



# HITRI

*plus*

Heavy Ion Therapy Research Integration

## HITRIplus Project – Its impact on boosting Research in South-East Europe and future perspective



This project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 101008548

**Hadron Therapy Workshop: Status and perspectives, plans for next generation facilities - 18 October 2024, Thessaloniki, Greece**

**Dr. Sanja Damjanovic, GSI Helmholtz Centrum for Nuclear Research, Darmstadt, Germany**

# HITRI *plus*

Heavy Ion Therapy Research Integration

**Opportunity to Develop Next-Generation  
Ion Therapy Facilities**

**Goal: Expand Access to Ion Therapy  
for a much larger number of patients**

**How: Leverage International Collaboration  
to advance accelerator technologies  
and new treatment techniques**



# SEEIIST a catalyst for HITRIplus

SEEIIST and HITRIplus form a powerful alliance

- HITRIplus leading the charge in beating cancer with cutting-edge ion therapy – setting ground for a new facility
- SEEIIST driving scientific growth in South East Europe as Strategic partner in HITRIplus and potential Reference user, empowered by the political support of SEEIIST member governments and the European Commission.



This collaboration shapes the future of the research and innovation in SEE

# How it started?



## Official launch: Government of Montenegro initiated SEEIIST in March 2017

### Background:

After 20 years working at CERN Minister of Science of Montenegro from Nov. 2016 to Dec.2020

### Rapid convincing:

Secured Government support just in 3 months  
Appointed as a political lead to setup SEEIIST's scientific framework.

## Political Milestone - SEEIIST goes Regional

Declaration of Intent signed at CERN on October 25, 2017 by SEE Ministers responsible for research (8 countries)



Memorandum of Cooperation signed by SEE Prime Ministers at the 6th Summit of the Berlin Process, Poznan, Poland, 2019



In January 2018 the SEEIIST Steering Committee was formed - I was elected to be the first Chair (2018-2021)

The question arose: What should SEEIIST be to have a direct impact on society and easily attract political support ?



# The proposal for SEEIST to be an **Accelerator-based Research Infrastructure for Cancer Therapy and Biomedical Research with Ion Beams**

came early 2017 from two key pioneers in the use of ion beams to treat cancer:



**Prof. Hans J. Specht at Uni HD**

- *Pioneer of ultra-relativistic heavy ion physics at CERN*
- *Pioneer of Ion cancer therapy as Scientific Director of GSI Helmholtz Centre for Heavy Ion Research*
- *He pushed and led the establishment of a pilot project at GSI , where the first 450 patients in Europe were treated with ion-beams from 1997-2008.*
- *Instrumental in establishing Europe's first hadron cancer therapy clinic, HIT, in Heidelberg*
- *The true author of IAEA RER6309 project*



**Prof. Ugo Amaldi at CERN**

- *A pioneer in the design of particle accelerators for cancer treatment, who was instrumental in establishing Europe's second hadron cancer therapy clinic, CNAO, in Pavia, Italy*
- *President of TERA foundation*
- *Editor of the Concept Study and pre-TDR for SEEIST*

# First promises of support from the EC and IAEA at the Forum in Trieste (Jan 2018) - where the Concept Study was presented

Basic concepts for a



Commission, leading to its first financial support in 2019.

#### Acknowledgements

The valuable advice by N. Sammut (University of Malta) and H. J. Specht (University of Heidelberg) during the development of the initiative is greatly appreciated.

to the successful RER6309 project.

# Support by the European Commission EU H2020 HITRIplus funded by the EC

## ❖ EC – Directorate General for Research and Innovation (EC DG-RTD)

First direct financial support for the SEEIST Design Phase

- 1.5 MEUR for the 1<sup>st</sup> stage of Design Phase (2019)
- Additional 5 MEUR via a competitive **Call EU-H2020 INFRAIA – HITRIplus (2021-2025)**

SEEIST is one of the 6 Leading EU-WB projects in R&I in the Innovation Agenda for the WB



