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ESTABLISHMENT OF THE NEW PARTICLE THERAPY RESEARCH CENTER (PARTREC) AT UMCG GRONINGEN

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Abstract

After 25 years of successful research in the nuclear and radiation physics domain, the KVI-CART research center in Groningen has been re-established as the PARticle Therapy REsearch Center (PARTREC). Using the superconducting cyclotron AGOR and being embedded within the University Medical Center Groningen, it operates in close collaboration with the Groningen Proton Therapy Center.

PARTREC uniquely combines radiation physics, medical physics, biology and radiotherapy research with an R&D program to improve hadron therapy technology and advanced radiation therapy for cancer. A number of further upgrades, scheduled for completion in 2023, will establish a wide range of irradiation modalities, such as pencil beam scanning, shoot-through with high energy protons and Spread Out Bragg Peak (SOBP) for protons, helium and carbon ions. Delivery of spatial fractionation (GRID) and dose rates over 300 Gy/s (FLASH) are envisioned. In addition, PARTREC delivers a variety of ion beams and infrastructure for radiation hardness experiments conducted by scientific and commercial communities, and nuclear science research in collaboration with the Faculty of Science and Engineering of the University of Groningen.

PARTREC FACILITY

The PARticle Therapy REsearch Center (PARTREC) is a newly established research facility at the University Medical Center Groningen (UMCG). It builds on the success of the former KVI-CART research center and utilizes the superconducting cyclotron AGOR (see Fig. 1) for experimental research, mainly in radiation physics and biology.

Built by a French-Dutch collaboration in Orsay in the period 1987 – 1994 and commissioned in Groningen in 1996, AGOR operated within the KVI-CART research center [1]. It was used for 25 years to perform research in nuclear physics and on fundamental symmetries [2] as well as for detector development, radiation hardness testing [3,4] and radiobiological experiments. Recently besides nuclear physics, radiation and accelerator physics and radiobiology,the research focus has been shifting towards medical applications and therefore the facility and its personnel was integrated into the University Medical Center Groningen (UMCG). Hence, the new structure, additional goals and the new infrastructure (described in the chapters below) have been formalized via a creation of the new research center named PARTREC (logo in Fig. 2) was created.

Figure 1: Photograph of the AGOR accelerator.

Working in close collaboration with the UMCG Groningen Proton Therapy Center (GPTC), PARTREC research activities encompass medical physics, radiation biology experiments, tests of different radiation therapy treatment modalities and development of detector technology. In addition, it provides opportunities for experiments in the domain of radiation hardness, for both the scientific and commercial communities, and nuclear science, in collaboration with the Faculty of Science and Engineering of the University of Groningen.

Figure 2: Logo of new PARticle Therapy REsearch Center (PARTREC).

BEAM DELIVERY CAPABILITIES

The magnetic field of AGOR has a varying value between 1.7 to 4.1 T. It is produced by two superconducting main coils and fifteen trim coils for the precise field shaping, with three iron hill sectors for focussing and defocussing of the circulating beam (see Fig. 3).

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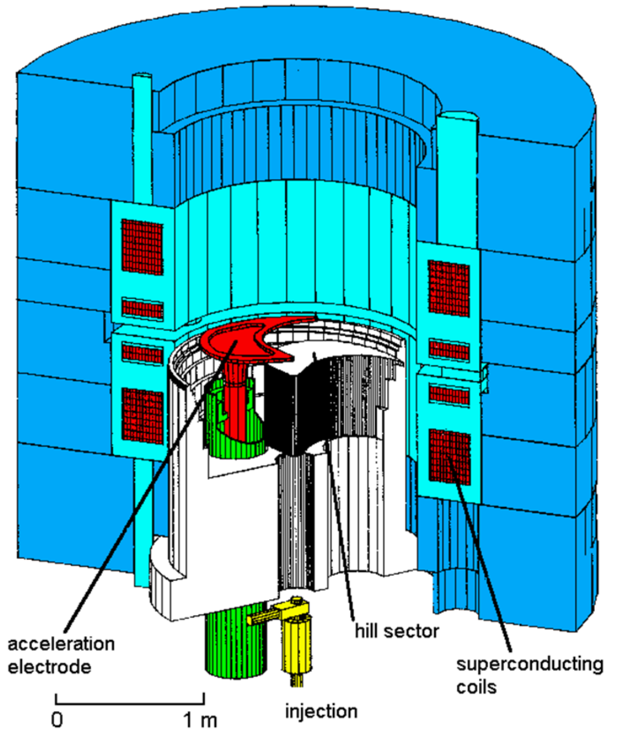

Figure 3: Schematic 3D-model of the AGOR cyclotron interior.

