Global Health: Enhancing Access to Cancer Radiation Therapy

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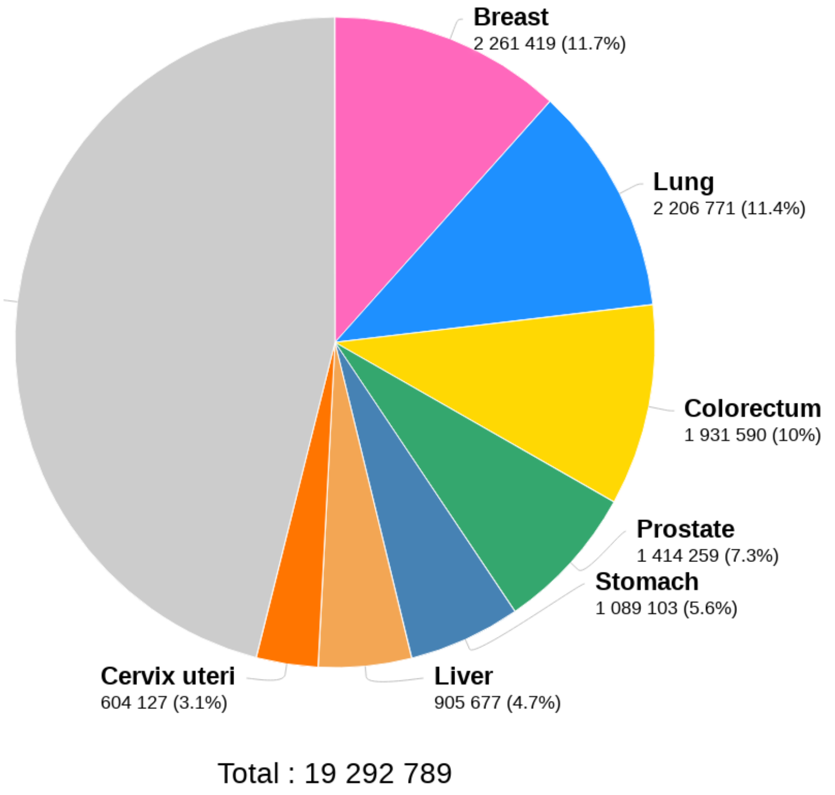
(on behalf of the STELLA collaboration)

Cancer is a growing global challenge

- In 2020 globally **19.3** million new cases per year diagnosed and **10** million deaths
- By 2040 this will increase to **27.5** million new cases per year and **16.3** million deaths
- **70% of these deaths** will occur in low-and-middle-income countries (LMICs)
- **9 out of 10 deaths** for cervical cancer and **7 out of 10** breast cancer are in LMICs



