CERN-ACC-2016-0072

EuCARD-2

Enhanced European Coordination for Accelerator Research & Development

Conference/Workshop Paper

Accelerators for Medical Applications

Schippers, J.M. (PSI) *et al*

06 June 2014

The EuCARD-2 Enhanced European Coordination for Accelerator Research & Development project is co-funded by the partners and the European Commission under Capacities 7th Framework Programme, Grant Agreement 312453.

This work is part of EuCARD-2 Work Package **4: Accelerator Applications (AccApplic)**.

The electronic version of this EuCARD-2 Publication is available via the EuCARD-2 web site <http://eucard2.web.cern.ch/> or on the CERN Document Server at the following URL: <http://cds.cern.ch/search?p=CERN-ACC-2016-0072>

ACCELERATORS FOR MEDICAL APPLICATION: WHAT IS SO SPECIAL?

J.M. Schippers, M. Seidel, Paul Scherrer Institute, 5234 Villigen, Switzerland

Abstract

Specific requirements of accelerators for radiation therapy with protons or ions will be discussed. The focus will be on accelerator design, operational and formal aspects. We will discuss the special requirements to reach a high reliability for patient treatments as well as an accurate delivery of the dose at the correct position in the patient using modern techniques like pencil beam scanning. It will be shown that the requirements of the accelerated beam differ from those in a nuclear physics laboratory. The way of operating such a medical device requires not only operators, but also the possibility to have a safe machine operation by non accelerator specialists at different operating sites (treatment rooms). It will be shown that the organisation and role of the control/interlock system can be considered as being the most dedicated in a particle-therapy providing facility.

INTRODUCTION

After the start of particle therapy mostly accelerators in (nuclear) physics laboratories were used. The first treatments have been performed with accelerators built for physics research in Berkeley (USA) in 1954 and in Uppsala (Sweden) in 1957. Typically the types of accelerators used for therapy were cyclotrons and synchrocyclotrons (the "old" way to reach high energies with a cyclotron). Often the existing facility was adapted to run a medical program next to the (nuclear) physics research program, but some, for example the cyclotron at the Harvard Cyclotron Laboratory became a machine dedicated to proton therapy [1]. In the 1990s the first synchrotron came into operation for proton therapy at the first hospital based proton therapy facility in Loma Linda, Ca [2]. Here the beam from the synchrotron was used in either of four treatment rooms.

At the end of the previous century, particle therapy slowly got more interest of commercial companies to produce the equipment. Due to such commercial enterprises the number of hospital based facilities has increased from 15 in 2000 to 49 in 2014 [3].

Already during the initial phase of proton therapy, it was clear that the requirements for the accelerators and the beam transport to the patient were different from those for the usual physics applications. Apart from the technological differences, also the way of operating such machines had to change. Routine patient treatment requires a simple, fast, safe and accurate reproducibility of the beam delivery, without the typical possibilities in physics experiments to tune, make a first test and improve the machine setting.

Apart from the accelerator, also the beam delivery at the patient requires dedicated equipment and well documented procedures. Usually the beam has to be aimed from several directions at a tumour in a patient lying on a treatment couch. This is done by a beam rotation device, a *gantry*. These large (diameter typically 6-12 m) and heavy (100-200 tons) devices require special attention with respect to mechanical accuracy, accessibility and beam optics. Here a lot of effort is going on in efforts to reduce the size and weight, while keeping the aiming precision and other important clinical parameters at their required values. Such clinical requirements are for example the maximum *field size* (the area that can be irradiated without shifting the patient) and the time it takes to perform an irradiation treatment. In this respect it is important to realize that long treatment times may lead to inaccuracies in the dose delivery due to a higher risk of motions of the patient.

A technical overview of particle therapy facilities can be found e.g. in [4], Most facilities have one accelerator and a beam transport system coupled to multiple (2-5) treatment rooms, each with either a gantry or one or two fixed beam lines. Although alternatives are being investigated, until now one can direct the beam to only one room at the time.

