Medical Applications

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JAI Advisory Board Meeting
7th April 2022

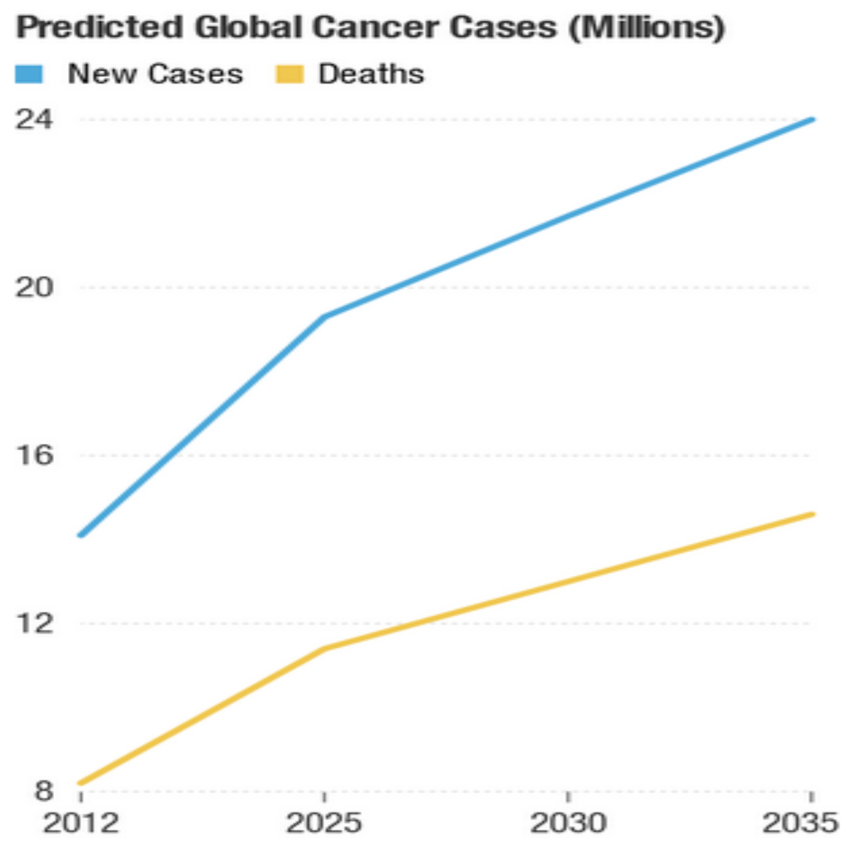
Medical Applications

Importance of establishing multidisciplinary programmes for delivering impact:

- STELLA (Smart Technologies to Extend Lives with a Linear Accelerator)
  - Robust, low-cost X-ray therapy for challenging environments
  - Nuclear Security and Cobalt 60 facilities
- VHEE and FLASH studies at CLEAR facility
- ITRF/LHARA (Nick Dover)
- BDSIM and instrumentation (Laurie Nevay)

Cancer is a growing global challenge

- Globally **18** million new cases per year diagnosed and **9.6** million deaths in **2018**
- This will increase to **27.5** million new cases per year and **16.3** million deaths by **2040**
- **70% of these deaths** will occur in low-and-middle-income countries (LMICs)



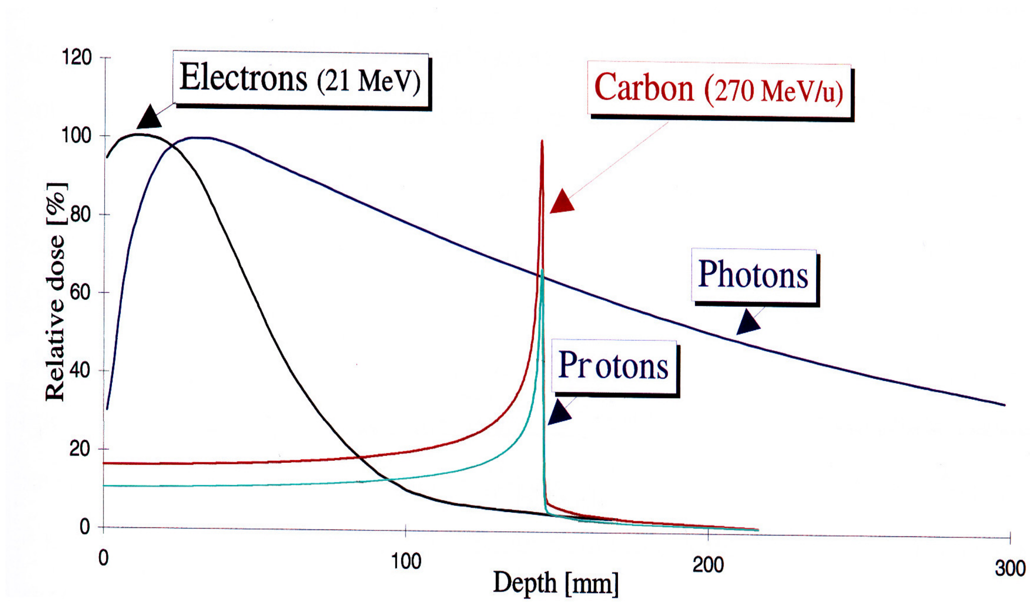
Radiation therapy is a key tool for treatment for over 50% patients

Aims of Radiotherapy:

- Irradiate tumour with sufficient dose to **stop tumour growth**
- **Avoid complications** and **minimise** damage to surrounding tissue

Current radiotherapy methods:

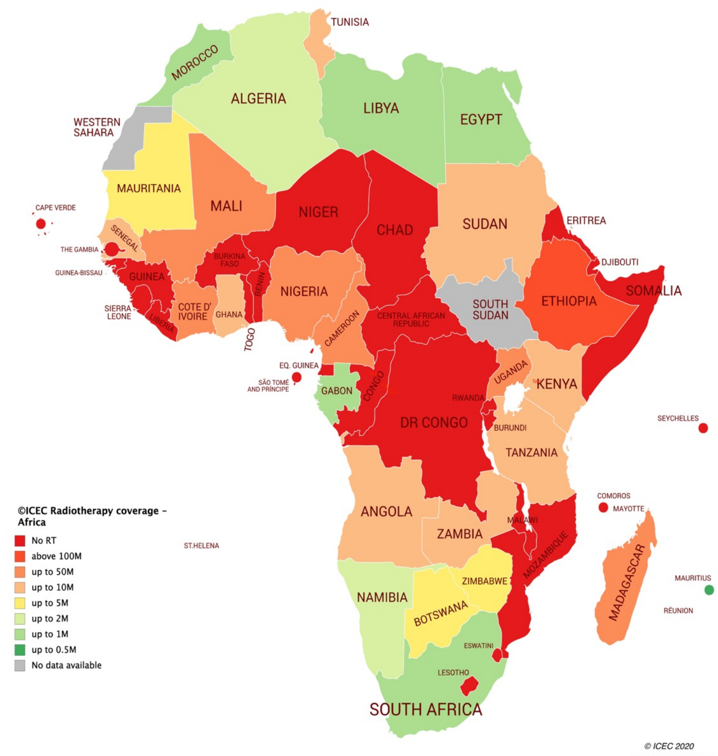
- 5 - 25 MV photons
- 5 - 25 MeV electrons
- 50 - 300 MeV/u hadrons



Current hot topics of research:
How to deliver RT cheaply and precisely
VHEE and FLASH with electrons and particles

Great strides have been made in the fight against cancer, but access remains a challenge

