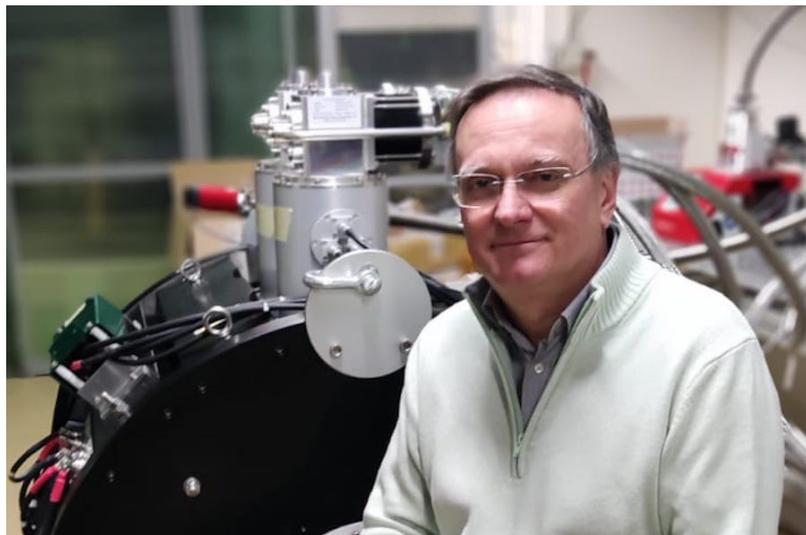


Newsletter Interview

A NEW BEAMLINER FOR RESEARCH AT CNAO | Interview with Valerio Vercesi, member of the INFN Committee for Life Sciences (INFN4LS)



A NEW BEAMLINER FOR RESEARCH AT CNAO

Inaugurated in February 2010, CNAO (Italian National Centre for Oncology Hadrontherapy) is one of the most qualified institutes in the world for treatment and research in Hadrontherapy, a particular form of radiotherapy that, instead of conventional X-rays, uses protons and atomic nuclei (ions) to destroy the tumour with great precision and effectiveness. CNAO is one of six centres worldwide and one of three in Europe - along with the Heidelberg Centre in Germany and the MedAustron Centre in Austria - capable of treating cancer through the use of carbon ions.

In addition to the beamlines dedicated to the clinical application, since 2022 CNAO can count on a new beamline developed in close collaboration with INFN, entirely dedicated to research. The new beamline will not interfere in any way with medical treatment due to its implementation in a dedicated experimental room. A third ion source, in addition to the two existing proton and carbon ion sources, is also planned to be installed during 2022, and will provide helium, oxygen, lithium and iron ion beams for multidisciplinary research activities. In addition to fundamental research objectives, radiobiology studies are planned for certain types of ions to evaluate their applicability to innovative clinical treatments that are potentially more effective than those currently available.

The collaboration with INFN is in place since the early stages of design of CNAO: INFN co-directed the high-tech part necessary for the implementation of the Centre's synchrotron, the particle accelerator realised thanks to the collaboration with INFN, CERN and the German GSI. In particular, the INFN has fielded the expertise and work of the INFN Genoa, Milan, Pavia and Turin divisions, the Frascati National Laboratories, the Legnaro National Laboratories and the Southern National Laboratories: an expertise based on decades of experience of INFN in the field of nuclear and sub-nuclear physics. Indeed, it is the precision of the CNAO synchrotron that is responsible for the effective application of Hadrontherapy, achieved by guiding the particles to selectively target cancer cells, causing multiple damage to their DNA while minimising damage to healthy tissue. In view of the high level of knowledge and technologies introduced for clinical practice objectives, extending the Centre's activities into multidisciplinary research has always been "the second pillar" of CNAO's strategy to keep the Centre at the forefront of innovation.*

We asked Valerio Vercesi, member of the INFN Committee for Life Sciences (INFN4LS), who has followed and follows the various joint INFN-CNAO programmes, to tell us about the state of the art of the beamline dedicated to research.

CNAO was founded as a Centre for the treatment of cancers. Could you please tell us about the genesis of the research programme with INFN?

Since the initial design of CNAO, with a clear vision of the future, an area was planned for a beamline totally dedicated to research. Indeed, the approval of the construction of the Centre by the Ministry of Health also included the idea that we could go beyond the clinical treatments that were possible in the original configuration and, for this to be based on a solid scientific and clinical foundation, a robust research activity was required. INFN institutionally has research as its fundamental mission and has therefore become not only a collaborator but often a promoter of several joint research projects that have seen the light in recent years. These projects have been directed, for example, at better understanding the action of particle beams on tumours, monitoring their effect so that the dose deposition process can be recalibrated according to its biological effectiveness. The fact, among other things, that CNAO is the only centre in Italy to allow irradiation with carbon ions has led many INFN groups and universities that traditionally collaborate with the Institute to propose measurement campaigns to validate radiobiological hypotheses or to study specific effects on detectors or their electronics. The hope is that CNAO will maintain the importance of this "second pillar" and that, having INFN as a partner, it will courageously address the challenges that allow research to improve, expanding also the resulting social repercussions.

What areas of multidisciplinary research will the new beamline be applicable to?

