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University Medical Center Groningen

partrec

The New PArticle Therapy REsearch Center (PARTREC) at the University Medical Center Groningen

L. Barazzuol[1,2], S. Brandenburg[1], R.P. Coppes[1,2], P. Dendooven[1], A. Gerbershagen[1], M.-J. van Goethem[1], E.R. van der Graaf[1], B. N. Jones[1,2], P. van Luijk[1,2], J.M. Schippers[1], S. Both[1]

[1] Particle Therapy Research Center (PARTREC), Department of Radiation Oncology, University Medical Center Groningen, University of Groningen, The Netherlands

[2] Department of Biomedical Sciences of Cells and Systems, University Medical Center Groningen, University of Groningen, Groningen, The Netherlands.

(a.gerbershagen@umcg.nl)

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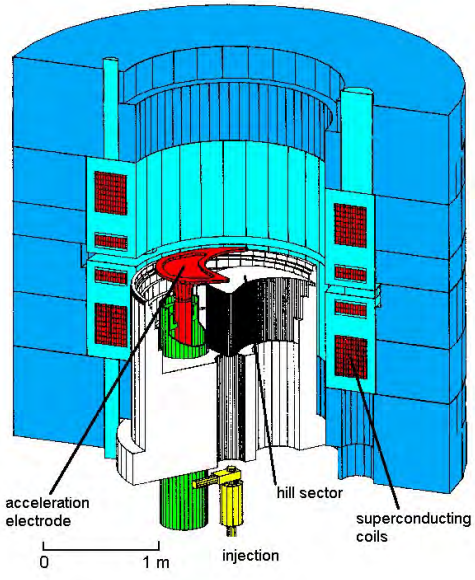

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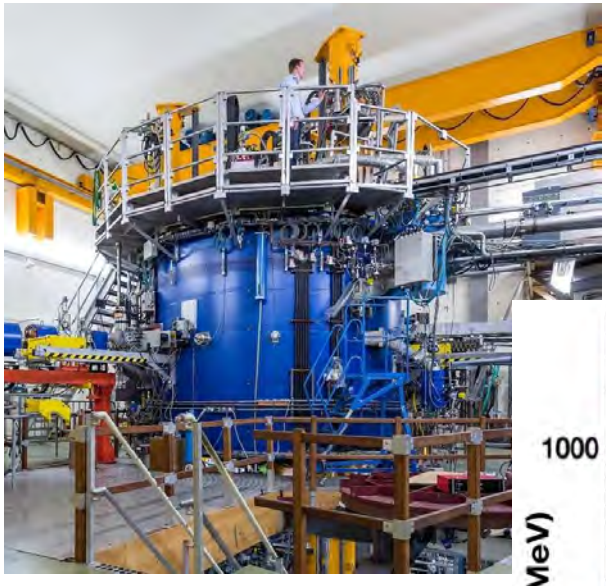
Our Facility

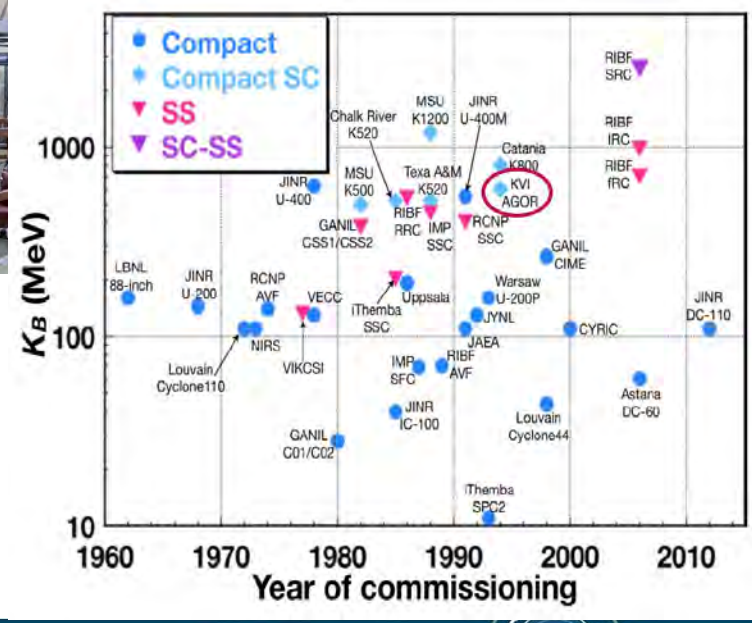
- We operate a large superconducting cyclotron for experimental research