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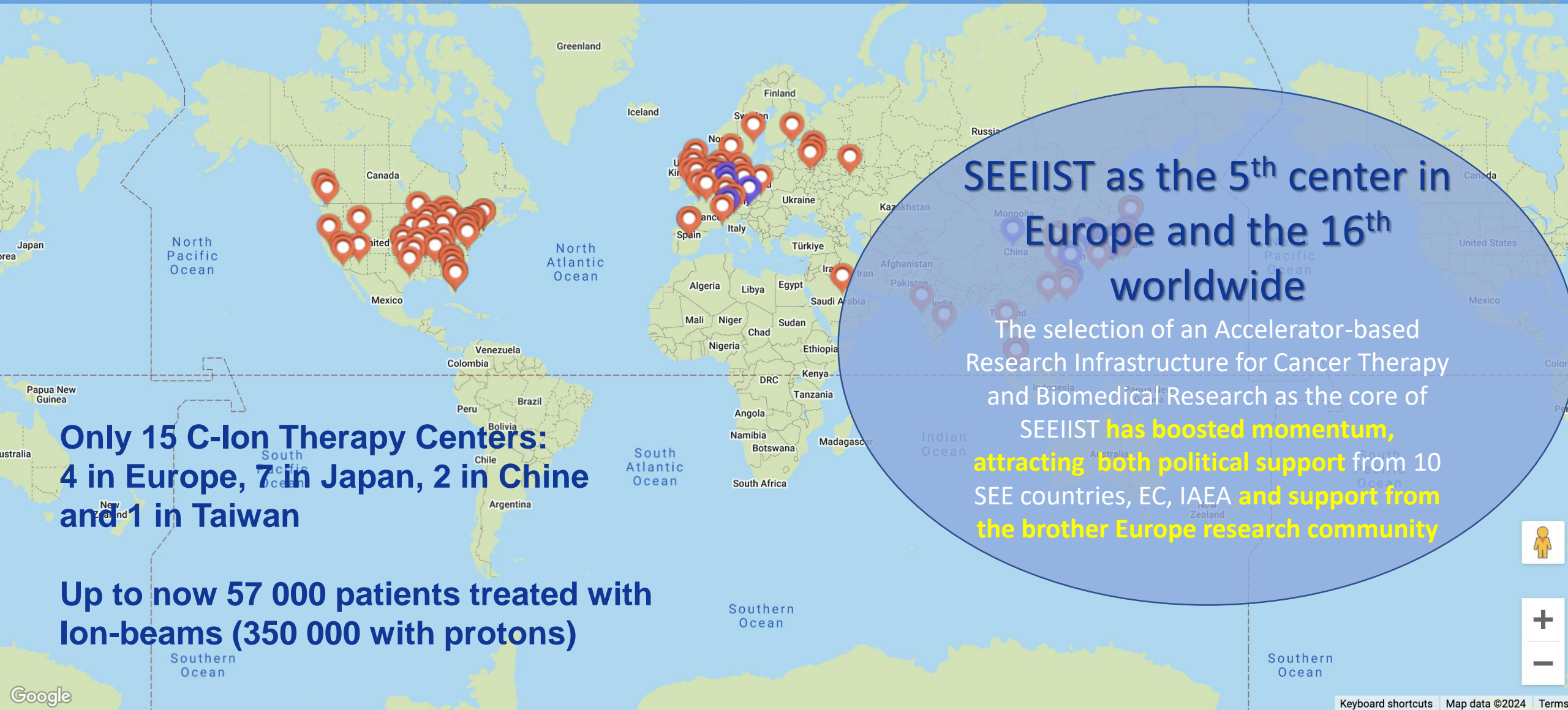
## ❖ EC - Directorate General for Neighbourhood and Enlargement (DG NEAR)

SEEIST became part of the Economic Investment Plan for Western Balkans (part of Global Gateway initiative) as the only Research Infrastructure – 9 billion EUR appointed for the WB 2021-2027, going up to 30 billion by 2030



# Particle Therapy Centers world-wide

## only 15 C-Ion Therapy Facilities



**Only 15 C-Ion Therapy Centers:**  
**4 in Europe, 7 in Japan, 2 in China**  
**and 1 in Taiwan**

**Up to now 57 000 patients treated with  
Ion-beams (350 000 with protons)**

**SEEIIST as the 5<sup>th</sup> center in  
Europe and the 16<sup>th</sup>  
worldwide**

The selection of an Accelerator-based  
Research Infrastructure for Cancer Therapy  
and Biomedical Research as the core of  
SEEIIST **has boosted momentum,**  
**attracting both political support** from 10  
SEE countries, EC, IAEA **and support from**  
**the brother Europe research community**





# Fight against Cancer

Cancer is the second leading cause of death globally, and was responsible for 10 million deaths in 2020 (WHO)

Globally, nearly 1 in 6 deaths is due to cancer (WHO) – Each year 400 000 children develop cancer

Cancer research declared by the **European Commission** as one of the **five Missions** in the **EU Horizon Europe Programme** - but presently entirely absent from the European RI landscape.