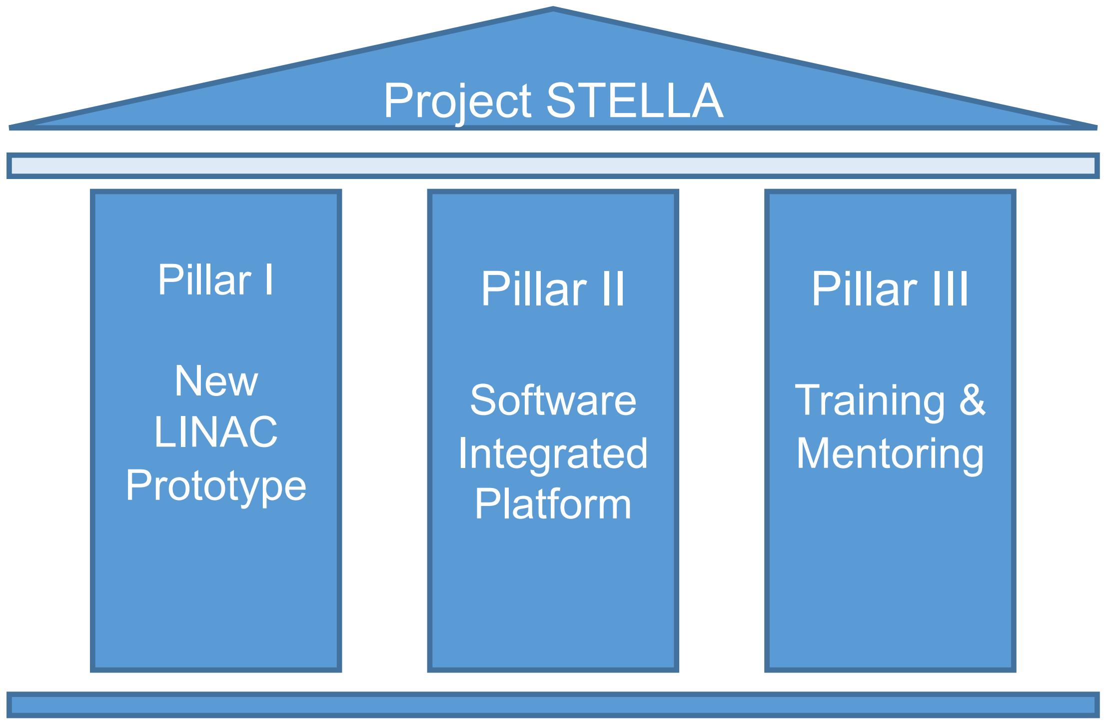
- Critical shortage of Radiation Therapy (RT) in rural communities in HICs and in LMICs results in disproportionately high rates of death
- Lack of access to basic cancer prevention and treatment in emerging economies results in $46 billion in lost revenue
- More than <u>one billion</u> people in Africa have either zero access or in many case one LINAC per 10 million people.



- USA: 1for 86,000 (3853 for 330M)
- Switzerland: 1 for102,000 (540 for 8.6 M)
- UK: 1for187,000 (358 for 67 M)

STELLA

(Smart Technologies to Extend Lives with a Linear Accelerator)