Data source: GLOBOSCAN 2020

Radiation therapy is a key tool for treatment for 50-60% patients

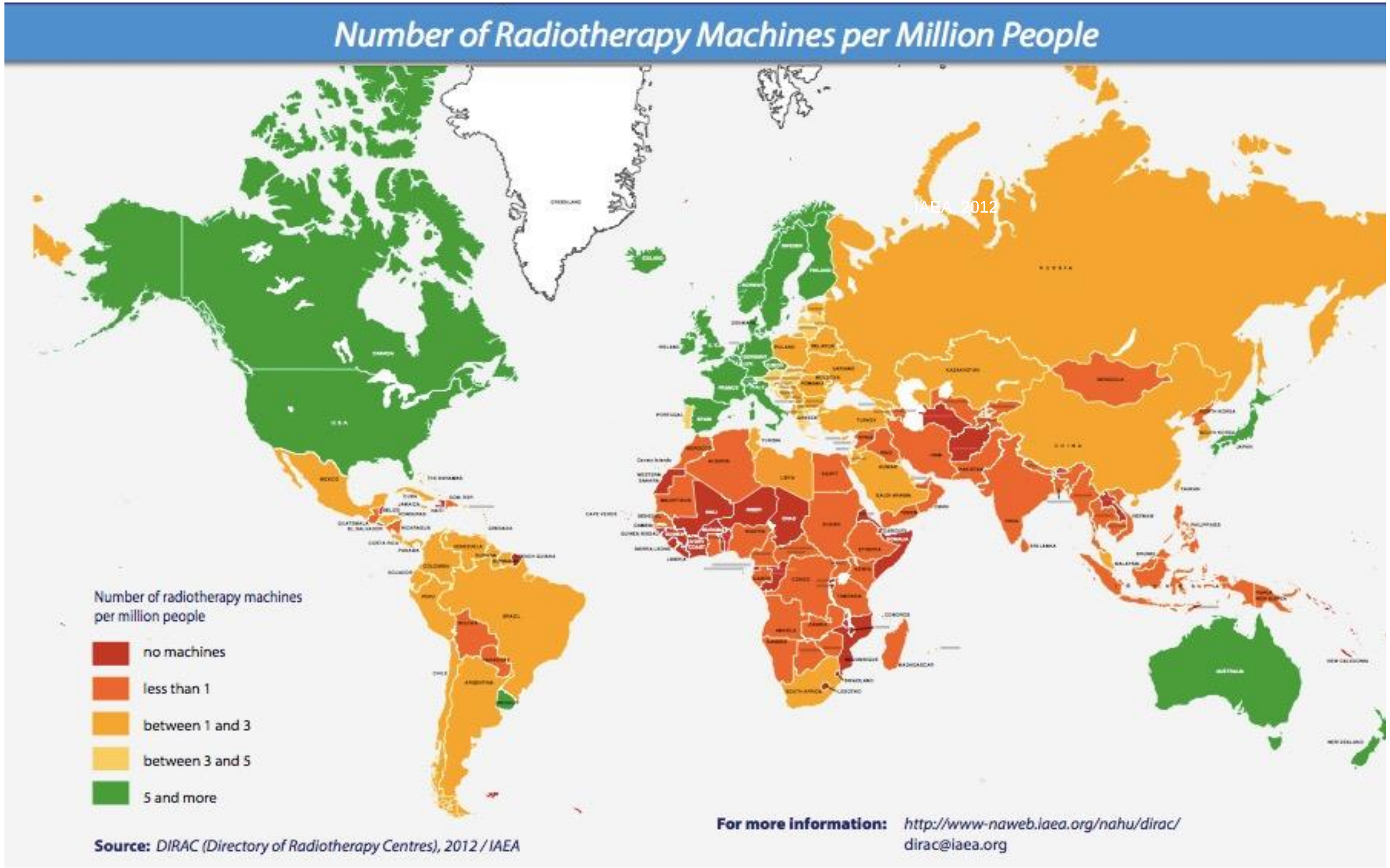
The Problem:
Much of the world has limited or no access to Radiation Therapy

Even though RT is one of the most useful tool for cancer cure or pain-relief:

- Inadequate supply of RT linear accelerators (Linacs)
- Gap greatest in low-middle income countries (LMICs)
- **Only 10%** patients in Low Income Countries have access to RT