It should also be realized that the legal aspects allowing operation of a medical facility for treatments have quite serious consequences. The equipment used, the procedures followed to treat a patient, the quality control (QA) procedures and the maintenance are subject to specific rules imposed by the certification of the equipment or even of the whole facility. The goal of such a certification (e.g. CE or FDA) is to increase the quality of the treatment and the safety for the patient. Depending on the national laws, this certification can be obligatory.

SERVICE

Compared to a machine for physics experiments, sudden changes in the beam schedule cannot be allowed. Especially since usually every day treatments are planned, patients would need to be rescheduled, which would not be desired. But also there is much less time for regular service: typically one evening a week, some nights and some weekends. A shutdown of a week or longer is usually not acceptable in a hospital, even when planned well ahead. This is due to the fractionation of an irradiation treatment of cancer. As with conventional photon treatments, the total dose to be delivered by protons is split into typically 30 daily fractions of about 2 Gy to spare the healthy tissue that is inevitably also being irradiated. (The dose given by ions, e.g. ^{12}C ions, has a different biological effect, which makes fractionation is

ISBN 978-3-95450-132-8

not so useful.) An interrupt of for example one week during a treatment course can not be accepted, since this could lead to a reduced cure probability. Therefore, if a shutdown is planned, no new treatments can start in the ~6 weeks preceding this long shut down. Furthermore the logistics is usually not capable of starting all new treatments in the first week after such a shut down. Therefore an accelerator shutdown of one week effectively yields a capacity reduction of 8-10 weeks. Apart from disappointed patients, this will also result in a significant income reduction of such a facility.

When service must be confined to short periods, this has implications for the design of the equipment. Of course a lot of attention is given to optimize the life time and to reduce the wear of components such as the ion source, components in the RF-system and cooling systems. Easy access, good and easy diagnostics, a modular design, easy exchange of components and a not too high radiation level due to activation are essential design requirements but not always easy to achieve.

Here it is also good to distinguish the situation between a treatment facility in a laboratory, where the amount of qualified experts, tools, spare parts and machine shops is usually not a problem, and the situation in most hospitals, where the technical support is usually supplied via a maintenance contract with a company. Also the equipment and procedures are usually under the rules of a certification as mentioned before. Although such a certification has the advantage of preventing uncontrolled and undocumented (or wrong) actions, it certainly leads to a less flexible operation and service.

BEAM PROPERTIES FOR DOSE DELIVERY

To deliver a radiation dose in a tumour, use is made of the so called *Bragg peak:* the dose increase at the end of the range of hadrons stopping in matter. To shift this Bragg peak to the desired depth, the range is adjusted by a corresponding change of beam energy. In synchrotrons this is be done by acceleration until any desired extraction energy. Until now (synchro-)cyclotrons are used for therapy with protons only. They are extracted at a fixed, machine dependent, energy. After extraction they are slowed down to the desired energy in an adjustable amount of material, a *degrader*. This can be done just after the extraction from the cyclotron, followed by a corresponding field change of all following beam line magnets, or just before the patient in the treatment *nozzle,* the last part of the beam delivery device. It is important that this energy change is sufficiently fast to limit the treatment time and to allow fast switching between treatment rooms, but above all it must be accurate (range!). Energy changes occur in two categories : the process of *range shifting*, to set the maximum depth needed at a certain incident beam direction, which may take several seconds and the much faster process of *range modulation*, which shifts the Bragg peak over the tumour thickness, typically with 2% energy steps, which ideally take <0.2 sec per step.

The typical beam diameter of 1-2 cm needs a lateral spreading system to cover typical tumour diameters of several cm up to 30-40 cm. The most commonly used method is *passive scattering* in which the beam is broadened by multiple scattering of the protons in a (set of) foil(s). Just before the patient, the broad beam is collimated to match to the lateral shape of the tumour.

The beam requirements are rather simple in this case: use a small beam diameter to hit the foils in the centre and have sub-millimetre beam position stability.