The acceleration is performed by three halfwave RF cavities, which can be mechanically extended or contracted to produce accelerating frequencies of 24–62 MHz with the harmonic numbers of h = 2, 3 or 4. The beam is axially injected from three external ion sources, with two ECR sources for heavy ions and a multi-cusp source for light ions. The extraction happens after 300–500 turns, depending on harmonic mode. The extraction radius is about 870–890 mm (depending on E/A of the beam), with the turn separation at the extraction being in the order of 2–3 mm, which corresponds to the width of the beam.

Given the flexibility of the magnetic field, RF frequency and ion sources, AGOR routinely delivers ion beams of all stable elements up to xenon, within an energy range dependent on the charge-to-mass ratio of the ions. For radiation hardness tests, the facility provides beams of protons at different primary energies and various ions (from He to Xe) at 30 MeV/amu (see diagram in Fig. 4 and setup in Fig. 5). Experiments can be performed at 90 MeV/amu with ions up to Ne. The changeover between the different particle types at the same energy per amu takes typically less than an hour. The possibilities of extending the palette of beams towards still heavier fully stripped ions and lower energies, as suggested by Fig. 4, are under examination [5].

Proton beams with energies relevant for clinical purposes (range in water up to 230 mm) are used for preclinical radiation biology research and proton therapy related physics since twenty-five years. They can be delivered with the continuous intensity of up to 10^9 particles per second per cm^2 with the dose homogeneity level within 1% for a scanned

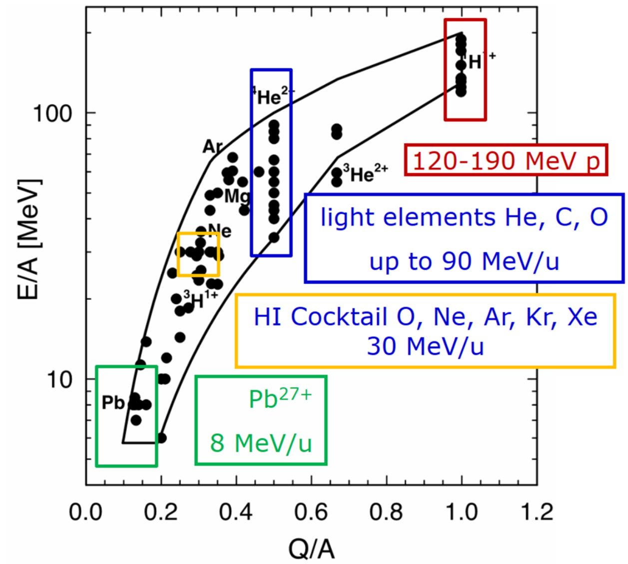

Figure 4: Ion types provided by AGOR, with their extraction energy plotted as function of their charge-over-mass-ratio.

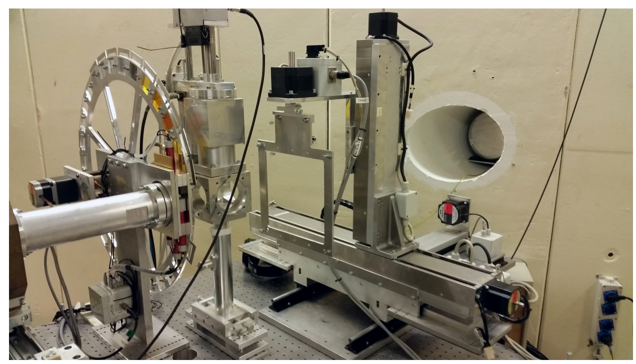

Figure 5: Photograph of the setup for heavy ion irradiations.

beam and within 2-10% for scattered beams, dependent on the irradiation field size. The intensity of the heavier ion beams depends on the ion type and can be varied in the range 10^2-10^5 ions / (s cm^2), with the field homogeneities comparable to the ones of proton beams. The LET can be tuned by means of a degrader system just before the sample location. The beam purity is very high (contamination below 10^{-5}) and is verified by means of a silicon detector telescope that stops the ions and provides particle identification.