International Cancer Expert Corps
Partnering to transform global cancer care

CERN

UKRI Science and Technology Facilities Council

Lancaster University

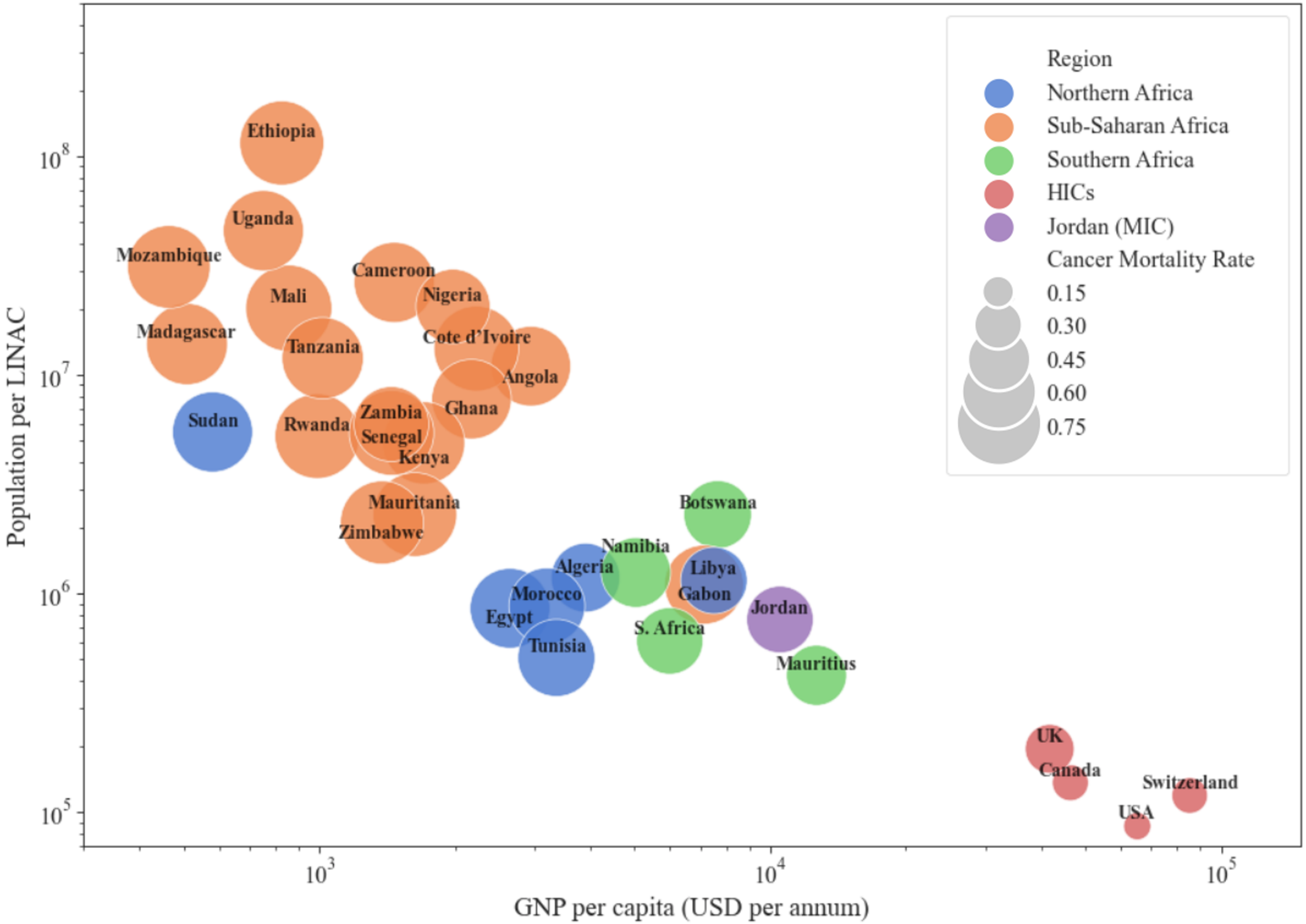
University of Oxford

Collaboration with 28 African Countries

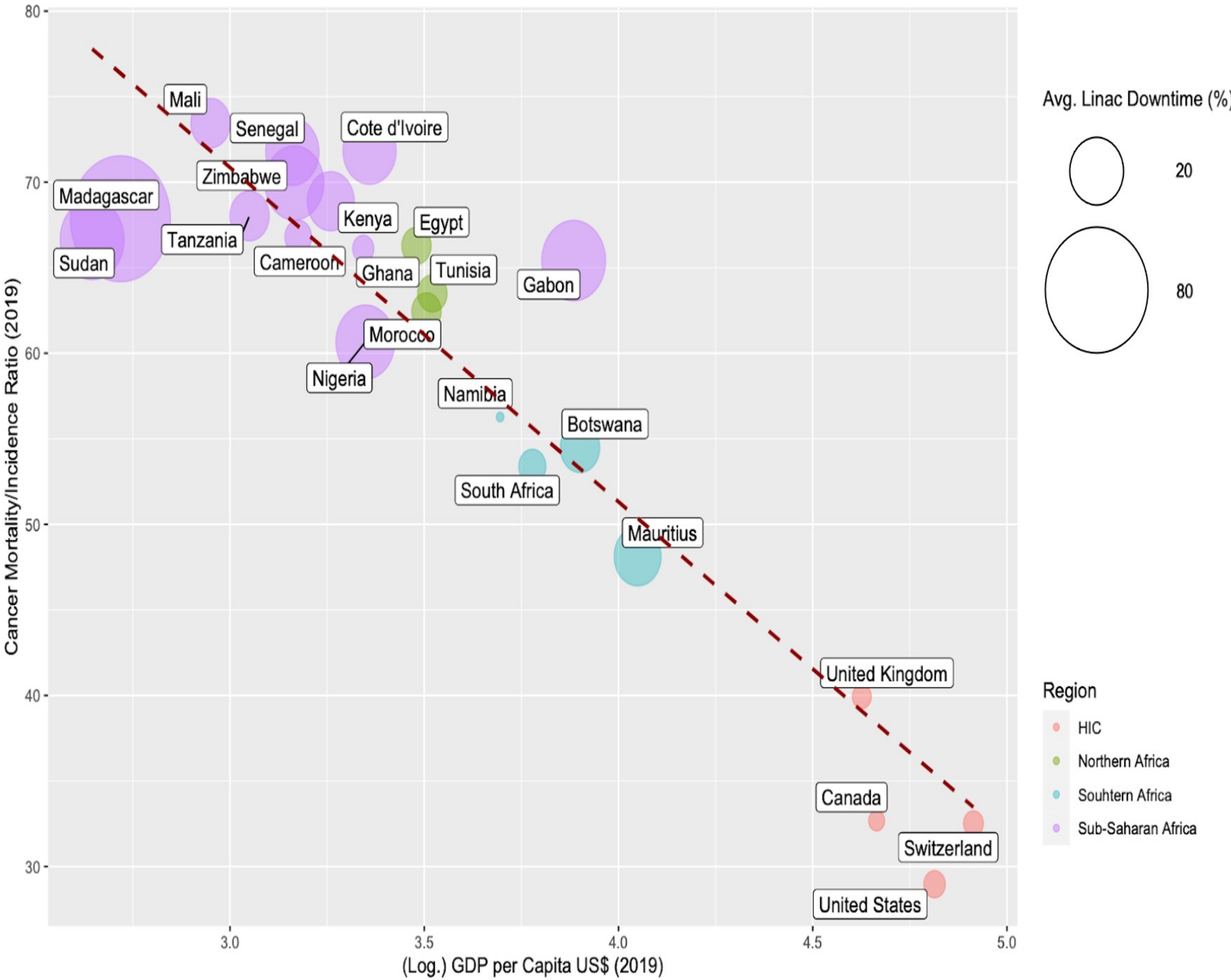
Looking for solutions for building affordable RT

- **Define the problem**
- **Gather information** from African hospitals/facilities regarding challenges faced in providing radiotherapy in Africa compare these to data from **HIC.**
- **Identify** the challenges from those who live with them day-to-day
- **Create design specifications** for a radiotherapy machine to meet these challenges for an improved design
- **Find a solution**
- Make the solution **available to all**

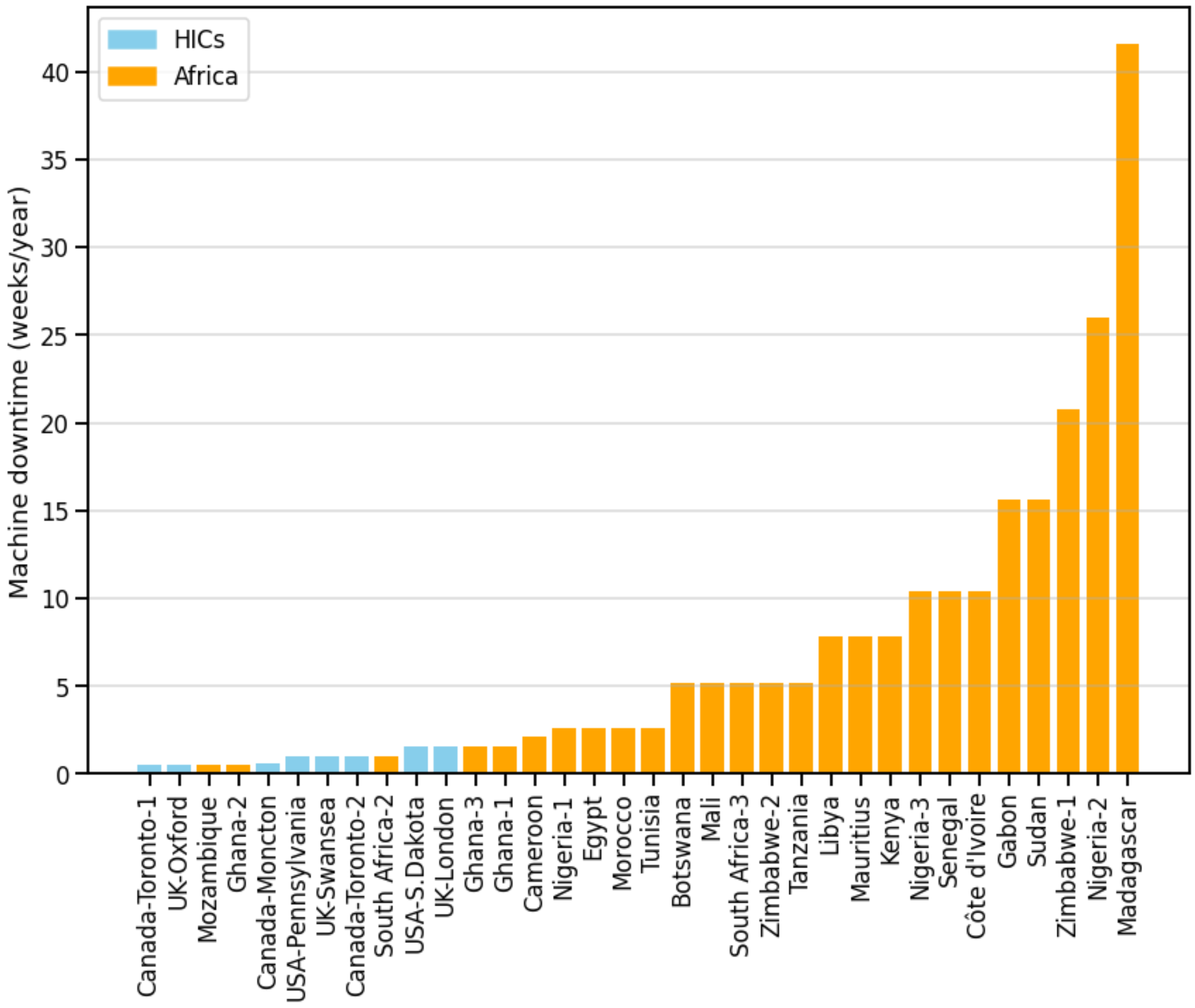
GNP per Capita and the Ratio of Inhabitants to RT Machines and Cancer Mortality Rates