The best coverage of the tumour is obtained when combining a fast lateral adjustment of a narrow (<cm diameter) beam with the fast energy changes: the *pencil beam scanning* technique. Here fast *scanning magnets* are used to aim the beam sequentially at volume elements (*voxels*) in the tumour volume. In each voxel a specific dose is deposited. This can be done in a discrete voxel-grid (*spot scanning*) using a "*step and shoot*" method [5], or by moving the pencil beam in a continuous way along a certain trajectory within the target volume (*continuous scanning*) [6]. Apart from aiming at the prescribed voxels with millimetre accuracy and within a millisecond, the main accelerator specifications are rather relaxed for spot scanning and concentrate on enough intensity, correct switching the beam on and off and a fixed shape of the beam cross-section. Continuous scanning techniques, however, either require a very precise and quickly adjustable beam intensity or a very constant intensity and fast reacting accurate scanning magnets.

TECHNICAL SPECIFICATIONS

The beam transport system needs to be reliable, reproducible, stable and must have well defined beam losses only at specific locations (e.g. slit systems). To be independent of their rotation, it is convenient to have a symmetric beam phase space and no dispersion at the entrance of the gantries. Especially when using beams from a synchrotron, which may have a very asymmetric phase space, this may require dedicated matching sections in the beam transport.

Important recurring actions are the switch-off and start-up of the accelerator and the beam lines. It makes sense to have different switch-off scenarios that depend on the reason for the switch-off request as well as on the expected time until restart. For example, there can be a short switch-off during the night or one could have a longer switch-off for a service. Depending on the magnet types, a fixed current ramping sequence must be followed during start-up and between patients. In case of frequent energy changes during a treatment, as it is the case when using pencil beam scanning, hysteresis should be taken care of. The easiest strategy is to change energy into one direction, e.g. from high to low, so that one always uses the same relation between magnetic field and magnet current. Magnet current ramping may be necessary in-between two treatments or in-between different beam directions (gantry angles). Also it may be necessary to spend some time to reach (temperature) stability in

bending magnets or in the RF system of a cyclotron to stabilize the quality of the extracted beam.

The dose to the patient is measured with a dedicated dose monitor (e.g. a large parallel air filled ionization chamber, traversed by beam and mounted just before the patient. Apart from switching the beam off when the dose has been delivered or in case of severe errors, like a too high or too low beam intensity or a wrong position of the scanning beam, such monitors are usually not suitable to be used in a feedback loop for beam control. Therefore, and since each treatment fraction must be done with an absolute dose accuracy of a few percent, stability and reproducibility of the beam parameters emittance, position and intensity are extremely important. Apart from frequent dedicated measurements between the treatments and performed in a standardized and well documented QA program, also many on-line measurements can be made with dedicated measurement equipment, such as beam intensity monitors, beam loss monitors, hall probes or separate current measurements in bending magnets and logging of many parameters at the beam delivery side as well as at the dosimetry side. Such logging can be very helpful in predicting services and decisions on preventive maintenance.

It is well known that measurements with interceptive beam diagnostics can influence the beam characteristics due to beam-material interactions. This may have consequences on beam energy due to energy loss in foils and emittance, due to multiple scattering in wires or foils. Therefore strict procedures must be followed when inserting beam diagnostics. One could decide that no devises are allowed to be inserted during treatments, or that a certain group of devices always has to be in the beam.

Although there are no special requirements on the vacuum system, one should realize that one needs thin vacuum windows at the end of each beam line. This location is rather close to the patient. Here one has to make a compromise between a thin foil to reduce multiple scattering of the beam and sufficient thickness to reduce the chance (and noise) of a foil break, which would cause a long interruption.

OPERATION AND CONTROL

To obtain a safe and reliable system, redundancy is often implemented. Parallel or sequential actions to intercept the beam are typical. But also critical measurements of beam characteristics or machine status should be performed with redundant methods. Redundancy can be implemented at low level. For example one can compare the outcomes of two different measurements in a local comparator and send an outcome- status signal to a safety control system. But also comparisons in the control system can act as a redundant check of the machine status. However, usually these higher level checks are not accepted in patient-safety systems, since there can be an unknown time delay in the signal processing. Also the signals of certain systems must be sent via “hard wired” connections.