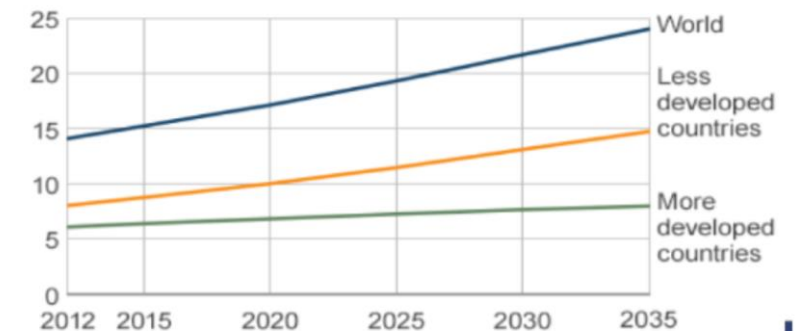
**SEEIIST addresses** this notable **gap in the European Research Infrastructure landscape**

GLOBOCAN 2012: Estimated Cancer Incidence, Mortality and Prevalence Worldwide in 2012



## Predicted Global Cancer Cases

Cases (millions)



Source: WHO GloboCan

# From Conventional to Ion-Beam Radiotherapy

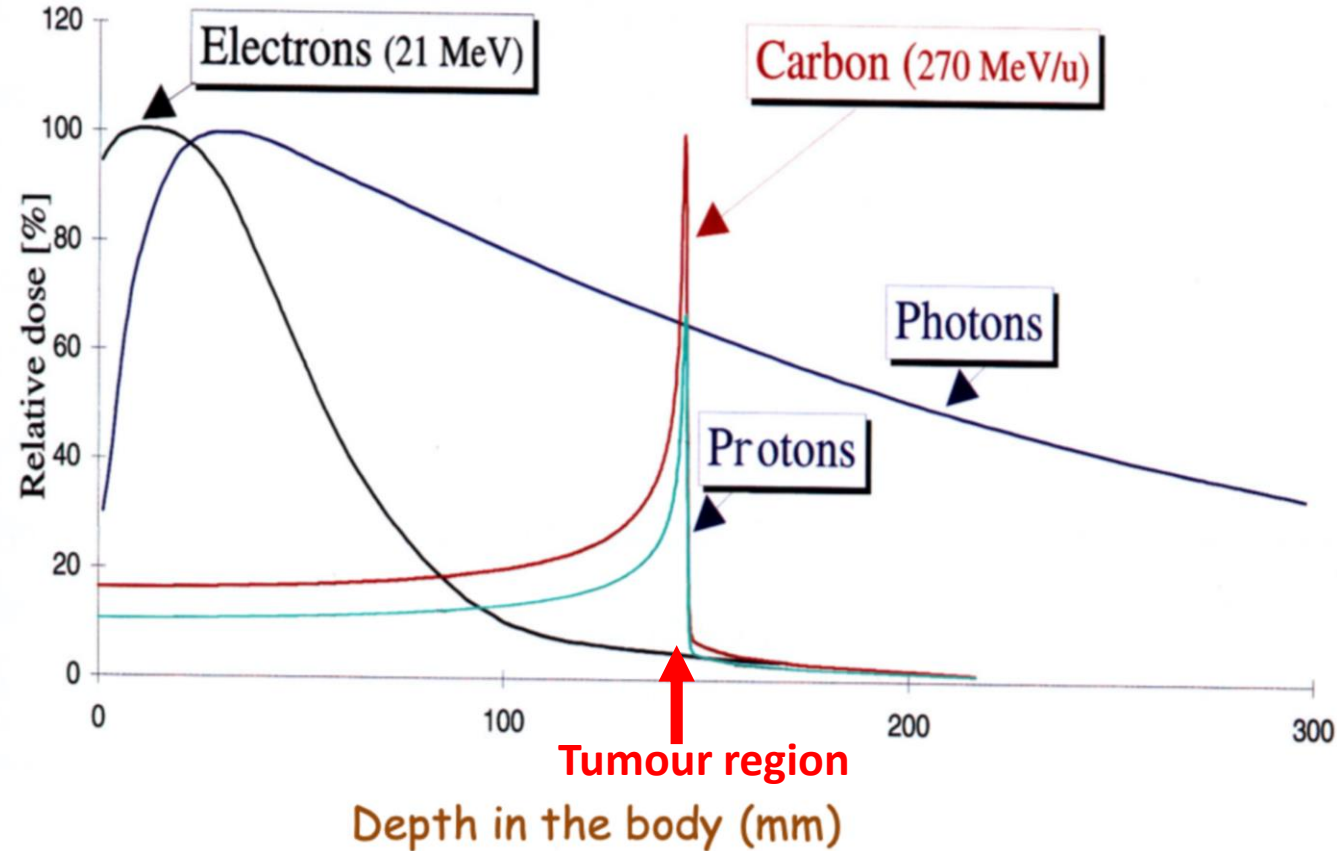


**Why Heavy Charged Particles are  
superior to any other radiation in  
tumour therapy?**

# The beauty of Bragg Peak



Deposited dose along the tissue depth



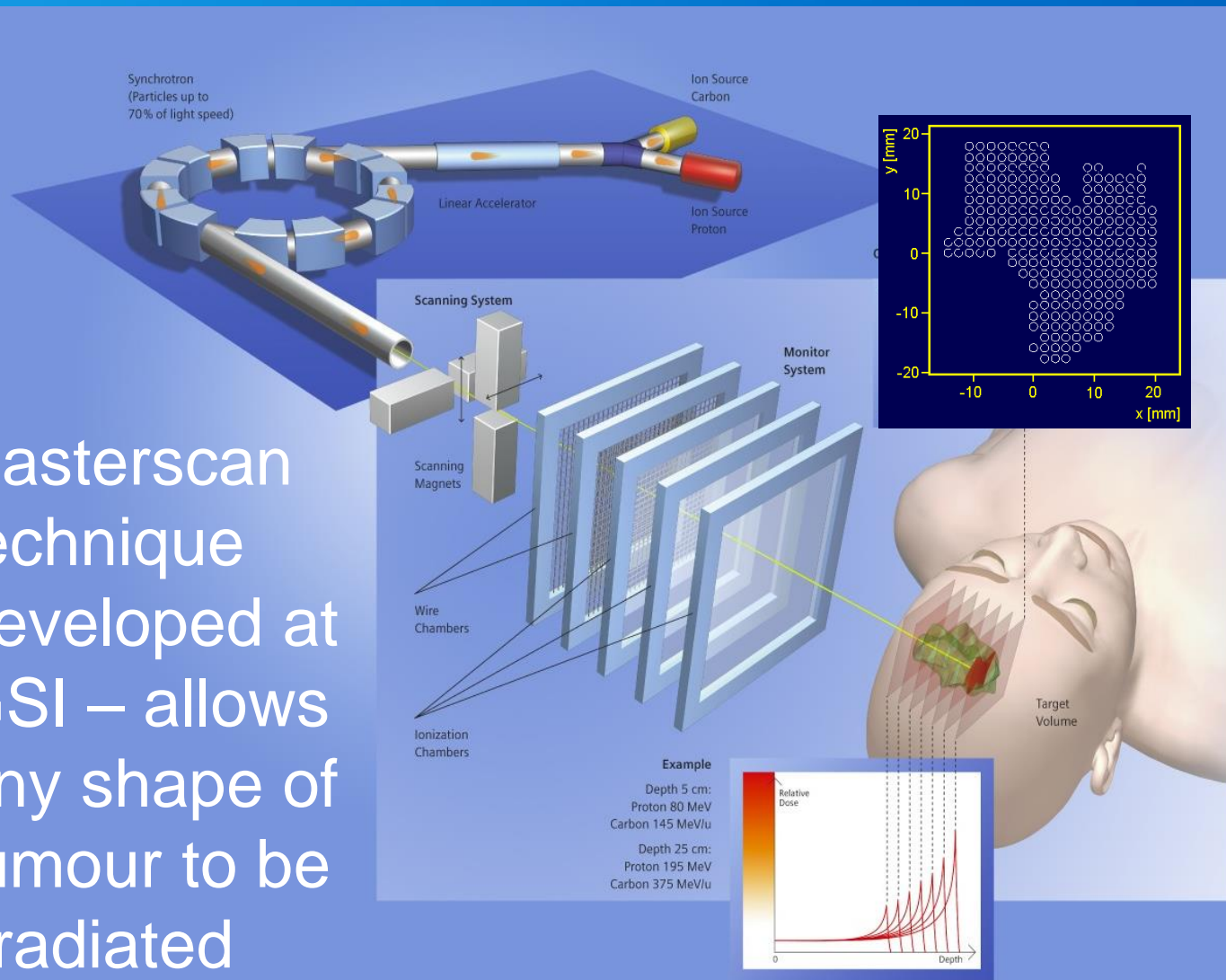
Different from X-rays and Electrons:

- Heavy charged particles exhibit minimal lateral and angular scattering.
- These particles travel in virtually straight lines and stop at a specific penetration depth, delivering a **high dose** precisely at the end of the ion path, known as the **Bragg peak**.
- The optimum dose of heavy ions can be **precisely localized at the tumour** inside the patient, **protecting surrounding healthy cells**, reaching the tumour wherever it is in the body

Ion therapy is particularly powerful for radioresistant tumours and tumours close to risk organs (C-ions more powerful than protons – much larger effective dose - proportional to  $Z^2$ )

# Ion Beams scan the Tumour Volume

Rasterscan technique developed at GSI – allows any shape of tumour to be irradiated



Ion beams scan the tumour volume of any shape in lines in the same way electrons do in the television tube.

**Three-dimensional Irradiation:** The depth controlled by the energy, while scanning in a plane at a fixed depth - isoenergy slice- achieved by two magnets changing the beam in vertical and horizontal position

**Three-dimensional imaging** of the irradiated tumour volume with millimeter accuracy – aligning with the precision of the treatment method

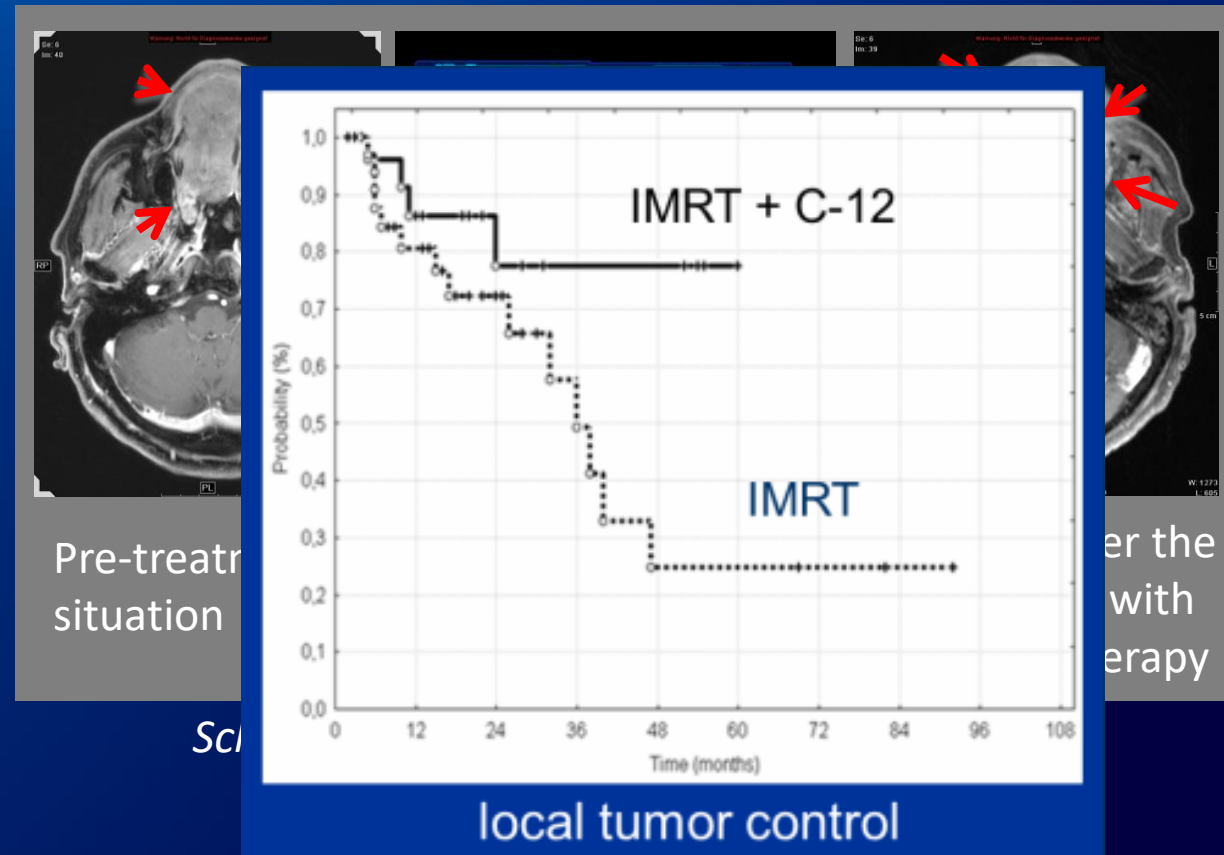
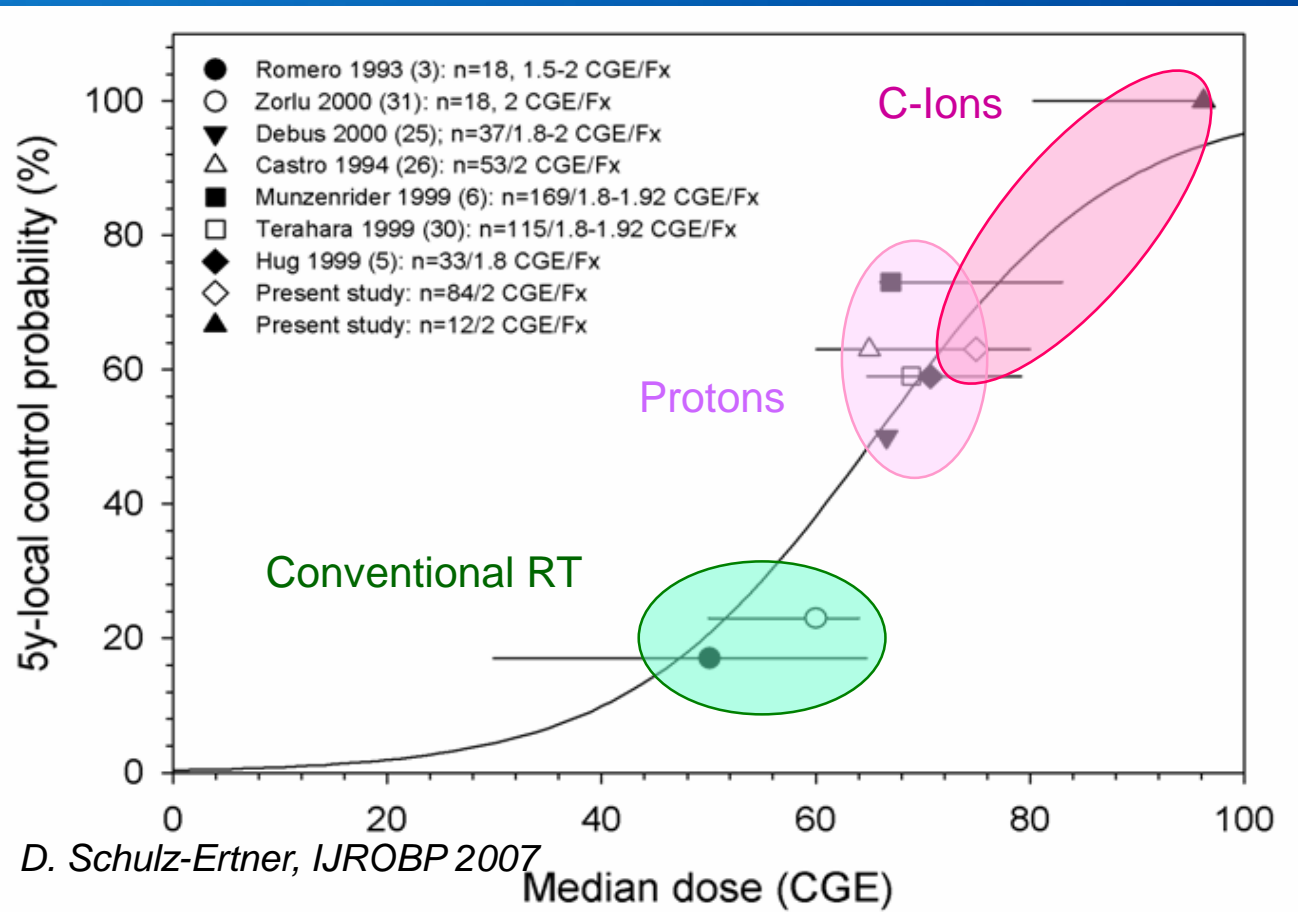
# Carbon-ion Therapy - High Effectiveness and Survival Probability