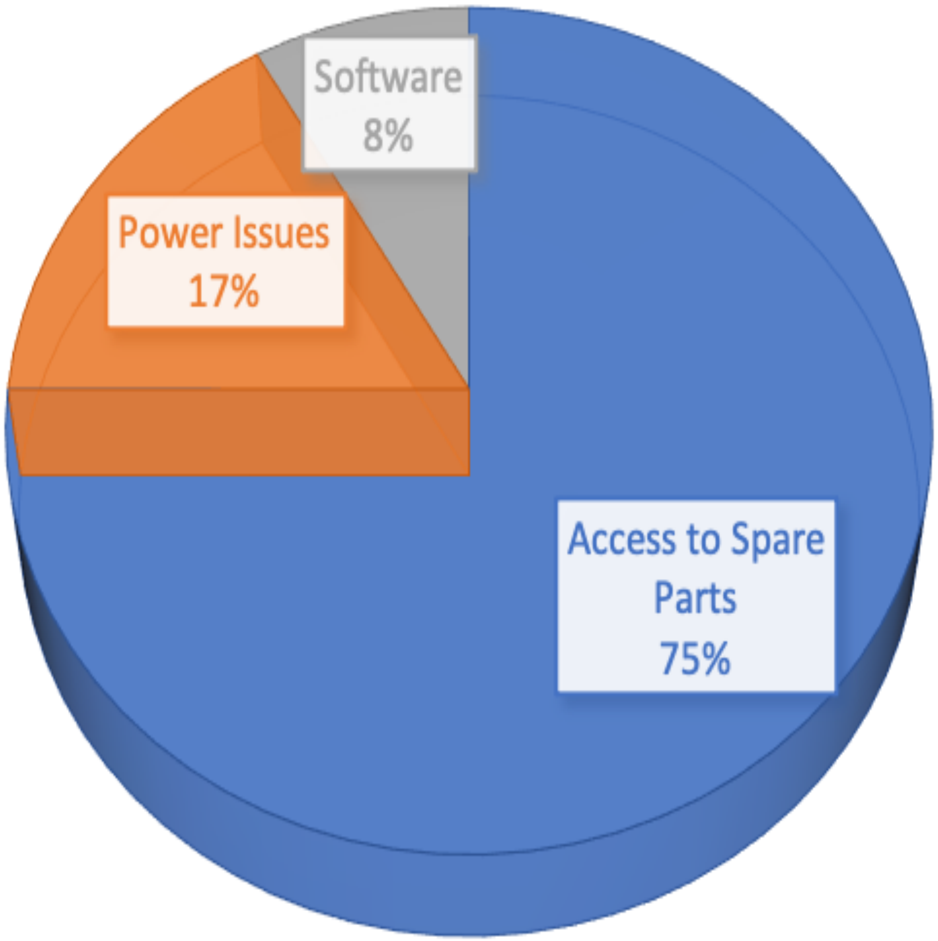
Impact of GDP and Linac Downtime on Mortality/Incidence Ratio



Downtime in weeks comparison African and HICs



Overall Reasons For LINAC Downtime from Survey



Data have been used for preparing STELLA CDR

STELLA

- Using the needs and data obtained a suitable Low-energy Linear electron accelerator is being developed, lead by STFC Daresbury and Lancaster team.

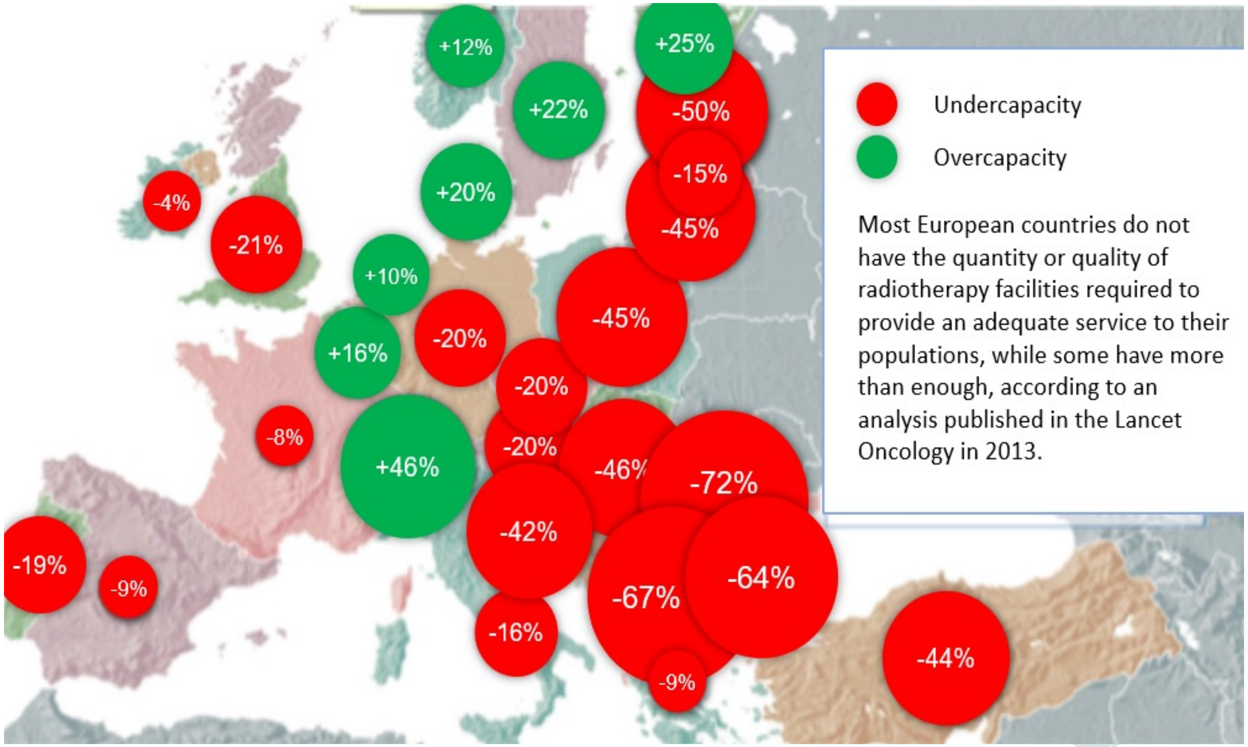
- A prototype solution for a cost-effective treatment:
  - Simpler installation
  - Robust operation
  - Easier to maintain
  - Reduced cost
  - Remote diagnostics and fault/breakdown detection

- CDR has been completed, evaluated and approved by an international committee

- Currently trying to secure funding for building the prototype

Collab: Oxford, CERN, STFC, ICEC, Daresbury Lab, Lancaster, African countries with RT

Not only an African Challenge



Radiation therapy capacities in Europe in 2013

Rosenblatt E, et al. Lancet Oncol 2013;14:e79–86

SEEIIST (Balkan Project)

SEE The SEEIIST needs reliable data from the SEE region

- Diagnostic and radiotherapy capacity;
- Cancer statistics;
- Human capacity, education and potential in research related areas;

[Questionnaire for Oncologists]

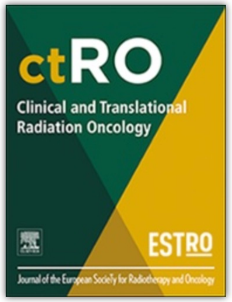
[Questionnaire for Scientists]

[Questionnaire for Regulators]