RESEARCH PLANS WITH THE NEW INFRASTRUCTURE

To extend PARTREC's research capabilities, new infrastructure is currently under development and is expected to become available in 2023.

This includes design, installation and commissioning of a new beam line for the biomedical research, which will free up additional capacities at the existing beam line (see Fig. 6). The new irradiation modalities developed in the framework of this extension will also become available at the existing beam line. These include scattering and pencil

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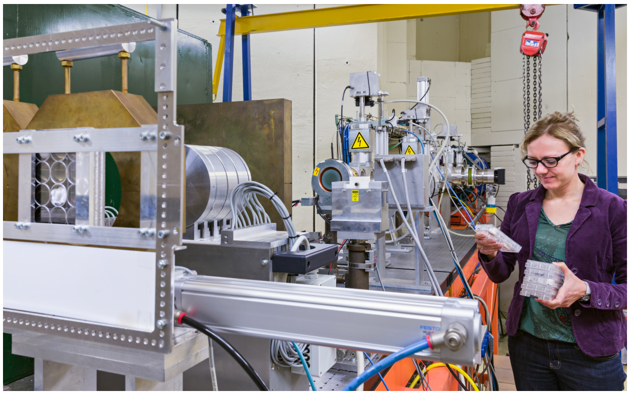

Figure 6: Photograph of the setup for radiobiological irradiations.

beam scanning, shoot-through with high energy protons as well as Spread-Out Bragg Peak for protons and helium. Additionally, the adaptation of the facility for the delivery of spatial fractionation and high dose rates in excess of 300 Gy/s (FLASH) is maturing. An active Proton Radiography program with a variety of detectors in collaboration with GPTC exists and advanced detector technologies, such as PET scanner panels around a head-shaped phantom [6, 7] for the optimization of margins for head-and-neck tumour treatment, are under development (see Fig. 7).

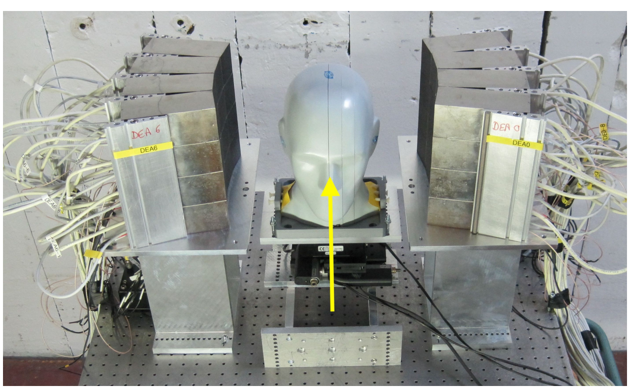

Figure 7: Experimental setup showing the head phantom in-between the 2 PET scanner panels. The head phantom sits on top of 2 orthogonal translation stages and a rotation stage. The direction of the proton beam is indicated by the arrow. The proton beam will be scanned vertically and horizontally with respect to this direction. The proton beam direction and entry point in the head phantom can be accurately controlled by combined translation and rotation of the phantom.

New experimental research [8] on the production of neutron-rich heavy nuclei using multi-nucleon transfer reactions between heavy nuclei (e.g. ^{136}Xe on ^{208}Pb) has recently been started. An upgrade to one of the electron cyclotron resonance (ECR) ion sources is under development, in addition to the work on improvement of transmission from the ion source to the cyclotron extraction. A new experimental station consisting of a 3 T superconducting solenoid fragment separator and MR-ToF mass spectrometer is developed in collaboration with the University of Groningen.

The new infrastructure will allow us and our users to address various research questions such as:

- Radiation effects on electronics.
- Testing of particle detectors [9].
- Biological and physical radiation effects in space.
- Studies of radiation sensitivity variations within normal tissue and tumour.
- Mechanistic studies using various tumour and normal tissue utilizing in vitro and in vivo models to investigate interaction between radiation and systemic treatments, such as chemotherapy, immunotherapy and DNA damage response (DDR) modulators.
- LET and RBE studies for biological treatment planning.
- Advanced radiotherapy dose delivery techniques, such as GRID and FLASH.
- Therapeutic window optimization and translation to the clinic.

