QA tests) are 16 per day (Monday to Friday, 6.00 a.m. to 10.00 p.m.), about 250 days per year, and at average 26 treatment fractions per patients (an average treatment fraction is estimated in 20 minutes).

The Supply shall be offered with the guarantee for defects and operating defects (art. 1490 cc), due to the lack of the promised and/or essential qualities to which it is intended (art. 1497 cc), as well as guarantee for proper functioning (art. 1512 cc).

The minimum warranty period required is 24 months from the date of the positive acceptance test signature. The warranty extension after 24 months is subject to evaluation in the Technical Offer.

During the warranty period, the Supplier shall provide all the technical assistance services required for preventive and corrective maintenance, according to the methods and conditions indicated in the Technical Offer and in any case in the Full Risk mode.

The warranty is extended to the entire Supply and to all its hardware and software components, whether they are installed during commissioning or following a replacement and/or upgrade.

During the warranty period, CNAO will not have to bear any financial burden for maintaining the supplied and/or updated equipment in perfect working condition. All charges for preventive/scheduled and repair interventions must therefore be understood to be included in the purchase price of the Supply.

At the end of the Full Risk Warranty and its possible extensions, the two-year Full Risk Maintenance period begins.

The offered Service - both in Warranty and post Warranty/Maintenance - is Full Risk, therefore it includes the repair and replacement of the Supply in all its components including accessories, consumables subject to wear (lubricants, filters, sensors, etc.), with the sole exclusion of the consumable material necessary for ordinary use (e.g.: disposable and single-patient material, if present).

The service will be performed by specialized personnel of the Supplier and compliant with safety standards and includes:

- the full system operation (Operations);
- the preventive maintenance;
- the system repair;
- the supply of spare parts;
- the full system upgrades (hardware and software).

These activities will be carried out as detailed below and in compliance with the minimum requirements.

<u>Uptime guarantee</u>

The Supplier guarantees the Uptime of the Proton Therapy System (“Uptime Guarantee”) in the value that will be declared in the Offer, which cannot be less than 98%. The Uptime shall be calculated in accordance with the definition below:

$U = (1-D/A) \times 100\%$

where U is Uptime, D is the downtime in minutes, A is calculated in minutes on the basis of the planned clinical activity hours, i.e. Monday – Friday 06.00 a.m. – 10.00 p.m.; all these values are evaluated over each quarter of the year.

For each percentage point the guaranteed Uptime, evaluated over a calendar quarter, is not fulfilled with respect to the offered value, the warranty/Maintenance period shall be prolonged by 1 calendar week (7 calendar days).

Example: if the offered Uptime is 98%, while the real Uptime is 95.98%, this implies that the service period shall be prolonged by (2.02 x 7 days = 14.14 days) 14 days.

Subject to agreement with CNAO, the prolonged service period (the 14 days of the aforementioned example) could be reduced by providing access to the proton therapy system to CNAO in agreed periods. The Parties shall discuss on a weekly basis the extent of downtime subject the dispute mechanism agreed upon.

If the achieved Uptime is equal to or less than 80%, the Client has the right to terminate the Contract.

Any extensions of the service periods do not exempt the Supplier from bringing the services concerning operations to the level laid down in the Uptime Guarantee as soon as possible.

In the Technical Offer the Bidder shall provide a Maintenance Plan [art. 16 lett. d) in the "Disciplinare di Gara" document], whose sections shall be entitled and ordered as the following 9.2 to 9.6 sections of the present document, complying with the minimum requirements.

9.2 OPERATIONS AND EXTRA-AVAILABILITY

The Bidder is committed to ensure that the System is operational and functioning from Monday to Friday from 6:00 a.m. to 10:00 p.m. in order to perform clinical activities and QA procedures.

In the remaining time, not specifically devoted to clinical or planned preventive maintenance activities, the Bidder is asked to provide a machine availability plan, not related to the clinical activities, for CNAO research activities ("Extra-Availability Plan" in the following).

9.3 PREVENTIVE MAINTENANCE

The Bidder shall detail the following ordinary maintenance activities:

- scheduling of the maintenance plan, to be agreed with CNAO;
- delivering of detailed technical intervention reports in order to test the status of the apparatus before and after the intervention, the performed maintenance activities, maintenance stop hours for the apparatus, complete list of replaced components;
- periodic checks, tests, adjustments and calibrations according to the manufacturer's specifications;
- replacement of spare parts and of parts subject to wear in order to recover the system quality standards and to assure its correct working so to prevent the system from stopping;
- verifications of electrical and mechanical safety in accordance with CEI Standards currently in force and with national regulations;
- supply of enhancements, upgrades, changes and improvements both for the hardware and the software;
- should any changes in the hardware be necessary due to new versions of the software, they should be in charge of the Supplier;
- supply of proper antivirus software bundles for the overall system and correlated sub-systems.

