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#### CNAO: TECHNOLOGICAL RESEARCH IN PHYSICS AT THE SERVICE OF MEDICINE

Interview with Gianluca Vago, physician and professor at the University of Milan, and, as of January 2019, President of CNAO (the National Centre for Oncological Hadrontherapy)

CNAO of Pavia, which was inaugurated in 2010, is a centre at the forefront of the treatment of tumours with hadrontherapy. This is a form of radiotherapy that exploits the extreme precision guaranteed by particle accelerators developed for basic research in physics. CNAO, the heart of which is a particle accelerator, a synchrotron realized in collaboration with INFN and CERN, is the second hadrontherapy centre in Europe and one of the few in the world to perform treatments that irradiate tumour cells with proton beams or, depending on the tumor, with carbon ions. CNAO is also the only one in Europe with the CE marking and with experience performing clinical trials to evaluate the safety and efficacy of such treatments. The use of proton beams or carbon ions has a great advantage when compared to the X-rays used in traditional radiotherapy, in particular in the treatment of deep cancers, as it allows the release of energy in proximity to the tumour mass, thus reducing the impact on healthy surrounding tissues and, therefore, consequent side-effects.

As well as being a cutting-edge centre, CNAO is in continuous evolution, adapting the techniques it employs to the most recent developments in the technology used in basic research in physics. Recently, CNAO launched the INSIDE (Innovative Solution for Dosimetry) trial, along with INFN, the University of Pisa, Sapienza University of Rome, and the Enrico Fermi Historical Museum of Physics and Study and Research Centre. INSIDE is an imaging system capable of "photographing" the proton beams and carbon ions used to strike tumours in hadrontherapy and of rendering therapies more precise and effective, by observing radiation in "real time".

We asked Gianluca Vago, President of the CNAO Foundation as of January 2019, and past Vice-Chancellor of the University of Milan, to describe the state of the art and prospects for development at the Pavia centre.



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# CNAO has a long history, from the first project design, to its construction, to the implementation of patient treatment.

CNAO is a concrete example of the collaboration between physics, medicine and engineering; it was conceived as an idea in 1991 thanks to the insight of Ugo Amaldi, particle and accelerator physicist, and Giampiero Tosi. At the time, Amaldi was working at CERN and Tosi was directing the Health Physics department at the Niguarda Hospital in Milan. Amaldi and Tosi's initial idea immediately received the support of INFN management, which – thanks to President Nicola Cabibbo – decided to directly allocate the first lot of funding. Subsequently, INFN kept supporting CNAO via research projects financed by Group V.

The centre, for which Amaldi and Tosi had laid the scientific foundations, first saw the light of day at the beginning of the 2000s under the impetus of Umberto Veronesi - in his capacity as Minister of Health – and Erminio Borloni. Borloni, thanks to his vision and his managerial skills, succeeded in providing Italy with a unique, cutting-edge facility, weaving around the centre a network of essential national and international collaborations. The most numerous and important collaborations were conceived with INFN's different laboratories and divisions - some 15 - and these contributed, in many different ways, to the creation of the centre's special technology and infrastructure.

In 2011, the first patient arrived and, up until today, 2,500 people affected by radioresistant or nonoperable tumours have been treated at CNAO with hadrontherapy. Since 2017, hadrontherapy has been part of the basic benefit package (LEA) that is funded by the National Health Service (SSN).

#### What makes CNAO a centre of excellence at an international level?

CNAO is one of only six multi-particle (protons and carbon ions) centres in the world able to treat tumours with hadrontherapy, an advanced form of radiotherapy that, instead of X-rays, uses proton beams and carbon ions. The latter are heavy particles that strike the tumour mass with greater biological efficacy, thus preserving the surrounding healthy tissues. It is an innovative cancer treatment that is used when traditional radiotherapy isn't effective or in the case of inoperable tumours.

At CNAO, we also do research with the aim of translating results into clinical practice and, in this regard, the link with INFN is strong and essential.

## Can you give us an account of CNAO's activities from when you began treatments on voluntary patients until today?

2,500 patients have been treated, and the results have exceeded expectations. The data, though only partial since the observation period is still short, tell us that hadrontherapy is capable of halting the disease in more than 80% of cases. Some of the diseases that we treat at CNAO include sarcomas,



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chordomas, chondrosarcomas, ocular melanomas, meningiomas, adenoid cystic carcinomas, paediatric solid tumours.

From the perspective of treatment precision, we have also observed a reduction in the toxicity in healthy tissue, which is essential for patients with a long life expectancy.

## The INSIDE trial, fruit of the collaboration between CNAO, INFN, the University of Pisa, Sapienza University of Rome and the Fermi Centre, was recently launched. What does it involve?

It is an important project that emerged from the combination of the different strengths and ideas of prestigious centres and universities. INSIDE is the first two-mode system in the world (consisting in a PET scanner and a charged particle tracking system) capable of monitoring the beams of carbon ions and protons used in hadrontherapy in real time. We will be able to observe in real time where the particle beams have their maximum destructive effect and, on the basis of these observations, recalibrate the particle beams' parameters to render treatment increasingly efficient.

## The new line of research at CNAO, which is also being undertaken in collaboration with INFN, is in the development phase. What activities will you be undertaking?

Since last May, the new line of research has been active in terms of testing and fine-tuning. It is a completely separate line from the patient treatment rooms and wholly dedicated to research. We will exploit the potential of our particle accelerator for research, for example, in the fields of radiobiology and radiation protection, to simulate the effects of radiation on materials used in aviation and in the aerospace industry. We will test new ions, such as oxygen and helium, to observe their action and to offer increasingly innovative treatments.

#### What do you foresee and plan for the future of CNAO in the short and long term?

We want to increase the scientific research that we undertake in collaboration with INFN and explore the potential of hadrontherapy in the treatment of tumours. It will be important to further increase the clinical collaborations that already exist with the main national treatment institutes in order to attain a complete, multi-disciplinary approach. We will also work a lot with advocacy groups to improve cancer patients', and their families', awareness and understanding of hadrontherapy.

Finally, we intend, in collaboration with INFN, to enhance the cutting-edge technological tools to have increasingly effective equipment available for the treatment of tumours.