Abstract— The use of charged particles (hadrons) for cancer treatment is an expanding field. Several countries are investing in dedicated centers in order to provide therapeutic beams with enhanced physical and radiobiological properties to treat radio-resistant tumors. The Italian national centre for hadrontherapy, (Centro Nazionale di Adroterapia Oncologica, CNAO), is currently being commissioned in Pavia. Politecnico di Milano is an institutional participant of CNAO since 2003, with specific responsibilities in terms of patient positioning, radiation protection and authorization issues. In this paper we update on the current status of CNAO/Politecnico di Milano partnership. The main activities mastered by the Bioengineering and Energy Departments of Politecnico di Milano in CNAO are described. Specific emphasis is given to the contribution of Politecnico di Milano to ensure radiation safety and to the design of dedicated patient positioning devices.

I. INTRODUCTION

Charged hadrons are characterized by the intrinsic capability of depositing the maximum of their energy in a well-defined and controllable location (Tobias et al., 1982). Hence, the use of hadron beams is a step forward in the historical development of targeted and effective cancer treatments, with better sparing of healthy tissues. The Italian national center for hadrontherapy (Centro Nazionale di Adroterapia Oncologica, CNAO) is currently being commissioned in Pavia (Fig. 1). The center will be providing hadrontherapy treatments with scanned particle beams (Goitein and Chen, 1983) at a national level. Politecnico di Milano is an institutional participant of CNAO since 2003. We report here the ongoing activities of Politecnico di Milano under the bioengineering and radiation protection aspects in the framework of such partnership.

II. METHODS

A. Patient positioning at CNAO

The upgrade of conventional radiation to heavy particles delivered by active scanning techniques is a major step forward in terms of conformality and effectiveness of the designed therapy. The drawback is that hadron beams exhibit higher sensitivity to positioning errors (Engelsman and Kooy, 2005). This implies the need for advanced positioning systems to ensure the highest standard in patient setup control. The technological challenge is to combine the most modern image guidance techniques with an high accuracy positioning device in an automated procedure for real-time setup control. This is the approach that was followed at CNAO for the CAPH system (Computer Aided Positioning in Hadrontherapy).

Patient setup procedures were designed to exploit state of the art technologies for accurate, automatic and highly organized patient treatment, where time consuming preparation activities can be handled in dedicated rooms. Imaging technologies, optical tracking devices and a high precision robotic patient positioner were selected as the key components. Multiple technological solutions were evaluated, taking into account setup accuracy and patient throughput optimization as specific goals.

B. Design of positioning devices

The selected approach is based on the integration of a non-contact Optical Tracking System (OTS) coupled with an in-room imaging device to monitor the patient position by means of external fiducials and anatomical landmarks. A six degrees of freedom robotic Patient Positioning System (PPS) automatically drives the patient to the nominal position using the feedback provided by the OTS, that is able to verify the positional repeatability in the marker configuration during treatment. A programmable laser projector allows to sample the surface of the patient as a point cloud that can be used to refine the initial registration obtained with the markers. The setup is then verified, before radiation is delivered, by means of image-based registration between images acquired in the treatment room through the Patient Verification System (PVS) and the treatment planning CT. The use of advanced optical tracking technologies for real-time patient monitoring during treatment is exploited to compensate breathing motion, and for updating at each session the geometric

Fig. 1. CNAO facilities in the town of Pavia.
relationship between internal structures and external fiducials. The PPS is a 6DOF robotic pantograph featuring a mechanical accuracy below ±0.3 mm and ±0.1°. The OTS is a three camera system able to localize passive markers and laser spots within 0.2 mm in a 3x2x2 m volume. The PVS installed in the bunkers with a fixed horizontal beam line is a stereoscopic X-ray imaging device suspended from the ceiling, that can rotate around the vertical axis according to the treatment table position (Fig. 2).

Fig. 2. Installation of patient positioning devices in the first treatment bunker at CNAO.

C. Patient positioning software implementation

The software for infrared patient localization with the OTS was developed in-house at the Bioengineering Department (Politecnico di Milano). The first step to achieve the desired level of automation is the development of an automatic segmentation algorithm to localize radio-opaque markers in the treatment planning CT with sub-millimeter accuracy. The algorithm is based on thresholded marching cubes, followed by geometrical filters to calculate the marker center coordinates.

Specific registration algorithms to quantify the setup quality have also been implemented, in order to calculate the patient setup corrections needed to align the tumor to nominal treatment position, using the information provided by the OTS. Positioning correction strategies based on fiducial markers and/or a combination of marker and surface topological information have been realized. The presented method is based on finding the rigid transformation such that the point cloud fits the corresponding patient surface model, and whose evolution is constrained by the physical markers that need to be placed within a given tolerance.

D. Commissioning of positioning devices

Several tests were performed to verify the mechanical accuracy of positioning and imaging devices. The accuracy of PPS and PVS motion was determined by means of repeated measures, carried out with a high precision laser tracker (±0.01 mm/m accuracy). Multiple reference points were monitored, so that the position of each component could be measured independently.