- From 1996 – 2013 beams mainly used for research in nuclear physics (light ions) and on fundamental symmetries (heavy ions)

- Emphasis has shifted towards detector development and radiation hardness testing (since 2005, mainly commercial with some funded experimental research) and biomedical research (since 2014)

- Reorganization:
KVI's accelerator facility, staff and medical physics group was integrated into UMCG and became PARTREC

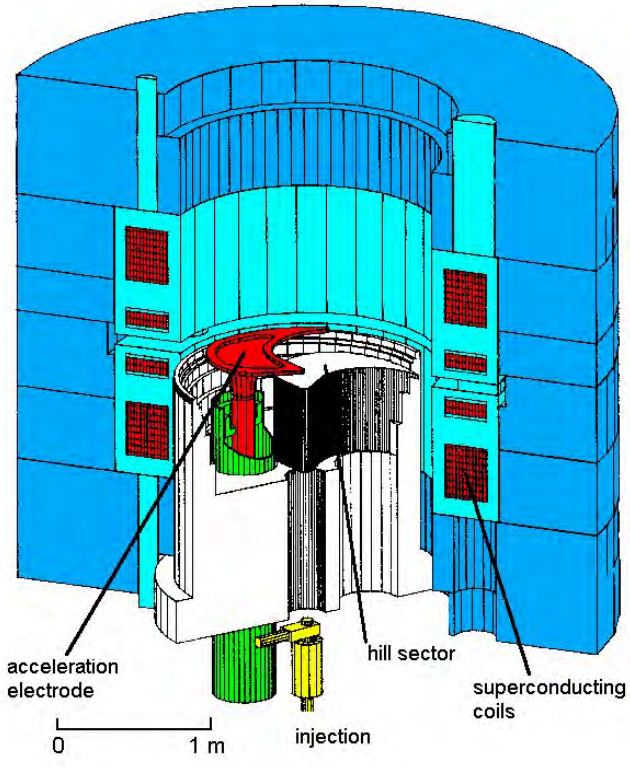


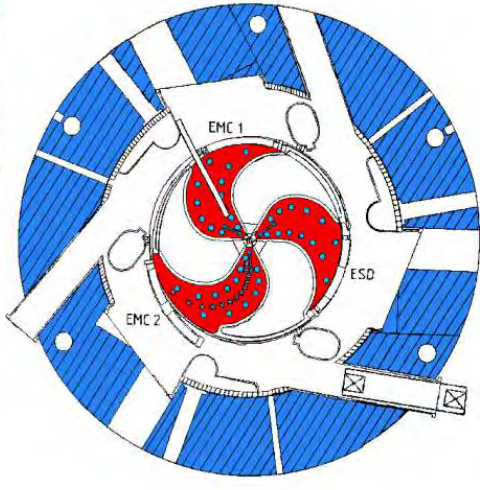


AGOR Cyclotron

- Superconducting AGOR cyclotron is a multi-particle, variable energy AVF-cyclotron
- French-Dutch collaboration built 1987 – 1994
- Operational since 1996
- Magnetic field (1.7 to 4.1 T) produced by
  - two superconducting main coils
  - fifteen trim coils
  - three iron hill sectors for focussing