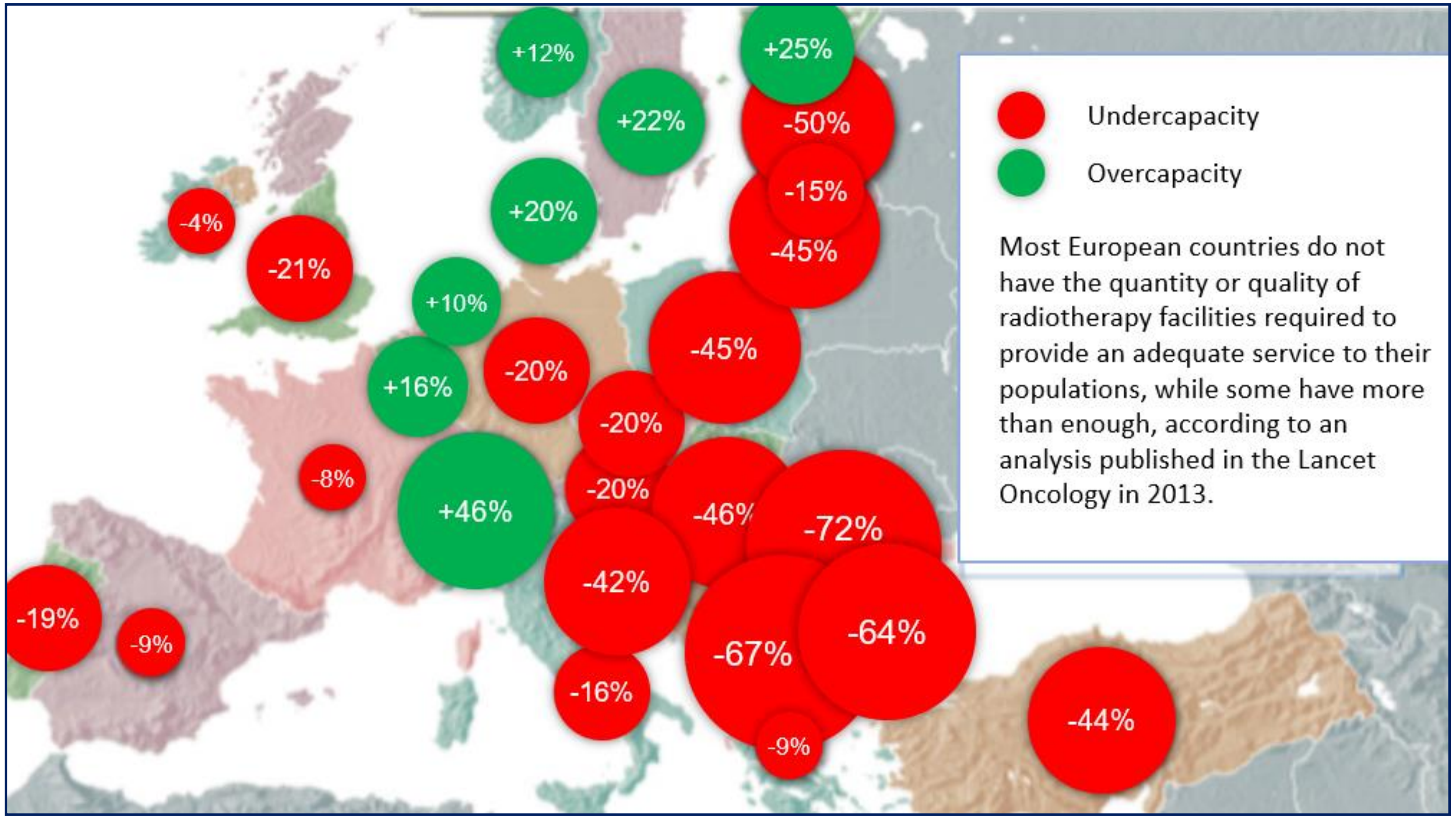
Three key reports highlighted the lack of access to RT

IAEA 2012 data showing huge disparities in global access



Most of the current 18,000 RT units are in HIC (High-Income Countries)

ESTRO Study: Access to RT technology in the European region (2013)



ESTRO – HERO Study (Health Economics and Radiation Oncology): Eastern and South-Eastern European countries need to expand and modernise their radiotherapy equipment.

2014 was an important year

- it was 60 years of CERN,
- 80th birthday of Ugo Amaldi who gave a public talk on “Physics is not only beautiful but also useful”
- It was the first time that Norman Coleman talked about ICEC (established in 2013) and his vision in the international arena.

ICTR-PHE
2014

Global Task Force for Radiotherapy for Cancer Control (GTFRCC) - 2015

The Lancet Oncology Commission

Lancet Oncol, 2015, 16: 1153

Expanding global access to radiotherapy

Rifat Atun, David A Jaffray, Michael B Barton, Freddie Bray, Michael Baumann, Bhadrasain Vikram, Timothy P Hanna, Felicia M Knaul, Yolande Lievens, Tracey Y M Lui, Michael Milosevic, Brian O'Sullivan, Danielle L Rodin, Eduardo Rosenblatt, Jacob Van Dyk, Mei Ling Yap, Eduardo Zubizarreta, Mary Gospodarowicz

Our results provide compelling evidence that investment in radiotherapy nc only enables treatment of large numbers of cancer cases to save lives, but also brings positive economic benefits.

The verdict is in: the time for effective solutions to the global cancer burden is now