ACCEPTED

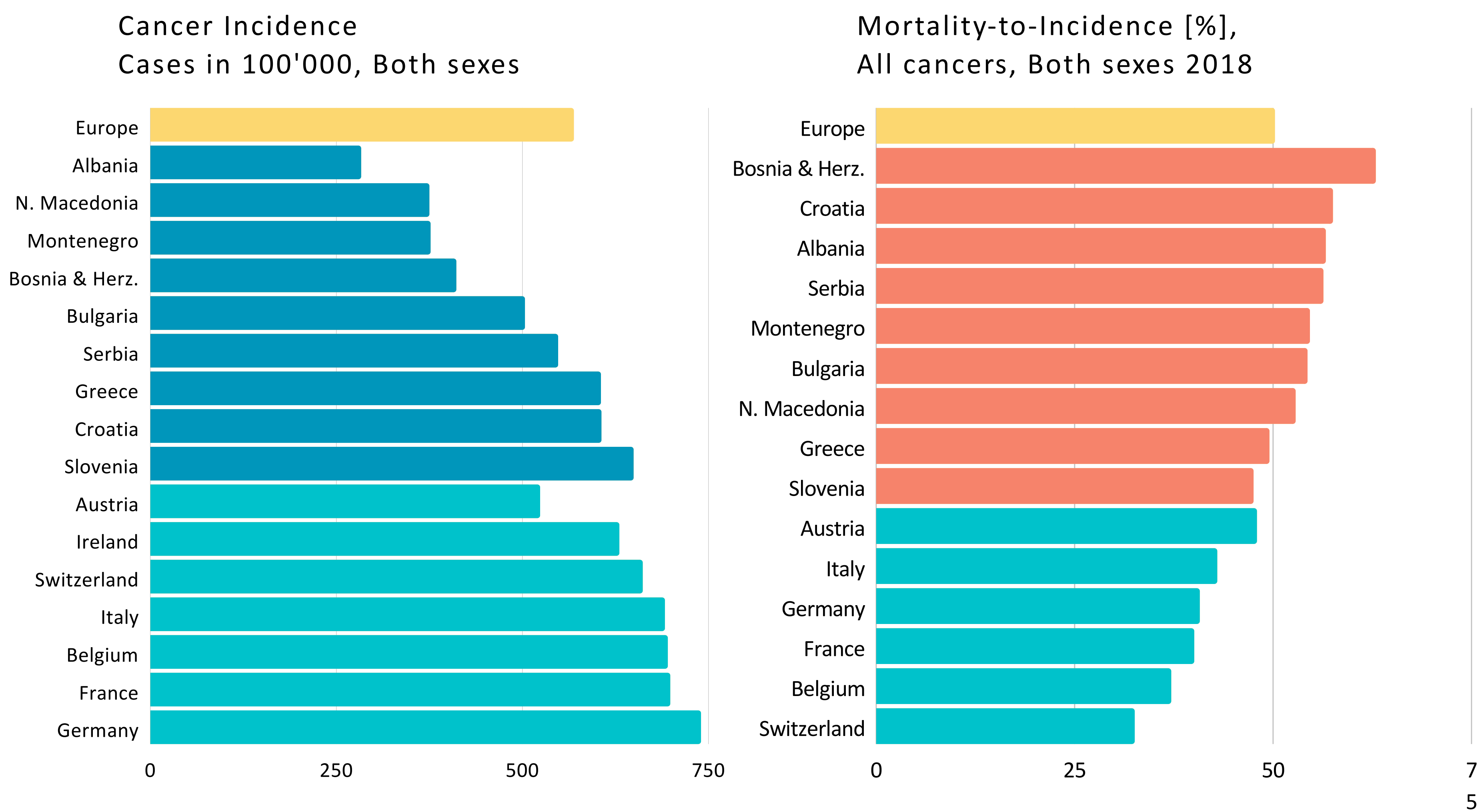
New publication

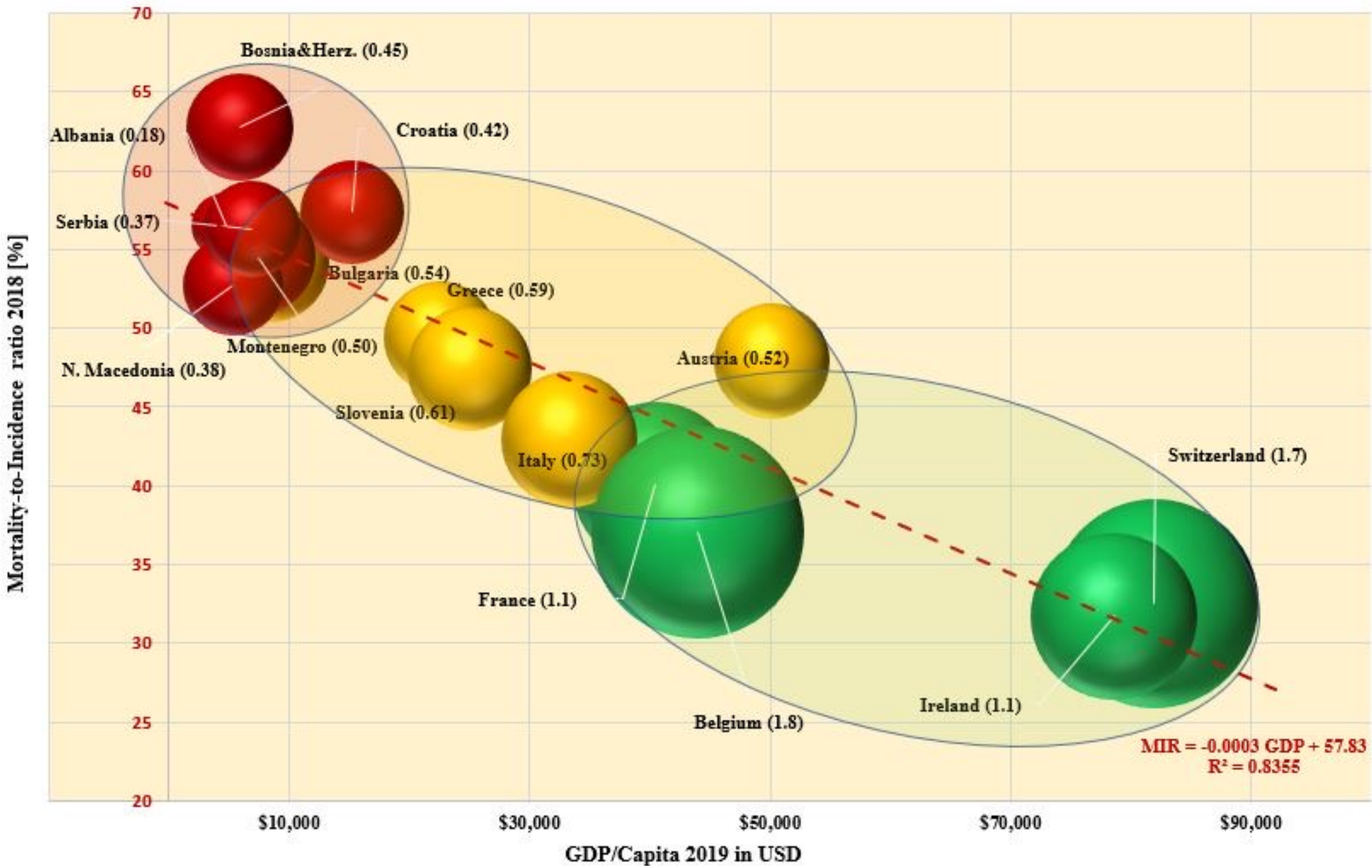
Manjit Dosanjh, Mimoza Ristova, Vesna Gershan, Petya Georgieva, Marijana Balin Kovacevic, Ledio Bregu, Irma Coralic, Tamara Djurovic, Deyana Dosieva, Yiota Foka, Ana Fröbe, Konstantinos Hatziioannou, Costas J. Hourdakis, Yllka Kabashi, Dimitar Kalev, Ilir Kurtishi, Leandar Litov, Beqir Mezelxhiu, Svetlana Nestoroska Madjunarova, Gordana Nikolova, Damijan Skrk, Velda Smajlbegovic, Snezana Smichkoska, Igor Stojkovski, Primož Strojan, Zdravka Tecic, Dušanka Tešanović, Vladimir Todorovic, Zdravka Valerianova



ISSN 2405-6308

Cancer data for SEE (Balkan region)



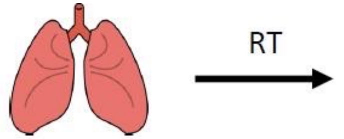


Dependence of the MIR on the GDP per capita and the density of conventional RT equipment. The radius of the spheres is proportional to the density of RT equipment per 100,000 population in the respective countries.