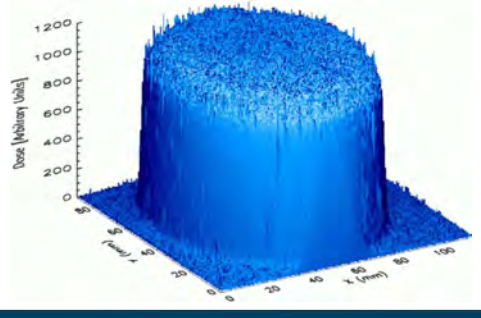
- 3 halfwave RF cavities, 24 - 62 MHz; h = 2, 3 or 4
- Three external ion sources (two ECR sources for heavy ions, multi-cusp source for light ions) are axially injected
- Extraction
  - 300 - 500 turns depending on harmonic mode
  - extraction radius 870 - 890 mm depending on E/A
  - turn separation at extraction 2 - 3 mm ~ beamwidth



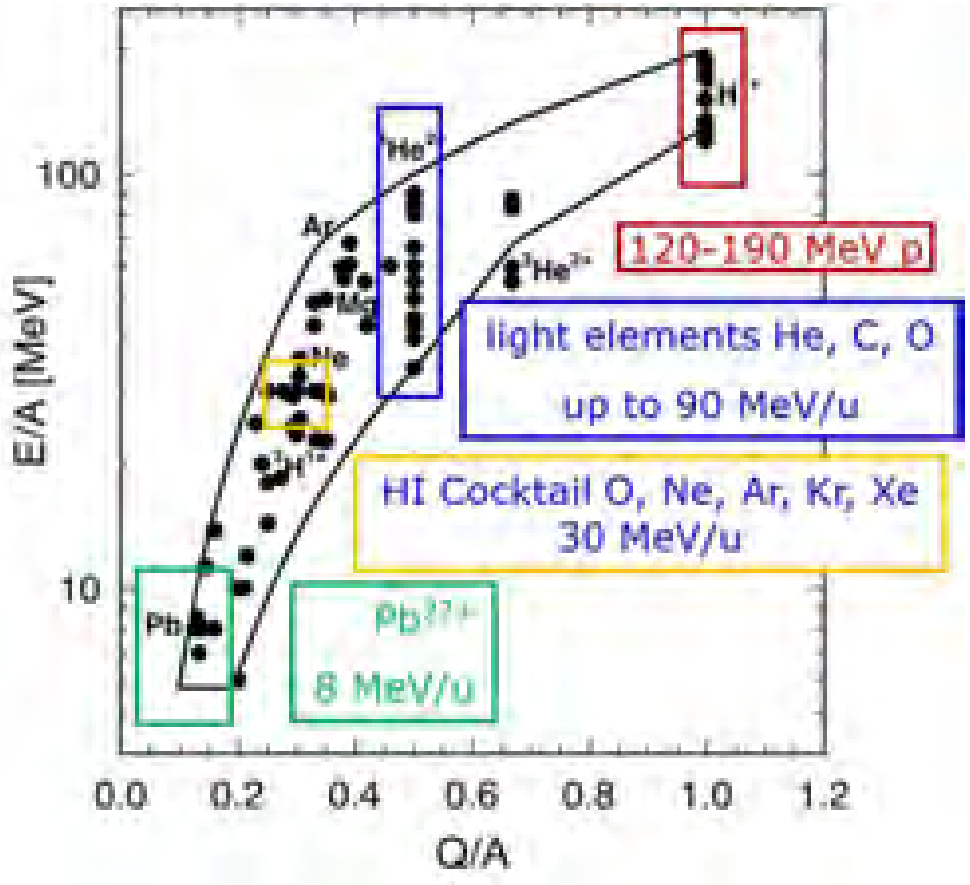


Beam Parameters

	Protons	Ions
Kinetic energy (MeV/amu)	≤ 190	≤ 90 for C and O ≤ 30 for all up to Xe
Attainable flux (particles per s)	> 10^{13}	≤ 10^{13} for Ne ≤ 10^{11} for heavier ions
Field size (cm^2)	≤ 10 x 10 (scanned beam) ≤ 8 x 8 (scattered beam)	≤ 7 x 7 for light ions (scanned beam) ≤ 3 x 3 for heavy ions (scanned beam)
Field homogeneity	± 2 % (scattered beam) ± 1 % (scanned beam)	± 2 % (scattered beam) ± 1 % (scanned beam)