**C Norman Coleman, Bruce D Minsky*

Lancet Oncol, 2015, 16: 1146

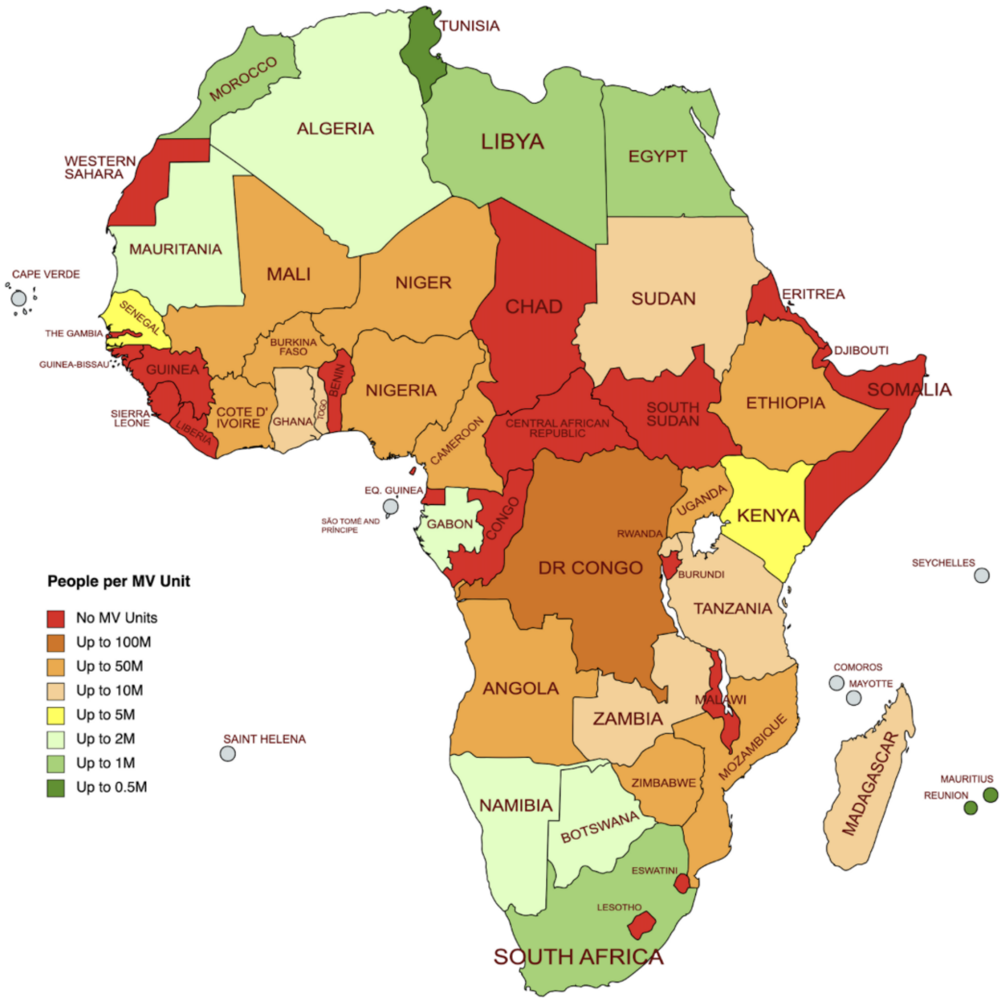
GTFRCC: "Our results provide compelling evidence that investment in radiotherapy not only **enables treatment of large numbers of cancer cases to save lives**, but also **brings positive economic benefits.**"

Number of people per functioning machine in countries in Africa

But there are dramatic disparities in Access

Africa: 420 MV RT units for around **1.4 billion** people
1 machine per 3.5 million people
US: **3879** MV RT units for around **340 million** people
I machine for 86, 000
UK: **357 MV RT** units for around **68** million people
1 machine per 190,000
Switzerland: 85 for **8.8** million people
1 machine for 100,000

- By 2030, there will be **1.4** million new cases of cancer and there will be **1** million cancer deaths in Africa
- In 2019 only **28** countries had RT facilities
- In 2024 there 34 countries
- Over **60% are in just 3 countries**: South Africa, Egypt and Morocco
- 20 countries have none



Created with mapchart.net

Africa’s Radiation Therapy Status

- **Acute shortage of RT** services both in quantity and quality
- **400 LINAC-**RT machines for more nearly **1.2 billion** inhabitants
- If current trends persist, GLOBOCAN forecast
  - By 2030, there will be **1.4** million new cases of cancer
  - and there will be **1** million deaths in Africa
- Only **32** countries have RT facilities **22** have none
- Over **60% located in just 3 countries**: South Africa, Egypt and Morocco
- **12** countries only one facility
- More than **18 countries** have Cobalt machines
- Africa has around **88 Co-60** machines (half of which are over 20 years old) proportionally more than any other continent
- Some of the **African countries lacking a Linac-RT** will consider buying Co-60 machine they are currently cheaper and easier to use