9.4 EXTRAORDINARY MAINTENANCE

The Bidder shall specify how it proposes to organise the corrective maintenance, differentiating between A) corrective action during the clinical activity time (i.e. from Monday to Friday, from 6:00 a.m. to 10:00 p.m.) and B) corrective action during the remaining time (i.e. nights, week-ends and public holidays) in accordance with the minimum requirements detailed in the following.

A) corrective intervention during the clinical activity time (Monday to Friday, 6:00 a.m. to 10:00 p.m.)

The Bidder shall clarify whether it is foreseen 1) to employ personnel permanently on site in Pavia or 2) personnel "on call".

In scenario number 1), the Supplier shall:

- employ on-site specialized personnel;
- guarantee an on line 24/7 technical support;
- guarantee an immediate action on a blocking breakdown (blocking stands for a failure which does not allow to perform clinical activities); continuous intervention till the failure resolution shall be assured;
- guarantee action on a not blocking breakdown at the end of the scheduled clinical activities; continuous intervention till the failure resolution shall be assured.

In scenario number 2), the Supplier shall:

- guarantee an on line24/7 technical support ;
- guarantee an immediate action on a blocking breakdown by means of specialized personnel within 4 hours from the call (blocking stands for a failure which does not allow to perform clinical activities); continuous intervention till the failure resolution shall be assured;
- guarantee action on a not blocking breakdown by means of specialized personnel at the end of the scheduled clinical activities; continuous intervention till the failure resolution shall be assured, so that the first scheduled clinical treatment can be performed without any delay.

B) corrective action during the remaining time (i.e. nights, week-ends and public holidays)

In the remaining time not specifically devoted to clinical or planned preventive maintenance activities, the Bidder shall assure to CNAO the System availability for research activities, according to the Extra-Availability Plan provided in the Offer and agreed with CNAO.

The Bidder shall specify its own proposal clarifying timescales and procedures, to be agreed with CNAO; the Supplier is also committed to manage restoration actions in case of a system breakdown.

On-line Support and intervention aimed to the speedy resolution of the blocking breakdown are considered as minimum requirements, in order to restore the System to be ready for the following clinical treatment.

Related to each performed intervention, the Supplier is asked to provide a detailed technical intervention report in order to verify the status of the apparatus before and after the intervention, the performed maintenance activities, maintenance stop hours for the apparatus, complete list of replaced components.

9.5 SPARE PARTS

Throughout the technology lifecycle, the Supplier shall guarantee the supply of every part necessary to keep all the equipment running efficiently and safely, in particular in compliance with the security and safety standards, as well as certifying full correspondence to expected parameters

coming from the equipment and their correct and proper use. The Supplier shall guarantee the same quality level of the equipment which passed the acceptance test.

In case some spare parts are no longer available on the market, the Supplier shall replace such parts with fully equivalent or even better parts with respect to the original ones. The equivalent spare parts shall guarantee the same quality level and lifetime as the replaced original parts, as well as be in compliance with the existing national and European technical standards.

In the Operation and Maintenance Plan the Bidder shall clarify if in CNAO is to be foreseen availability of an area for storage of spare parts; connected storage area requirements shall be specified.

CNAO shall be responsible for the storage area, whereas the Supplier shall be in charge of the stored material, especially in terms of number of spare parts, shipping charges and correct functioning of spare parts.

9.6 HARDWARE AND SOFTWARE UPGRADES

Throughout the Guarantee and the Full Risk maintenance period, the Supplier undertakes to deliver, install and start for free any hardware and software upgrade aimed to keep and/or improve the system performances, functionality, safety and reliability.

The Supplier shall report annually all the upgrades developed during the year for all the hardware and the software installed in the offered configuration.

Free upgrade shall include but is not limited to: electronic circuits, PC and server replacement, operating systems updates and software packages, replacement of parts of the system including components necessary to guarantee the complete apparatus functionality, together with its own ancillary systems.

10 TRAINING AND EDUCATION

Establishment of a commercial proton therapy system does not represent a brand new treatment modality for the relevant professions in particle therapy present at CNAO; however, for the specific case of a different accelerator concept and treatment delivery modality, hands-on training is essential both for the radiation oncologists, technologists (radiographers), medical physicists, accelerator technicians and system operators.