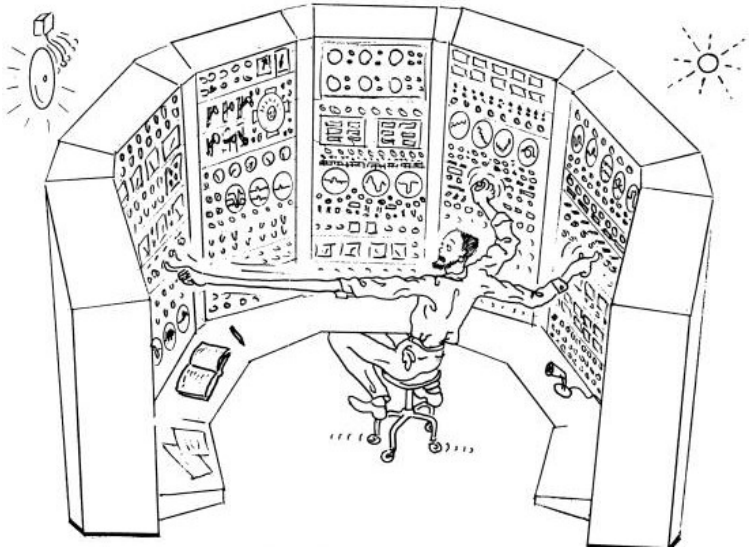


AGOR can deliver beams of all elements up to Xe



Our Team

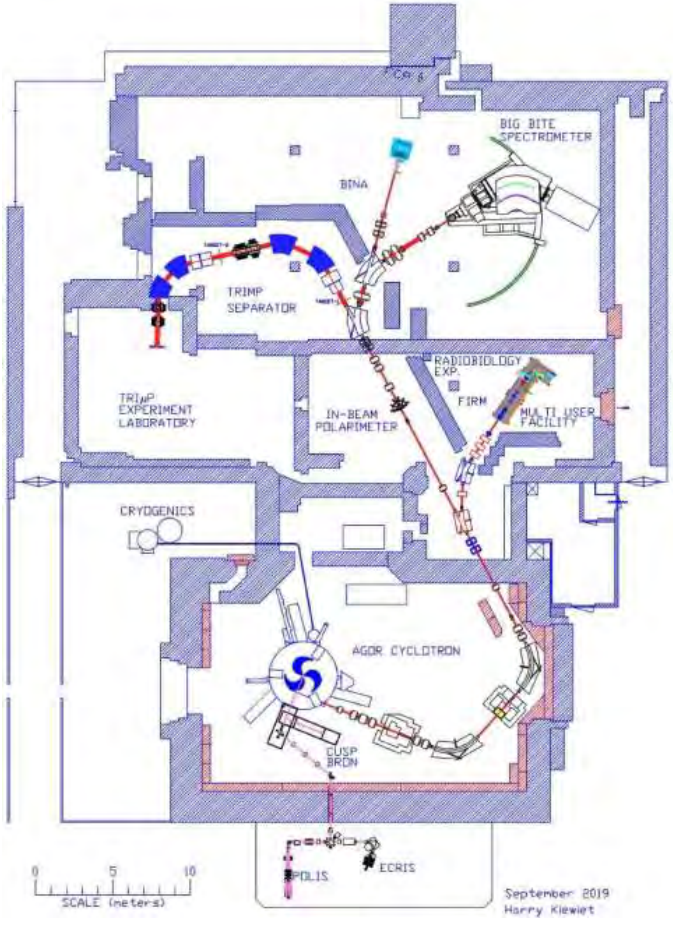
- Technical staff (24)
  - Operators to operate and maintain the accelerator (5)
  - Cryogenics, cooling, compressed air and vacuum (2)
  - Design/Mechanical: mechanical repairs, design and construct mechanical components that have become obsolete and contribute to scientific and infrastructure projects (5)
  - Electronics: maintenance of the magnet power supplies, RF-amplifiers, low level RF-electronics, PLC-systems and interfaces of all these systems to the central control system of the accelerator (5)
  - IT Support needed for operation, maintenance and upgrading of the accelerator control system as well as the irradiation control system (3)
  - Experimental and project support provided to internal/external scientists as well as companies, ECR sources (4)
- Faculty (4)
- Post-docs (2)
- PhD-students (5).