In carrying out the experiments which I have mentioned, the researchers had to deal with the limitations imposed precisely by the availability of CNAO beams that are obviously used primarily for clinical purposes. This placed limits on both the types of projects that could be proposed and their time frame. In the current configuration, for example, it is not possible to leave experimental installations always active and most of the research activity can be carried out only at certain times of the night or at weekends. With the availability of the new research line, many of these limitations, if not all, will cease to exist and thus the range of activities will expand considerably. In addition to the already-mentioned activities of radiobiology, dosimetry and radiation resistance for studies related to fundamental research, new possibilities in research and development contexts are now feasible for strategic sectors of industry, such as aerospace or for studies on new materials for avionics. Disciplines such as biology (e.g. in the field of plants) or genetics (e.g. for the study of new genotypes) will also be able to take advantage of these new irradiation possibilities. All this will be further expanded with the installation of the new ion source.

What is the specific role of INFN in the design and implementation phases of the new line and in the definition of research programmes?

As mentioned, the experimental room was built at the same time as the construction of the Centre, but the original funding did not allow the necessary technology to be installed. It was essentially thanks to a MIUR (Italian Ministry of Education, University and Research) Reward Project won by INFN (IRPT, with Principal Investigator G. Battistoni and Technical Coordinator for INFN A. Lanza) that it was possible to proceed with the installation of the new beamline. INFN has invested approximately 2.5 million euros for this purpose (in addition to the costs of the personnel involved) and has participated in all phases, including design, component acquisition and beamline installation. INFN has been involved in every element, including the functional specifications, the beam optics, the vacuum system, the diagnostics and the controls. The layout of the room was chosen following a questionnaire organised by CNAO, to which both national and international potential users responded: the solution adopted, with four possible irradiation positions, satisfies 97% of applicants. The rules for the use of the experimental line are in the final approval phase: INFN will be granted free slots and priority in the experimental proposals. As is the case for other research infrastructures, an Operating Committee will be formed to evaluate proposals and will be advised by an international Advisory Board. The Committee may also include other entities that become active components of the infrastructure, both public and private.

When do you expect research activities to start?

The gestation of this new research beamline has been long and at times troubled. In my experience, which ended two years ago, as Director of the INFN Pavia division, there were many obstacles that stood in the way of a more rapid implementation. In general, high technology implementations can suffer from physiological delays because one is working at the limit of existing technologies and on the development of something that has new potential and limits, to be constantly verified; I am aware of these also thanks to my years at CERN, in large collaborations such as ATLAS at the LHC. In the case of CNAO, there were also other elements: it should not be forgotten, for example, that the Centre is in an area subject to very stringent environmental constraints (the Ticino Park) and this rightly requires the utmost attention to be paid to certain aspects of the infrastructure and that the authorisation process is more complex than for basic research infrastructures.

Nevertheless, the beamline has long since finished its fine-tuning phase, and all permits have been acquired. Unfortunately, the advent of the pandemic prevented it from being opened immediately to users so that research programmes could begin (a precaution also dictated by the need to limit the influx of people in the Centre). It is quite reasonable to expect scientific activities will begin in the second half of this year.

A third ion source is also planned to be installed by the end of 2022, in addition to the proton and carbon ion sources. What is its objective?

For the treatment of patients with hadrons, CNAO has two ECR (Electron Cyclotron Resonance) sources that fully meet current treatment protocols. These sources, however, are not adequate for the requirements of research programmes, regarding the production of other ions, in particular metal ions such as Li, as well as possible current increases aimed, for example, at future developments for shortening treatment times. Therefore, it is necessary to have a third source that, above all, allows the two existing ones to be left always ready, efficient and with their production parameters constant, to always provide the same ion beam used for the therapeutic routine. The source that has been identified is based on the AISHA (*Advanced Ion Source for HAdron therapy*) prototype that was built and characterised at INFN Southern National Laboratories. The implementation of this second version, further improved to include the production of ions up to ^{56}Fe ionised 19 times, was made possible thanks to the award of a Lombardy Region grant (Research and Innovation Call Hub POR FESR 2014-2020 - INSPIRIT Project - ID 1161908), led by CNAO and with INFN and an Italian industrial company as partners.

The intensities that can be achieved with this new source are higher than those of commercial sources and, in particular, the production of iron ions is possible only in very few laboratories in the world and is becoming increasingly important, for example, for space missions. Indeed, from the characterisation of materials to be used in the equipment employed, to the consequent problems of radiation protection for astronauts due to the biological damage induced, the study of this ionic species becomes essential for long stays due to interplanetary travel or permanent bases on the Moon. Numerous simulations of biological effects, particularly for DNA damage, are also in progress and may guide future experiments. Construction of AISHA-2 is in progress and its installation and characterisation is planned for late 2022. Its implementation will be a further demonstration that knowledge and technology transfer between excellent basic research and cutting-edge, socially impactful applications is an unparalleled driver of innovative, not just incremental, progress.

*CNAO synchrotron accelerates the carbon protons and ions to an energy that allows them to penetrate the human body up to 27 cm. The particle beam that strikes the cancer cells acts like a "brush" with a precision of 200 microns (two hundredths of a millimetre). The level of precision is ensured, on the one hand, by the continuous three-dimensional monitoring of the patient and of body movements and, on the other hand, by the action of two scanning magnets that, based on the indications of the monitoring, guide the "brush" along the tumour outline. The extreme precision achieved

is largely the result of research in high-energy physics. The synchrotron was implemented (mainly) thanks to the collaboration of CNAO with INFN, CERN, GSI (Germany), LPSC (France) and the University of Pavia, heavily relying on technology produced in Italy.