## Chordomas of the Skull Base

90% Survival probability 5 years after C-treatment

Carbon ion Boost and IMRT highly effective for **Salivary gland tumors**



# Hadron therapy the most powerful, yet still a niche in cancer therapy

Main factors for limiting growing:  
Cost and Size

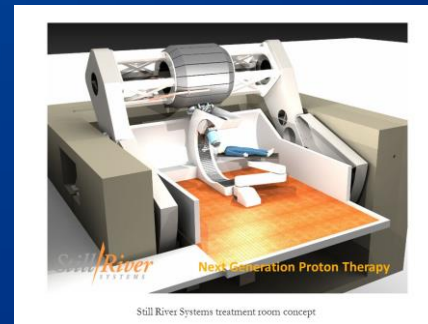
250 MEUR



Ion therapy  
(protons + carbon ions)



Proton multi-room



Proton single-room

2 MEUR



X-ray linac

E.g. in 2018 world-wide 22,000 patients were treated with hadron therapy (p,C). In contrast, 25,000,000 patients were treated with conventional radiotherapy

# Scientific Milestones – SEEIIST attracted support from the broader European Research Community

**HITRIplus** - 18 European Research Centers, Clinics and SMSs across 14 European countries

Collaborative partners in the HITRIplus project: CERN, GSI, HIT, CNAO, MedAustron, MIT, Bevatech GmbH, CEA, CIEMAT, COSYLAB, INFN, PSI, Uni Malta, Philipps Uni Marburg, Uppsala Uni, Wigner RC, Technical Uni Riga and SEEIIST

**Opportunity to Develop Next-Generation Ion Therapy Facilities to Expand Access to Ion Therapy for a much larger number of patients**

- *More Compact & Cost-Effective, and Higher Performance Designs*
- *Incorporating R&D Innovations for treatment, like FLASH Therapy*

# CERN Next Ion Medical Machine Study (NIMMS)

+ large number of international partners:

## Towards a new generation of accelerator for cancer therapy

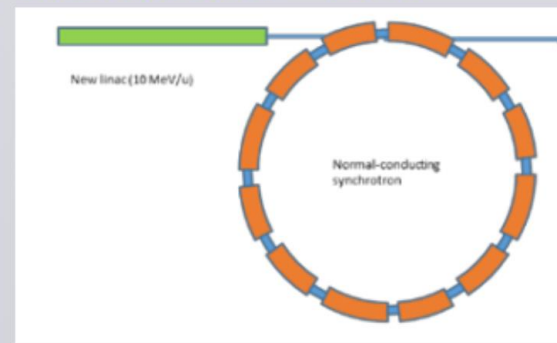
### Three alternative accelerator designs

Maurizio Vretenar,  
CERN, 19 Oct 2020

#### Improved synchrotron (warm)

Equipped with several innovative features: multi-turn injection for higher beam intensity, new injector at higher gradient and energy, multiple extraction schemes, multi-ion.

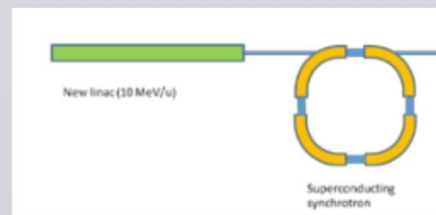
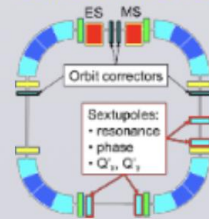
Circumference ~ 75 m



#### Improved synchrotron (superconducting)

Equipped with the same innovative features as warm, but additionally 90° superconducting magnets.

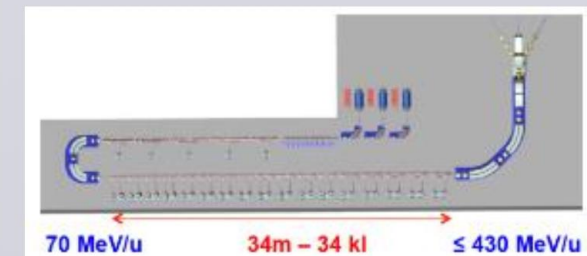
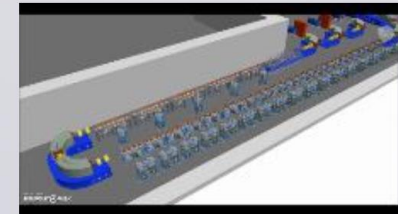
Circumference ~ 27 m



#### Linear accelerator

Linear sequence of accelerating cells, high pulse frequency.