PARTEC Operation

- We strive to provide a reliable and reproducible ion beam to satisfy the needs of the user
- We also provide support
- Operational 120 hours/week, 26 weeks/year
- Beam requests: irradiations.partrec@umcg.nl
- With shift from fundamental physics to radiation biology and physics and technology of particle therapy the number of individual experiments increased while their duration has decreased
- Over the past few years proton beams provided for over 80% of beam time

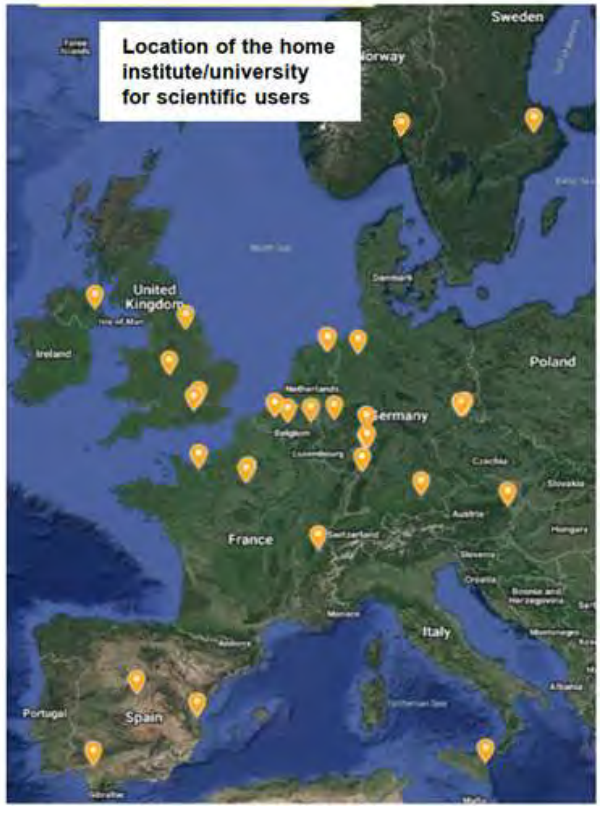
KVI facility layout before PARTREC upgrades



Our Users and Funding

- Recognized by ESA as Ground-Based Facility (CORA-IBER, Investigating biological effects of space radiation)
- Supported by EU as Large-Scale Facility (IAs RADNEXT, INSPIRE)
- Commercial Funding:
  - Mainly proton in-air irradiations
  - Expanding heavy ions
  - Mostly non-domestic aerospace
- Local and national funding (RUG, UMCG, KWF, NWO)
- Examples
  - Determination of the lateral dose response functions of detectors in proton beams
  - Prediction, prevention and treatment of radiotherapy-induced complications
  - Proton SOBP irradiation of cell cultures and organoids
  - A test measurement to study recombination effects at high dose rate
  - Evaluation of proton and carbon-ion RBE for cell killing in radio resistant and hypoxic patient derived Glioblastoma stem cells
  - The interaction of chemotherapy with high and low LET radiation in pancreatic cancer cell lines
  - Measurement of the production cross section of the short-lived b+ emitters of interest in proton therapy
  - Neuronal responses to particle irradiation and potential interaction with stress hormones