The PPS was also benchmarked vs. the OTS by means of a head phantom fitted with 4 passive markers. The PPS was moved in 6DOF within a ±5 mm and ±3° range from isocenter and the final position was measured with the OTS. Finally, the implemented OTS software modules for automatic patient positioning control based on markers/surface information have been tested on synthetic and clinical data.

E. Shielding design and authorization issues support

Since the CNAO synchrotron accelerates protons up to 250 MeV and carbon ions up to 400 MeV/u, radiation protection problems are completely different from those related to conventional radiotherapy facilities. The impact of beam particles with the patient, the beam dumps, or the machine structure, gives rise to nuclear reactions that result in the emission of high energy particles, among which protons, neutrons, photons and nuclear fragments play a crucial role for the radiation safety of both patients and workers.

High energy neutrons are the most important issue for the radiation safety of workers, since they are the main component of the secondary radiation field emitted by the beam interaction, and they can be shielded with a very reduced efficiency. For this reason, the accelerator vault and the treatment rooms shielding in hadrontherapy centers are made of a few meters of concrete; hence radiation safety calculations need to be carried out in the very early stages of the facility design, since they impact in the structural and architectural layout.

Politecnico di Milano has been involved in the very early stage of CNAO design, and has given strong support in setting up the methods for calculating the shielding, as detailed in Agosteo et al. (1996) and Agosteo (2001). In these earlier works, the attenuation curves of secondary neutrons in concrete walls were calculated with Monte Carlo simulations using the FLUKA code, together with the source terms, given as the ambient dose equivalent per impinging primary beam particle. Using this formalism, it is possible to estimate the dose rate at any point of the plant by knowing the primary beam current, and the structural parts of the machine where they are expected to impinge (beam loss points).

One of the most important and delicate issues in the CNAO shielding design is the calculation of the radiation component reflected through the entry mazes to the treatment rooms. These latter separate the treatment rooms from the clinical area, which is expected to be crowded by medical and technical workers.

The preliminary design has been carried out using the universal transmission curves (Mauro and Silari, 2009), and the reflected dose has been estimated for the final design with Monte Carlo simulations, by using MCNPX 2.6.0. The same approach has been used for the piping ducts passing...
through the synchrotron shielding. The synchrotron hall roof has been designed with the aim of reducing the dose at the neighbourhood due to neutrons scattered in the air (skyshine effect). This is a particularly important issue, since CNAO is located within a densely populated city and within a few hundred metres from a research reactor (LENA), University of Pavia departments and two major hospitals. A big effort has been made in order to keep the skyshine doses to the neighbourhood within irrelevant values. All these calculations, that are at the basis of the CNAO shielding design, have been embedded in the report submitted to the supervising authorities for the required authorizations.

F. Radiation measurements and instrumentation setup

One of the major tasks of the radiation safety laboratory at CNAO concerns the measurements of the neutron fields inside and outside the synchrotron hall and the treatment rooms, for environmental dosimetry and for the characterization of the radiation field inside and outside the shielding.

The cooperation between CNAO and the Politecnico di Milano resulted in the development of innovative neutron detectors, both passive and active. A dual detector rem counter has been designed (Agosteo et al., 2010), to be used as a neutron survey meter for monitoring the neutron dose throughout the plant. The rem counter consist of a polyethylene sphere with cadmium and lead insets, designed to have a response proportional to the fluence to ambient dose equivalent conversion coefficients, over an energy range up to 1 GeV. The rem counter is designed to host two types of detectors: the active version hosts a \(^3\)He proportional counter (SP9, designed by Centronic\(^TM\)) and the passive one a CR39 nuclear track detector, coupled with an enriched boron converter (BE10, supplied by Dosirad\(^TM\)). In the passive version, the neutrons thermalised by polyethylene are detected via the \((n,\alpha)\) reaction on the boron converter, since \(\alpha\) particles create tracks on the CR39 track detector. The CR39 detectors are etched in a 6.25 M NaOH aqueous solution at 98°C. The tracks are read with the PoliTrack system (Caresana et al., 2008), that is a scanning system consisting of a high-resolution optical microscope coupled to a digital video-camera. A noise reduction procedure has been implemented, based on the tracks image parameters (Agosteo et al. 2009).

The passive version of the dual detector rem counter is currently used at CNAO as an environmental dosimeter, and 27 passive rem counters have been spread throughout the plant in order to have a detailed mapping of the neutron field in both controlled and unregulated areas. One prototype of the active version is in use at CNAO to perform punctual measurements when a fast evaluation of the neutron dose is required.

An innovative active detector, named LUPIN (Logarythmic amplifier based Ultra wide dynamic range PHe up free Neutron detector) (Ferrarini at al., 2010) has been developed for beam loss monitoring inside the synchrotron hall, both for machine diagnostics and for radiation protection, in order to give a posteriori control on the parasitic beam loss inside the synchrotron vault. This detector is based on a BF\(_3\) proportional counter. The current generated by the \((n,\alpha)\) reaction on \(^{10}\)B inside the proportional counter is converted by an amplifier to a voltage proportional to the logarithm of the current. The voltage is sampled by a high frequency ADC (up to 1 MHz), and for any sample the current value corresponding to the voltage is calculated and integrated over time, to get the total charge released in the tube. For any given time interval, the total charge is divided by the average charge released by a single \((n,\alpha)\) reaction, so that the total number of reactions in the time interval is calculated.