Access to Radiotherapy Technologies (ART) in Baltics, Eastern Europe, Central Asia and the Caucasus

Another point to consider is replacement of Cobalt 60 machines with LINACS because not only do they offer state-of-the-art -treatment less security risk

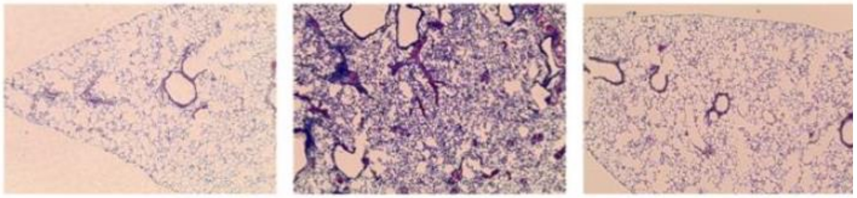
FLASH Radiation therapy



Electron beam
~ 5 MeV energy
Pulsed beam

Dose Rate $\times 10^6$

	Conventional RT in clinics	FLASH-RT
Mean Dose Rate	0,1 Gy / sec	>50 Gy / sec
Time to deliver 10Gy	100 sec	1.8×10^{-6} s



Collaborating with radiation oncologists on accelerator delivery of FLASH:

- **Undertanding/optimising beam energy, intensity, time structure, profile**
- **JAI providing expertise on beam delivery, instrumentstion, feedback and control**
- **Collaborating with colleagues at:**
  CERN/CLEAR/DESY/Gronigen beam:electrons: 50-250MeV-1GeV
  Daresbury/Gronigen: electrons, protons
- **Dosimentry is key-PP expertise important**

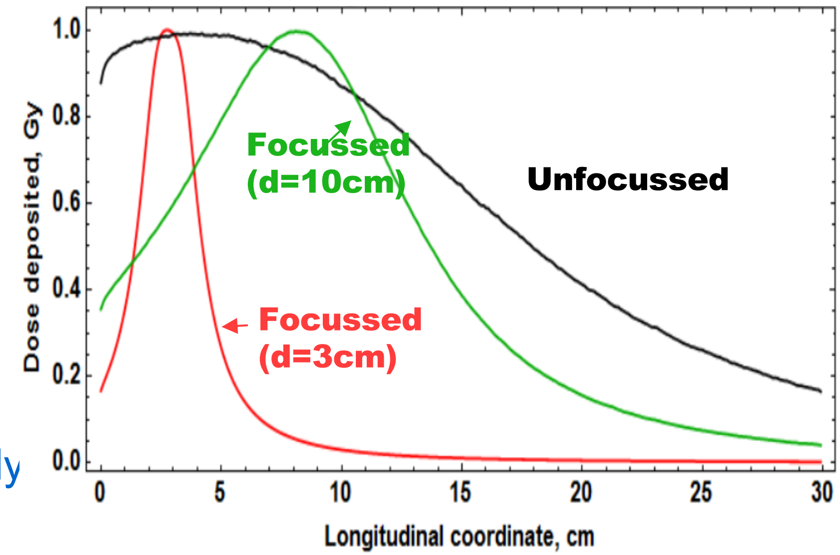
Imperial College London | Royal Holloway University of London | University of Oxford

FLASH RT – many questions

- Dose rate
- Energy range
- Compare electrons vs. protons vs. photons
- Scanning
- Focusing
- Dosimetry
- Treatment planning tools
- New real time-imaging
- Tests in vivo, in vitro

VHEE (Very High Energy Electrons)- Beam Delivery

- **VHEE** :
  - Superior treatment for deep seated tumours
  - Less sensitive to inhomogeneities in tumour compared to conventional RT
  - **Allows scanning, focussing**
- **High gradient** RF technology -> **compact** acceleration
- FLASH effect – healthy tissue sparing at extremely high dose rates
  - **VHEE could be used to deliver FLASH** treatment for **deep seated tumours**



- Figure from Dosanjh et al. 'Very high Energy Electrons for cancer therapy' (2020)

Cameron Robertson
Oxford, 2nd Year

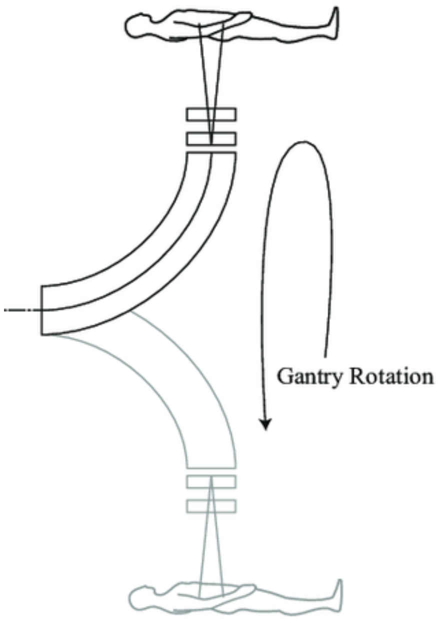
A.Gerbershagen
CERN/BE

A.Latina
CERN/CLIC

Imperial College London | Royal Holloway University of London | University of Oxford

Beam Gantry Optics for VHEE (FLASH) Beams

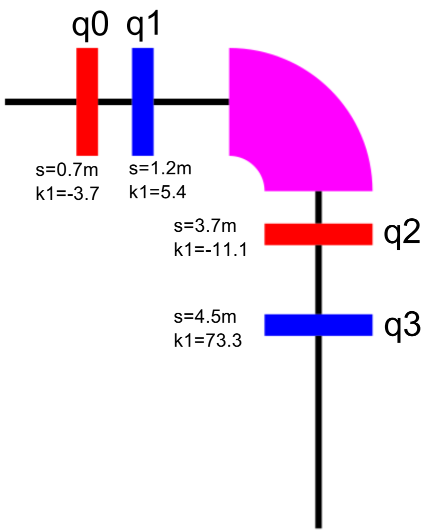
- Optics design for Transfer line/gantry required to transfer beam from accelerator to patient and meet **treatment specifications:**
  - **Magnification** of beam to cover entire tumour
  - **Flattening** of beam to ensure consistent lateral dose distribution
- Design carried out for toy model (**Riesenrad Gantry**)
  - Single dipole transfer line

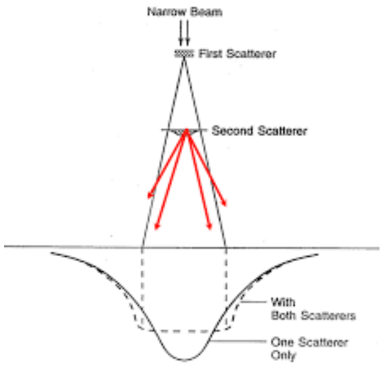


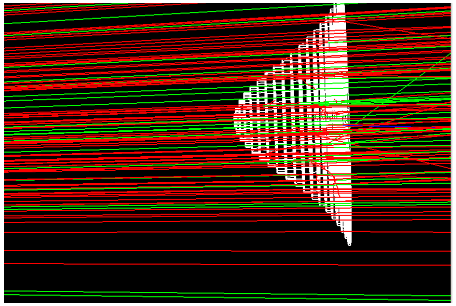
Owen et al. (2013)

Optics Designs

- Design carried out using two principal methods
  - Matching of beam parameters with **quadrupole optics**
  - Matching of beam parameters with **quadrupole optics and dual scattering foil**
- Constant beam distribution up to **75mm radius** achieved in both cases (magnified from **1mm radius initial beam**)
  - Dual Scattering foil results in significantly less mass to be rotated by gantry
- Experimental verification of dual scattering principle in progress at CLEAR