esa
European Space Agency

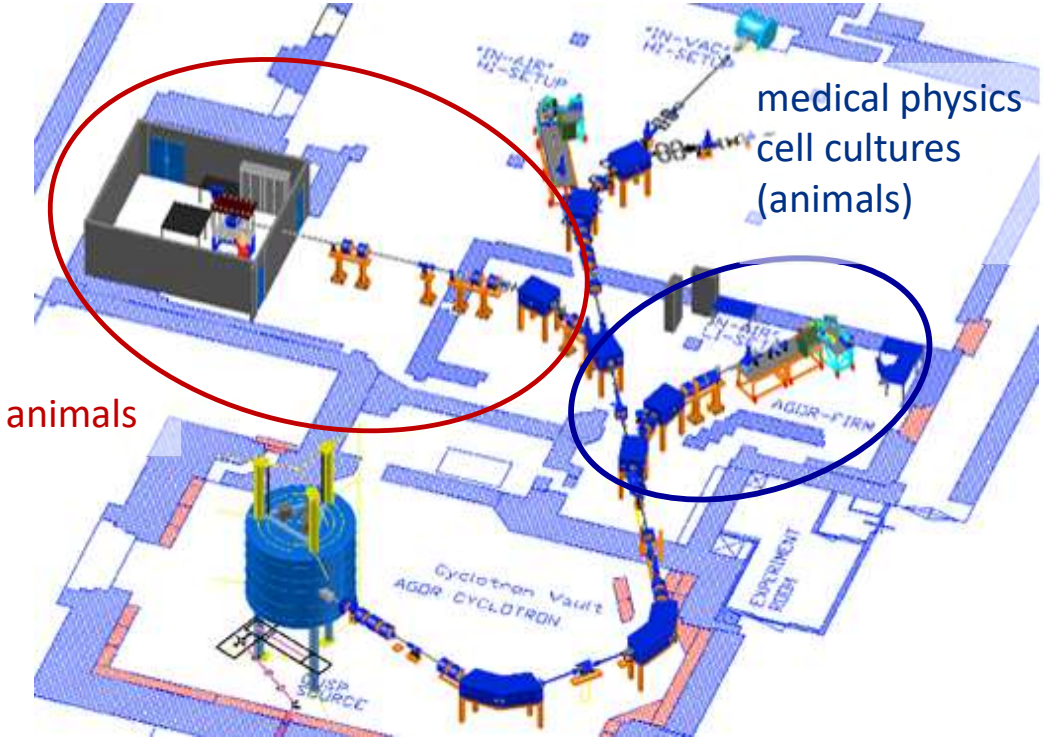


Ongoing Upgrades

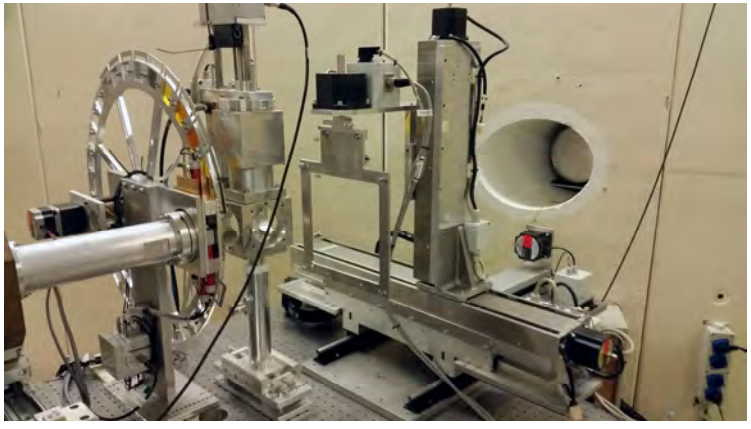
- Radiation hardness testing is expanding

- In 2018 funding has been obtained for further expansion of the biomedical research as well as for a project investigating the properties of neutron-rich heavy nuclei