This kind of detector does not suffer for saturation due to dead time, or to pile up, that is a typical limit of pulse-operated proportional counters, and has a very wide dynamic range that is limited only by the space charge effects inside the BF\(_3\) tube. For this reason, it can be used to detect very intense neutron bursts, and it can be successfully used in pulsed neutron fields. On the other hand, a single neutron reaction over a long time can be discriminated from the background, so that the detector behaves like a pulse-operated proportional counter in weak or continuous neutron fields. A prototype of the LUPIN detector is now in use inside the CNAO synchrotron vault and utilized as a beam loss monitor, and seven more detectors are scheduled within the next six months.

III. RESULTS

A. Mechanical accuracy of positioning devices

The robotic couch motion was proved to be repeatable within the design specification under different loading conditions (in the range 0-200 Kg). A maximum deviation of 0.1 mm was observed over a ±180° continuous PVS rotation, independently of the rotational direction. The absolute PVS rotational accuracy, as determined by repeated PVS rotations at a 60° step, was never beyond the measurement precision. The accuracy of X-ray tubes and flat panels motion when they are deployed for imaging measured 0.13 mm and 0.02 mm, correspondingly. The head phantom study performed on site showed an agreement between PPS and OTS (mean±SD) within 0.1±0.1 mm and 0.06±0.07° in 30 repeated measurements.

B. Patient positioning software tests

Results show that radio-opaque marker can be detected with an absolute maximum error within 0.3 mm in a DICOM dataset featuring 3 mm slice thickness and 1.27x1.27 mm in-plane pixel spacing. A sensitivity of 92.27% with no false positive has been reported in the localization of 233 markers in 35 patients. This value was obtained as the result of selective filters aiming at the required sub-millimeter accuracy: these filters prevent the identification of markers that are not rendered as
sufficiently spherical due to manufacturing defects or partial volume effects.

The implemented algorithm for marker based rigid registration provided adequate results, showing an average error of 0.036 mm on a test dataset consisting of 180 simulations in which a rigid body transformation was applied in the 10mm and 10° range for translation and rotations, respectively. The reduced computational time allows real time execution, consistently with the sampling frequency of the optical localizer (70Hz) and clinical procedure time constraints.

Hybrid registration based on a combination of marker and surface information proved to be comparable with dedicated libraries for constrained registration (Matlab® Optimization Toolbox) if at least two corresponding points are provided to the optimization function. We measured registration errors that are within the resolution of the utilized surface dataset.

C. Radiation measurements and instrumentation setup

The dual detector rem counter has been calibrated at Politecnico di Milano, and then inter-compared to other commercial and experimental rem counters at the CERF facility at CERN, where a neutron field with a predominant high energy component is available, that is quite similar to the neutron field that is expected to leak through the CNAO shielding. The experimental results show that the detector can provide a correct measurement of the neutron dose in a high energy field.

The first measurements at CNAO have proved that the passive rem counter can give a nonzero response even when measuring the cosmic ray neutron background (9 nSv h⁻¹), integrated over a measurement lasting two months. On the other hand, the same dose rate can be measured by the active version in an hour measurement with a 15% uncertainty.

These instruments can so be used to detect very small neutron leaks coming from the synchrotron, and so to verify the evaluations on which the shielding design is based. The beam losses that have been assumed for these calculations will be checked using the LUPIN detector. The behavior of this detector has been characterized with measurements in several neutron fields, both pulsed (like the PUNITA facility at JRC, Ispra), and continuous (inside the experimental cave at CERF, CERN), showing no sign of saturation up to a few million reactions per second (Ferrarini et al. 2010).

IV. DISCUSSION

Dedicated solutions for patient setup in hadrontherapy were designed, installed and tested, in the framework of a tight collaboration between Politecnico di Milano and CNAO. The presented results show that sub-millimeter accuracy is available in PPS motion and OTS/PVS monitoring for accurate patient setup.

The cooperation on the radioprotection side has resulted in the design of the shielding and in the development of instrumentation devoted to the measurement of the neutron fields. Detectors have been developed both for measurements outside the shielding, requiring a very high sensitivity and effective background suppression, and for measurements inside the shielding, where the pulsed neutron field and its intensity required the development of an innovative detector based on a logarithmic amplifier.

REFERENCES

- Agosteo S. Radiation protection at medical accelerators, Rad Prot Dosim 96:393-406, 2001
- Engelsman M, Kooy HM. Target volume dose considerations in proton beam treatment planning for lung tumors, Med Phys, 32:3549-3557, 2005
- Goitein M, Chen GT, Beam scanning for heavy charged particle therapy, Med Phys, 10:831-840, 1983