Length ~ 53 m






# GSI Biophysics, alongside international research efforts – Advancing Innovative Flash Radiotherapy - a novel approach using ultra high dose rate

## FLASH Therapy with heavy ions – Powerful waepon in the fight against cancer - Killing tumours in less than 1 second with reduced toxicity

With FLASH Therapy – Ultra-High Radiation Dose Delivered in a very short time (Dose Rate of  $> 40$  Gy/s, delivered time  $< 200$  ms). For Comparison: Conventional Radiation Dose Rate is 1 Gy/min.

**GSI in one of the 10 breakthroughs of 2022: Investigating new weapons in the fight against cancer**

World's leading oncology journal dedicates its cover story to the FLASH method in which GSI has a leading role



The cover of „Nature Reviews Clinical Oncology“.

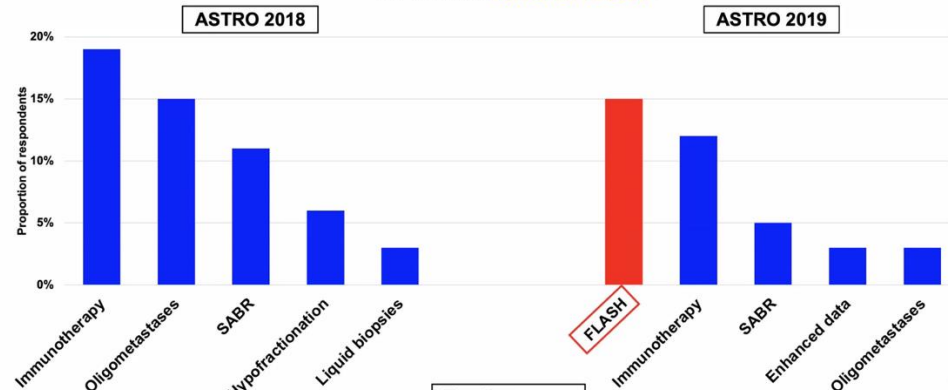
19.01.2023 | It could become a powerful weapon in the fight against cancer and open up completely new possibilities for tumor therapy with charged particles. FLASH irradiation – the application of an ultra-high radiation dose in a very short time – is in strong focus worldwide and is being advanced with high expertise at GSI and FAIR. FLASH clinical implementation is one of the top 10 Breakthroughs of the Year 2022 according to "Physics World". In its December issue, the world's

**The Hottest Topic in Radiation Oncology!**

# FLASH „boom“

EDITORIAL  
Responses to the 2018 and 2019 “One Big Discovery” Question: ASTRO Membership’s Opinions on the Most Important Research Question Facing Radiation Oncology...Where We Headed?

**ASTRO Meeting Survey:  
What is the One Big Discovery that needs to be translated into the clinic RIGHT NOW?**



Treatment	ASTRO 2018 (%)	ASTRO 2019 (%)
Immunotherapy	~19	~12
Oligometastases	~15	~3
SABR	~11	~5
Hypofractionation	~6	~3
Liquid biopsies	~3	~3
<b>FLASH</b>	0	~15

Top 5 answers

Marco Durante, 2023, GSI

# Future Direction for HIRIplus aligned with SEEIST in shaping the scientific landscape in SEE

Leveraging complementarities and synergies:

- synergies of structural/ cohesion/ IPA funds with national and EU funding progr. cross-cutting need

Leveraging EU Horizon Europe Instruments:

- Explore new funding instruments requiring collaboration among 3-5 countries and co-funding – e.g. Innovation Valleys

Political advocacy for new European Partnerships



Average salaries in Europe

# Key to success:

**International Cooperation and Collaboration  
among different stakeholders**

Shared Vision

“Together, we can shape  
the future of cancer  
treatment and science in  
South-East Europe.”



- BKP

# New Growth Plan for the Western Balkans

Boosting the Western Balkans' socio-economic convergence with the EU & accelerating EU reforms



NOVEMBER 2023

#WesternBalkans  
#EUEnlargement

**€6 billion**

**€2 billion** in grants

**€4 billion** in loans



SEE

ST

South East European  
International Institute  
for Sustainable Technologies

# SEEIIST: A potential Flagship project for EU Enlargement