- Image guidance
- Individual planning
- Multiple modalities
  - PBS/scattering
  - Shoot through/SOBP
  - Grid
  - FLASH
  - Protons; helium



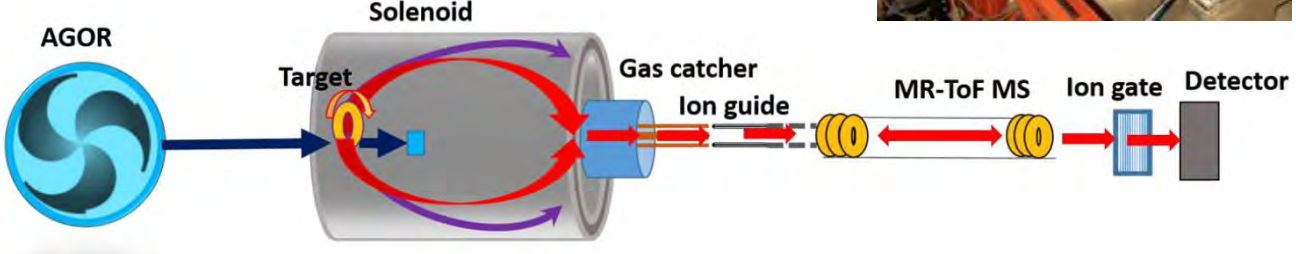
Heavy Ion Beams



- Research areas
  - Radiobiology (RuG, UMCG, PSI)
  - Detector tests & development (ESA)
  - Experiment development (ESA)
  - Radiation hardness (ESA, companies)

- At the moment, AGOR can deliver beams of all elements up to Xe

- New experimental research 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
- ECR ion source development, improvement of transmission from source to extraction
- A new experimental station consisting of a 3 T superconducting solenoid fragment separator and MR-ToF mass spectrometer is developed with RUG and will be installed



Biomedical Research

Currently performed :

- Animal (rats) experiments: protons, helium
- Cell cultures and organoids: protons to neon
- Physics: mainly protons, helium, carbon

• University of Groningen and the University Medical Center Groningen (UMCG) have recently established a clinical proton therapy center (first patient at the start of 2018)

• A new beam line with 3D X-ray and bioluminescence imagining at the irradiation position (individually optimized small animal irradiations) will be built in the coming years

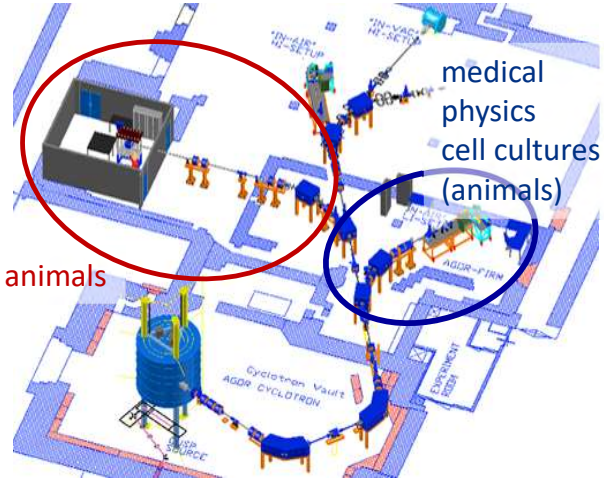
• Several new dose delivery modalities will be available, including pencil beam scanning, spatial fractionation and very high dose rate (>1000 Gy/s)