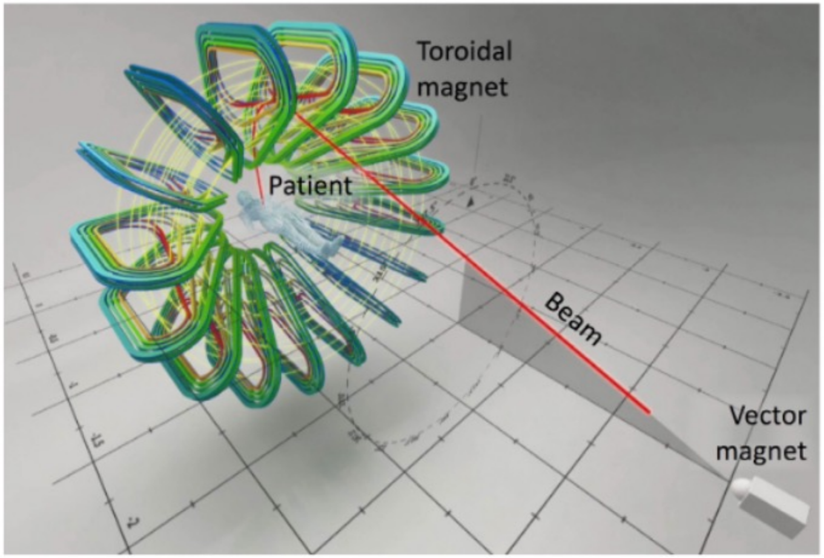






Future Studies - GaToroid

- Gantries contribute significantly to the overall cost of particle therapy facilities
  - Precise (~0.1 mm) movement of heavy (100s of tonnes) objects requires costly mechanical implementation.
  - Far too slow to be considered for **FLASH therapy** from multiple angles
- **GaToroid** is a novel concept for a **static** gantry
  - Beamline lattice composed of circularly symmetric **toroid magnets**
  - Angle of treatment beam defined by **single vector magnet**
- Optics design for **VHEE Gatoroid** is being studied



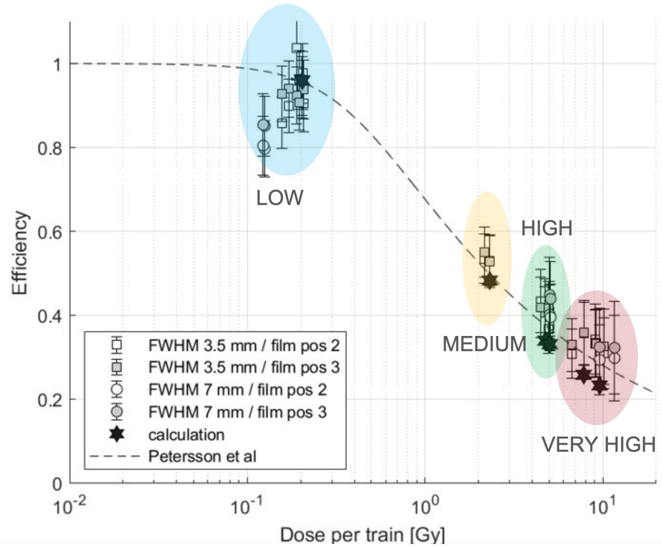
Bottura et al. (2020)

CLEAR

CERN Linear Electron Accelerator for Research

VHEE High Dose-Rate Dosimetry - Motivations

- Ionisation chambers, currently used for reference dosimetry and beam-dose monitoring, have a non-linear response at ultra-high dose rates required for FLASH (>100 Gy/s).
- More established real-time dosimetry methods are required to be able to characterise and fully understand the effects of UHDR VHEE beams for RT.
- For the clinical implementation VHEE FLASH-RT need a beam-dose monitor with the following properties :
  - A dose-rate independent response.
  - A temporal resolution high enough to resolve bunches/trains.
  - A response time that is fast enough to trigger a safety interlock in between pulses.
  - Minimal perturbation on the beam



Source: D. Poppinga, [The challenge of high dose rates for ionisation chambers]

Joseph Bateman, Oxford, 2nd Year

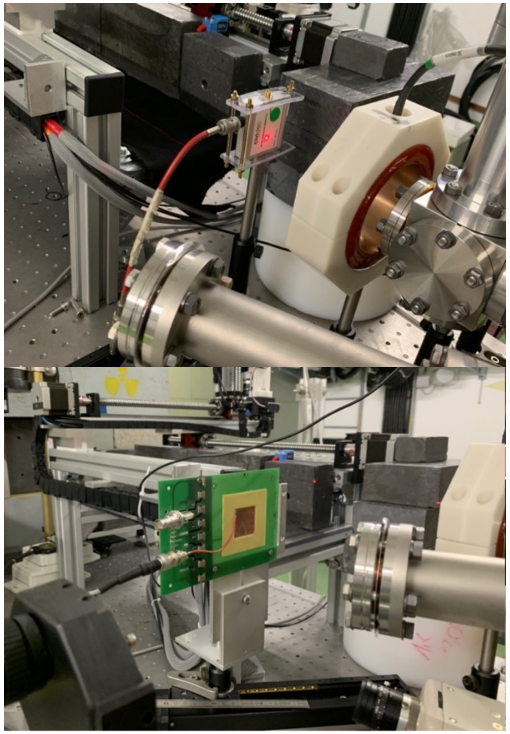
A.Gerbershagen CERN/BE

R.Corsini CERN/CLEAR

Imperial College London · Royal Holloway University of London · University of Oxford · JAI John Adams Institute for Accelerator Science · clear

VHEE High Dose-Rate Dosimetry –Status

- Carried out a feasibility evaluation using Monte Carlo simulations of *in vivo* dose range verification methods currently used in hadron therapy (PET Imaging, Prompt Gamma Measurement etc.) for their application to VHEE (submitted for publication).
- Currently optimising radiochromic film dosimetry protocols and establishing reliable reference dosimetry methods for VHEE FLASH RT.
- Carried out initial tests on detectors/instrumentation that are readily available at CERN on CLEAR for their suitability for VHEE FLASH Beam-Dose Monitoring i.e. determining which charge-per-bunch they saturate at, such as:
  - Diamond Detector (pCVD dBLM)
  - TimePix3 ASIC
  - GEM Foils



dBLM (top) and GEM foil (bottom) detectors in the CLEAR In-Air Test Stand

VHEE High Dose-Rate Dosimetry – Future Steps

- Further tests on detectors and beam instrumentation for the purpose of VHEE FLASH Beam-Dose Monitoring (e.g. solid-state detectors, scintillating fibres and screens).
- Investigate the use of beam diagnostics equipment, characterised against reference dosimeters, for beam-based dosimetry, e.g. electromagnetic pick-up monitors, resonant cavities etc.
- Calibration of detectors/instrumentation against reference dosimeters (e.g. film) and Monte Carlo simulations.
- Experimental validation of some of the simulations for the most promising *in vivo* dose range verification methods (e.g. bremsstrahlung measurement).

Also started collaboration within Oxford Physics

- Collaborating with a DPhil. student in the Particle Physics detectors group at Oxford, who is working on developing and testing Si LGAD (Low Gain Avalanche Detectors)
- We will test the LGAD at CLEAR for possible uses in medical applications, e.g. dosimetry, beam monitoring, *in vivo* dose monitoring, electron radiography etc.
- Opens the possibility for further collaboration with the Oxford detector group for the development and testing of detectors for medical applications.