Medium-term, it is envisaged for PARTREC to provide users a one-stop-shop facility. This implies that PARTREC will support the users during the complete process of experiment development, the actual irradiation and its follow-up. For the animal irradiations, PARTREC will guide the users with the ethics authorisation process, animal procurement logistics, and will provide on-site animal accommodation with individually ventilated cage (IVCs) with a capacity of 200 rats and mice. For the follow-up the laboratory for animal handling prior and post irradiation could be used. The GronSAI imaging center will provide the possibilities to perform optical, structural and functional imaging of the animal models prior and post irradiation using fluorescence, bioluminescence, PET, CT, MR and multi-modality imaging systems. In addition, the local data management facilities could be used to store, process and analyze the irradiation-related data.

CONCLUSION

The new PARTREC facility will provide the physics, radiation hardness, radiation biology and medical communities with a state-of-the-art, open access research infrastructure for cell/tissue culture and small animal research. The upgrades to the infrastructure will become available from 2023.

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REFERENCES

[1] S. Galès for the AGOR project group, "AGOR: A superconducting cyclotron for light and heavy ions", in *Proc. ICCA'11*, Tokyo, Japan, Oct. 1989, paper f01, pp. 184–190.

[2] H. W. Wilschut and K. Jungmann, "Trapped Radioactive Isotopes: micro-laboratories for fundamental Physics (TRIμP)", *Nuclear Physics News*, vol. 17, no. 1, p. 11-15, 2007. doi:10.1080/10506890701225114

[3] E.R. van der Graaf, R.W. Ostendorf, M.-J. van Goethem, H.H. Kiewiet, M.A. Hofstee, and S. Brandenburg, "AGOR-FIRM, The AGOR Facility for Irradiations of Materials", in *Proc. RADECS 2009*, p. 443, 2010. doi:10.1109/RADECS.2009.5994694

[4] F. Diblen, T. Buitenhuis, T. Solf, P. Rodrigues, E. van der Graaf, M. J. van Goethem, S. Brandenburg, and P. Dendooven, "Radiation hardness of dSiPM sensors in a proton therapy radiation environment", *IEEE Transactions on Nuclear Science*, vol. 64, no. 7, pp. 1891–1896, 2017. doi:10.1109/TNS.2017.2705522

[5] B.N. Jones, S.Brandenburg, and M.-J. van Goethem, "AGOR status report", in *Proc. Cyclotrons'19*, Cape Town, South Africa, Sep. 2019, pp. 256–258. doi:10.18429/JACoW-Cyclotrons2019-TUC03

[6] I. Ozoemelam, E.R. van der Graaf, M.-J. van Goethem, M. Kapusta, Nan Zhang, S. Brandenburg, and P. Dendooven, "Feasibility of quasi-prompt PET-based range verification in proton therapy", *Phys. Med. Biol.*, vol. 65, no. 24, p. 245013, 2020. doi:10.1088/1361-6560/aba504

[7] I. Ozoemelam, E.R. van der Graaf, M.-J. van Goethem, M. Kapusta, Nan Zhang, S. Brandenburg, and P. Dendooven, "Real-Time PET Imaging for Range Verification of Helium Radiotherapy", *Front. Phys.*, vol. 8, p. 431, 2020. doi:10.3389/fphy.2020.565422

[8] X. Chen *et al.*, "Stacked-ring ion guide for cooling and bunching rare isotopes", *Int. J. Mass Spectrom.*, vol. 477, p. 116856, 2022. doi:10.1016/j.ijms.2022.116856

[9] T. Teichmann, M.J.G. Torres, M.-J. van Goethem, E.R. van der Graaf, J. Henniger, A. Jahn, H.H. Kiewiet, M. Sommer, W. Ullrich, C. Weinhold, and T. Kormoll, "Dose and dose rate measurements in proton beams using the luminescence of beryllium oxide", *J. Instrum.*, vol. 13, p. 10015, 2018. doi:10.3389/fphy.2020.565422