The control system of the machine plays an important role in the safety of the patient but also in a high availability of the system [7]. These two goals can be achieved when at least several requirements are fulfilled: a clear diagnostics of the situation, well documented and tested changes only under supervision of dedicated staff and a clear concept of “who is allowed to do what” during treatments. Especially this last issue is of importance, since usually the machine can be operated from different locations: workstations at each treatment room, in a service room near the accelerator and in a main control room. Therefore a kind of *mastership*-concept within the control system(s) can be helpful, to have a unique definition of who is running the machine. For example this can be the medical operator in one specified treatment room (the “master”). This concept also prevents unwanted actions from somewhere else, like from another treatment room or from a main control room. The actual granting of the mastership is must be done via a clear procedure. Well defined operation modes of the facility are needed to define the allowed actions in each situation. In *service mode* almost all normal accelerator and beam line actions are allowed and treatments are forbidden, whereas in *treatment mode* the allowed actions are restricted to specific actions, such as setting the gantry angle, loading the treatment steering file for automatic performance of energy changes and scanning procedures, “start” and “stop” the treatment. But tuning the beam optics to improve the beam quality, is not allowed in this mode.

In most facilities machine operators perform the start-up of the accelerator and beam lines, do some machine specific tests and stay alert in case of problems. The person responsible for the execution of the treatment is present in the control room of the selected treatment room (the “master”). Usually these persons are not accelerator experts. Therefore they need clear status overviews and unique instructions from their local control systems. In case of technical problems they will fall back on the machine operator. But for standard situations the control system should provide a simple enough interface to allow the operation without deep knowledge on the accelerator.

There are many reasons for stopping a running irradiation: for example a wrong value of a machine parameter, an out-of-range reading in a monitor or a problem in the dose-delivery (e.g. the patient moves). Interpreting the relevant signals and initiation of such actions (*interlocks*) is the role of the interlock/safety system. The sensitivity to cause such an interlock strongly depends on the system in which the failure occurs and on the possible consequences. For patient safety the highest sensitivity is desirable. However, if the error margins are too small, this yields unnecessary beam-offs and longer treatment times, which increases the chance of failures.

Consider, for example, a dose monitor in a treatment room, which generates an alarm when a signal is detected in a situation where no beam is supposed to be present in that treatment room. However, when its detection

ISBN 978-3-95450-132-8

threshold has been set so low that it could react to noise in the room during preparation of the next treatment, it could cause an interrupt of the treatment in the other room.

Table 1: Patient Safety Related Interlock Signals of the System at PSI and Examples of their Causes, Illustrating the Different Beam-switch-off Levels

Interlock type	General cause	Example
ALOC	error detected within the local therapy control system	Crossing of a threshold in the local dose delivery.
ATOT	severe error that might lead to an uncontrolled deposition of dose or injury of a person	Time-out in a dose monitor in the nozzle
ETOT	emergency signal generated in any safety system	Emergency button pushed

Table 2: Hierarchy of the Interlock Signals of the Patient Safety System at PSI and Related to Switch off the Beam

Interlock type / Beam switch-off level				Measures for Beam-Off
ETOT	ATOT	ALOC	Routine Beam Off command	Kick beam into dump
				Close beam stopper to specific treatment room at area entrance
				Close beam stopper at beam line start
				Reduce cyclotron RF power to 80%
				Switch off cyclotron RF
				Switch off ion-source

Thus the design of the interlock system also includes the definition of reasonable alarm thresholds. In Table 1 and 2 patient-safety related interlock signals at PSI and their hierarchy are shown as an example.

There are different reasons for stopping the irradiation. A normal (or routine) beam-off request happens at the end of each treatment when the requested dose has been reached. In the PSI system, the beam is then kicked into a beam dump. But a detected error needs a more reliable and redundant shut off. At PSI an ALOC signal (see Table 1) causes the beam to be kicked into a beam dump and a beam stopper is closed in parallel (Table 2). Again one has to balance between safety and availability. On one hand one has to be sure that the beam is switched off, but on the other hand one has to consider the time it will take to get the beam back in good conditions. Due to temperature and other effects, it may occur that the characteristics of the extracted beam have changed. Another aspect to be considered is the impact of frequent on-off switching on the lifetime of certain components in the accelerator.