Training program for the CNAO personnel: training and educational program in the ramp-up/commissioning period (before start and until full clinical capacity) shall be included for all relevant professions and shall be included in the total price of the Supply. In particular, the level and content of the offered educational program and how this is proposed for the different professions shall be specified.

At the end of the installation phase, and possibly even during installation for the technical aspects, the Supplier, responsible for related charges and procedure, shall train CNAO personnel for the correct use and maintenance of the supplied apparatus.

The training shall be generally performed after the acceptance tests and shall be agreed with CNAO. In particular, the following topics shall be issued:

- use of the apparatus in all its functionalities;
- safety issues related to the different professional roles involved in the running, management and maintenance of the system;
- starting the routine clinical activity in collaboration with CNAO personnel;
- procedures for the nominal functionality restoring after failures and common procedural errors;
- Quality Assurance procedures ;
- details, clarifications and additional information during the initial period of the clinical use of the system;
- any other subject that the Supplier deems useful for a complete and useful training of the CNAO personnel.

Two different phases of the training should be identified as detailed in the following:

1. at the start-up of the system (basic education, start-up of the clinical activity), according to the training plan agreed together with CNAO. The estimated duration of the training shall be indicated by the Bidder.
2. after the start-up of the system (advanced education, advanced functionalities and applications of the system), according to the training plan agreed together with CNAO. The estimated duration of the training shall be indicated by the Bidder.

At the end of the training phase, qualification of the trained personnel shall be certified by the Supplier by means of a detailed and signed declaration. Such a document shall be a proof of the performed and received training to the CNAO personnel.

11 DELIVERY, INSTALLATION, COMMISSIONING AND ACCEPTANCE TEST

The Bidder shall provide a detailed time plan [art. 16 lett. d) in the "Disciplinare di Gara" document], including all the phases from delivery to Acceptance Tests, considering a total available time of 36 months.

Once the availability of the spaces suitable for installation is communicated by CNAO, the Supplier will start the delivery, free of charge, of all the components of the Supply. The term of 36 months, from the stipulation of the contract, for the Acceptance Tests of the Supply may therefore be extended, waiting for the Client to acquire the necessary legal authorizations and the availability of the spaces in which the accelerator must be installed. From now on, the Supplier accepts not to advance any right and/or economic claim for any possible delay.

The Supplier shall undertake the responsibility for completeness, of the correctness and of the logistics of the delivery.

The Supplier will proceed with the installation in compliance with the final EBI document (*Documento Definitivo di interfaccia macchina ed edificio*).

The Supplier will carry out all the calibration, testing and verification activities necessary for the commissioning, which must take place within the approved time plan.

The end of the commissioning phase will be communicated by the Supplier and recorded in a specific report. From the date of the end of commissioning, CNAO will have 30 days to start the Acceptance Tests.

Acceptance Tests will be carried out in compliance with the list discussed, agreed and integrated by CNAO, as reported in Chapter 1 of this document.

In the event of a negative test result, the Supplier shall be available to reprogram it promptly and to work continuously to resolve the critical issues. Passing the test will be recorded jointly by the Parties and will be considered as acceptance.

The entire Supply will be deemed accepted on the date of the last positive acceptance report; Warranty period begins from this date.

The overall acceptance of the Supply will certify that the equipment can be formally used in complete safety, demonstrating its overall installation, complete and correct operation, in compliance with the requirements of this specification and with what was declared in the technical offer as well as in compliance with applicable regulations in force.

The Supplier remains responsible for the deficiencies and defects that may occur later and attributable to the Supply, even after the Acceptance and until the end of the Warranty period.

After the positive Acceptance of the Supply, the Supplier must deliver the necessary documentation required by the regulations, including, among others, the following documents:

- declaration of conformity of the product by the manufacturer according to Regulation (EC) n. 765/2008;
- CE certificate according to Regulation (EC) n. 765/2008;
- user manuals for the operator in accordance with Regulation (EC) no. 765/2008;
- technical assistance manuals for the maintenance of the equipment offered, including electrical, electronic and mechanical diagrams and lists of component parts.

The Supplier shall also provide the insurance policy on product liability, valid and effective for the entire life cycle of the proton therapy system, with a maximum limit of € 10,000,000.00.

All the documents shall be supplied in n. 2 paper copies in English, n. 2 copies in Italian and n. 2 digital copies (both in English and in Italian).