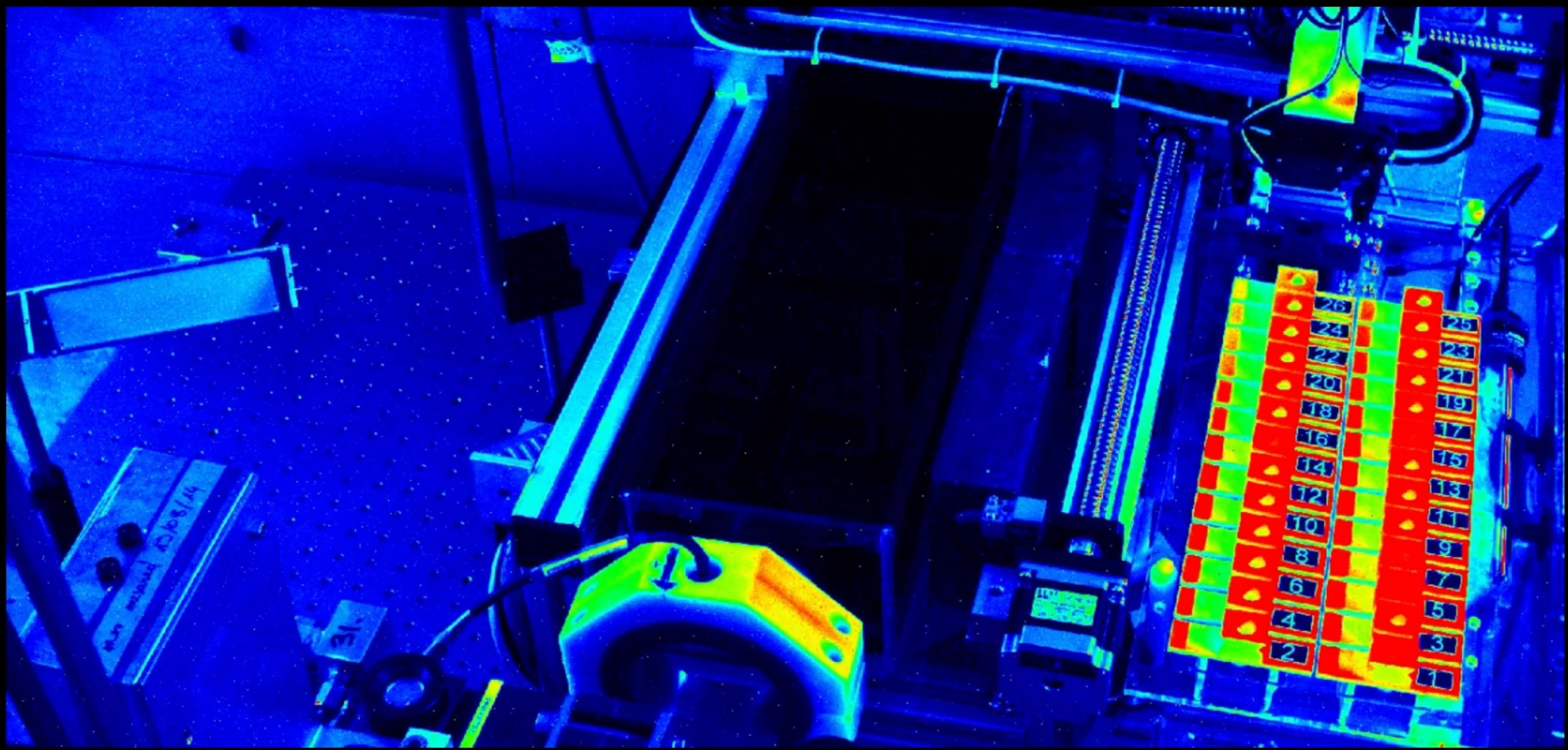
In vitro radiobiological measurements at CLEAR

Collaborating with Marie-Catherine Vozenin's CHUV group

- Effect of conventional vs Flash
- Dose effect
- Plasmid
- Zebra fish eggs

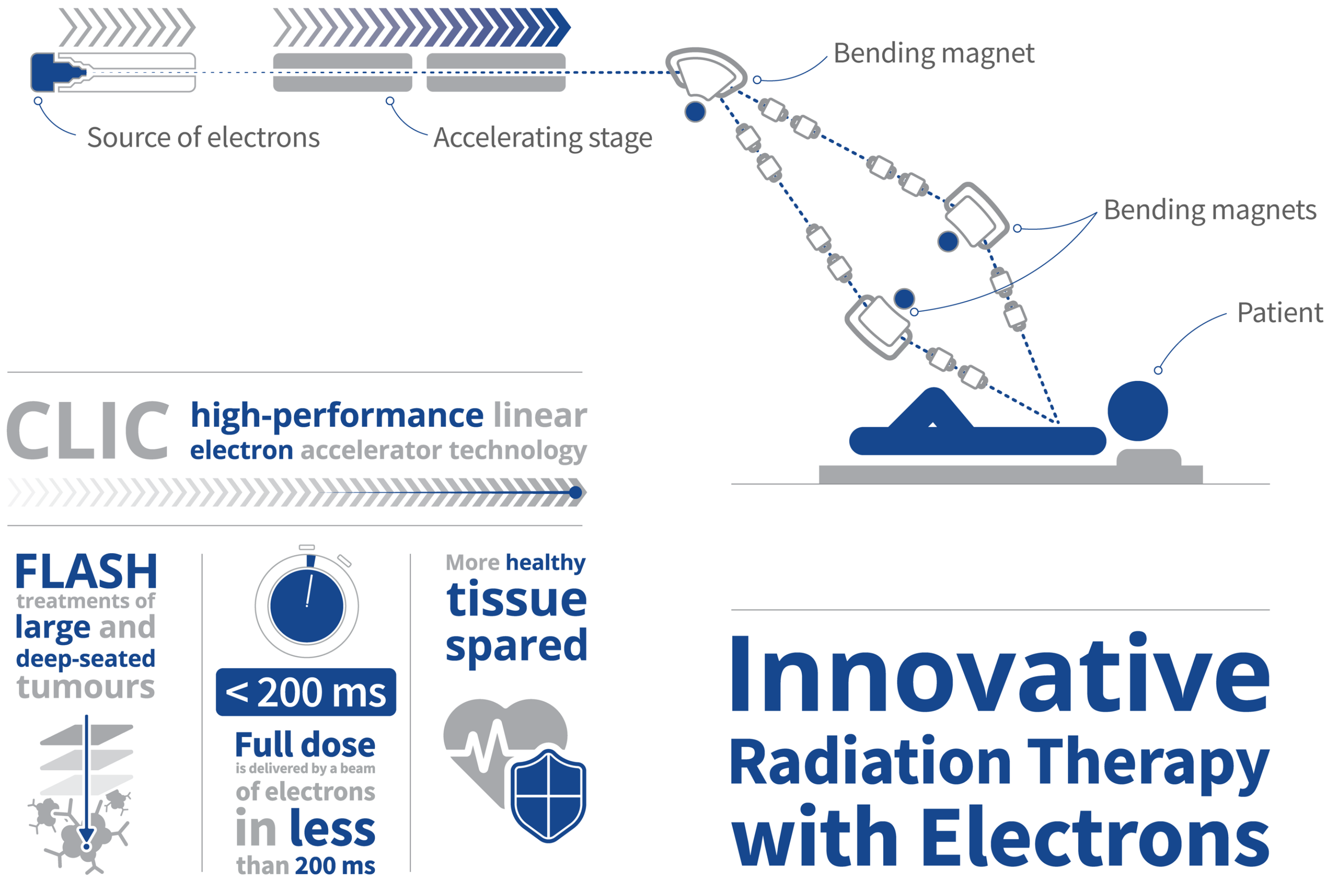
Measurements at CLEAR

(Pierre Korysko, Oxford postdoc - robot and CLEAR operation)



DEFT (Deep Electron FLASH Therapy)

CHUV-CERN facility funded, Luke Dyks from Oxford involved



In summary

- STELLA is progressing …..
- FLASH, lots of interest and progress but much remains to be done