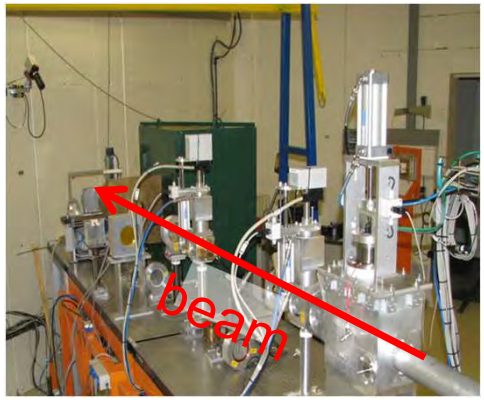
• Operated as an open access facility

• Individual imaging

  • Anatomical variations between animals

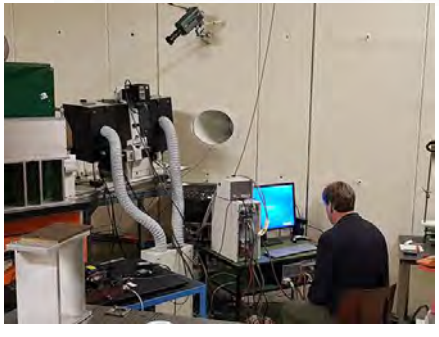
  • Individually optimized irradiation plan





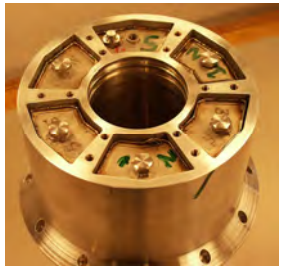
One Stop Shop

- Experiment development
- Ethics authorisation process
- Irradiation + follow-up
- Animal procurement logistics
- On site animal accommodation with IVCs
  - capacity 200 rats and mice
  - no long term stay
  - two additional accommodations planned
- Laboratory for animal handling prior and post irradiation
  - GronSAI imaging center
    - optical
    - molecular
    - CT
    - MRI
- Data management facilities



FLASH Irradiations

- FLASH effect occurs at high irradiation rates (100s Gy/s)
- FLASH radiation damages healthy tissue less, while delivering full damage to the tumour tissue -> increases therapeutic window
- Beam intensity
  - protons ≤ 6×10^{13} pps
  - helium ≤ 10^{13} pps
  - carbon ≤ 10^{10} pps
    → proton, helium dose rate 10^2 - 10^4 Gy/s, dependent on field size
    → 90 MeV/A carbon SOBP dose rate up to 200 Gy/min
  - further increase under development (improvement of the source performance and transmission into the cyclotron)
- Development of dose control (diamond detector, N_2 thin dual cap ionization chamber, CW current transformer) and high dose rate dosimetry (Gafchromic Film, Faraday Cup)
- Establish beam parameters, dose delivery and control methods in conformity with ones clinically achievable for FLASH beam irradiations
  - at GPTC and
  - at other facilities.



Summary

- UMCG has unique combination of treatment facility (GPTC) and research center accelerator facility (PARTREC)
- PARTREC delivers protons (<190 MeV) and ions up to Xe for
  - Commercial and institutional irradiation tests
  - Radiobiology and medicine
  - Nuclear physics research
- Ongoing upgrades include
  - Very heavy ions acceleration (up to ^{209}Bi)
  - Higher dose rates for FLASH
  - New infrastructure for animal, organoid and cell irradiation
- Acknowledgement
  - Research funding
  - Access funding
  - Host institutions and all colleagues for contributing

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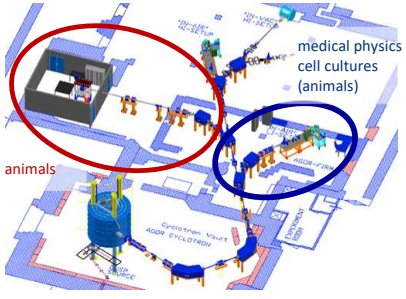

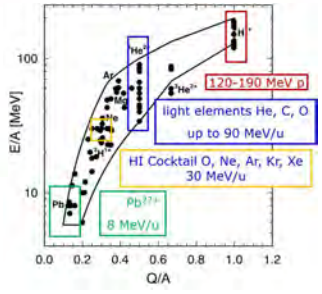

DUTCH CANCER SOCIETY

NWO Netherlands Organisation for Scientific Research

ZonMw

esa European Space Agency

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Thank you

Acknowledgements:

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