To reduce such effects the interlock system should be designed such that detected errors will cause different interlock levels, all according to the type, severity and possible consequences of the failure, Each interlock must have the possibility to act specifically on certain subsystems. Also, and in any case a check must made on the action caused by an interlock: if a switch-off action has failed a next level must be activated and a more rigorous action must stop the beam.

In defining these hierarchies in interlock levels and redundancies, one has to consider that the reaction times vary when different systems are utilized for safety purposes. For example, the time it takes to reduce the beam intensity to zero by kicking the beam into a beam dump, is much faster and a simpler action, than switching off an ion source.

The complete interlock/safety system should be setup in a logic and modular way. In PSI it has been organized into three independent systems:

1. machine interlocks: react when accelerator and beam line devices are technically not working well.
2. patient safety interlocks: react when dose delivery signals are outside their tolerance region.
3. area/access supervision: checks doors, emergency buttons and radiation levels.

Each system decides on the necessary level of switching-off and sends the so derived “off” signal directly to the involved components. In Tables 1 and 2 this has been illustrated for the patient safety system at PSI. The machine-interlock system in a facility for medical treatments is conceptually more or less similar to the one at any accelerator facility. The patient safety system, however, is of course extremely dedicated to the medical application. The area/access supervision is partly similar to the one in physics laboratories, but is adapted to the patient access.

In practice, the most important aspect of an interlock/safety system is the explicit presentation of the switch-off cause(s) to the (medical) operator. The information given by the control system must allow the operators in the control room as well as in the treatment room to react immediately and efficiently when a failure occurs. If one only detects the interception of the beam and has no idea of its cause, it will not only affect the availability but also the working pressure, the alertness and the motivation.

CONCLUSIONS

So, an accelerator facility for particle therapy implements a variety of technical measures to ensure an accurate and reproducible dose delivery to patients. In comparison to an accelerator for classical research purposes the medical facility implements a complex interlock system for patient safety, monitoring a large number of parameters. Furthermore the safety measures related to the irradiation treatment are imposing a stringent discipline on the operation of an accelerator facility. Of course one has to follow global requirements at high level, but details of these requirements have turned out to be the most difficult ones to deal with, especially in relation to the desired high availability of the machine for treatments.

This deals with a very complex balance between safety and availability. Availability has an immediate impact on the number of patients to be treated (so: financial consequences) and many interruptions during a treatment will also increase the inaccuracy of the treatment and could thus have negative consequences on the success of the treatment.

But especially in the last 15 years, particle therapy has grown out of the accelerator laboratory status of "interesting experimental application" and worldwide more than 100,000 patients have been treated with particle therapy. Nowadays new facilities are built as separate institutes or within a hospital. However, facilities in accelerator laboratories remain essential to guide and perform the technological developments to make the systems cheaper without a loss of quality.

REFERENCES

[1] R. Wilson, A Brief History of the Harvard University Cyclotron, Harvard University Press, 2004.
[2] J.M. Slater et al., Int J Radiat Oncol Biol Phys 22 (1992), pp. 383–389.
[3] Particle therapy coordinating group, (PTCOG) http://ptcog.web.psi.ch/patient_statistics.html
[4] J. M. Schippers, Beam Delivery Systems for Particle Radiation Therapy: Current Status and Recent Developments, Reviews of Accelerator Science and Technology (2009) 2, 179-200.
[5] E. Pedroni et al, "The 200 MeV proton therapy project at the Paul Scherrer Institute: Conceptual design and practical realisation", Med. Phys. 22 (1),1995.
[6] T. Haberer et al., Magnetic scanning system for heavy ion therapy, Nucl. Instr..Meth. A 330 (1993) 296–305.
[7] N. E. Ipe et al. (Ed.), Shielding Design and Radiation Safety of Charged Particle Therapy Facilities, PTCOG Report 1 (2010), http://www.ptcog.ch/index.php/ptcog-publications

ISBN 978-3-95450-132-8