Africa's Environment - Challenges

Situation Today

Rapid machine failure and long down time

- End – of – Life machines
- Delay in spares funding approval and shipment

Increasing cancer care demands

- Machines not adequate to meet demands
- High cost of care
- High mortality

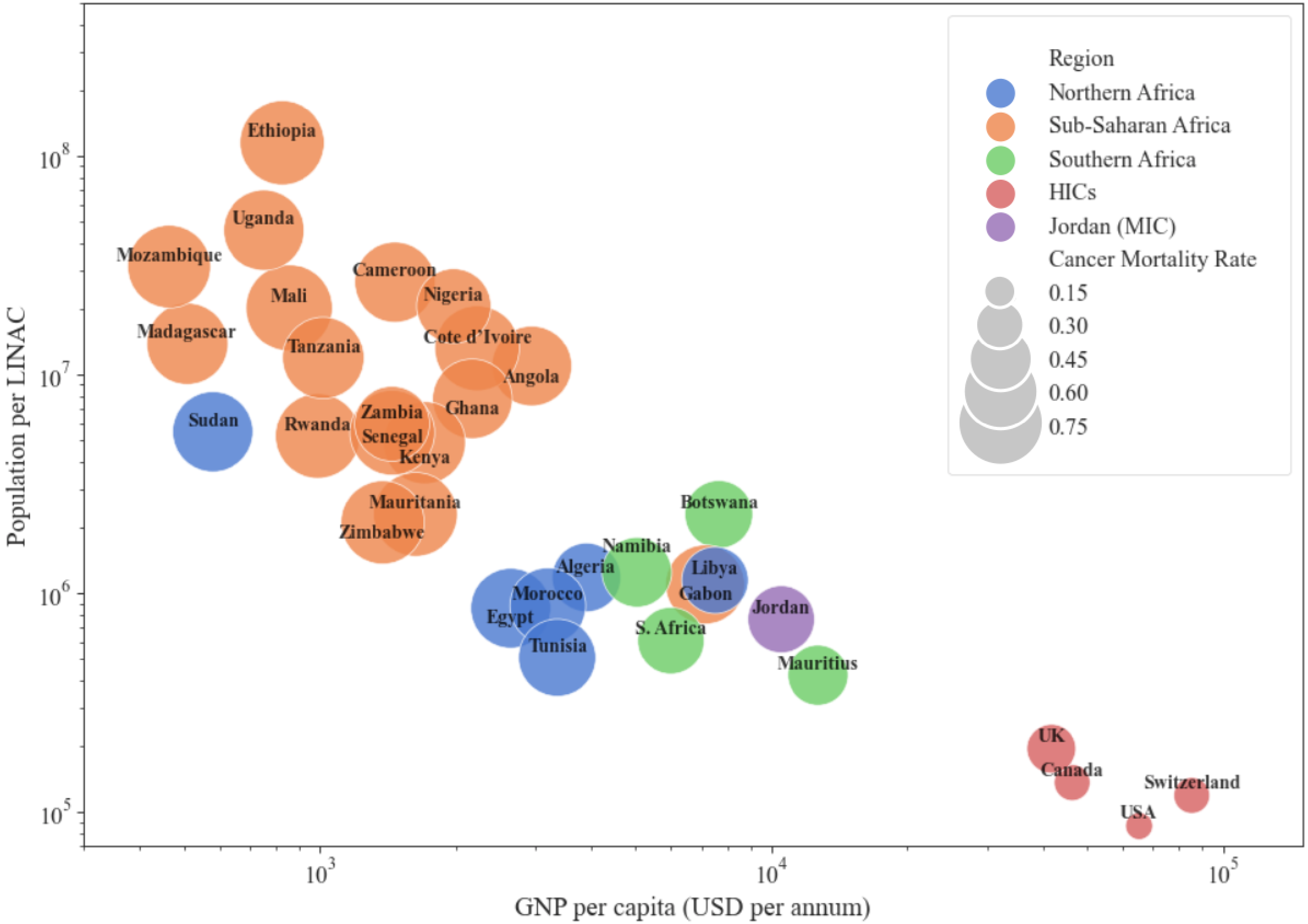
Capacity for Multi-disciplinary teams

- Clinical skill gaps
- Need for training programs following global trends
- Lost time and high cost of short training time abroad

AFRICA’S ENVIRONMENT - CHALLENGES

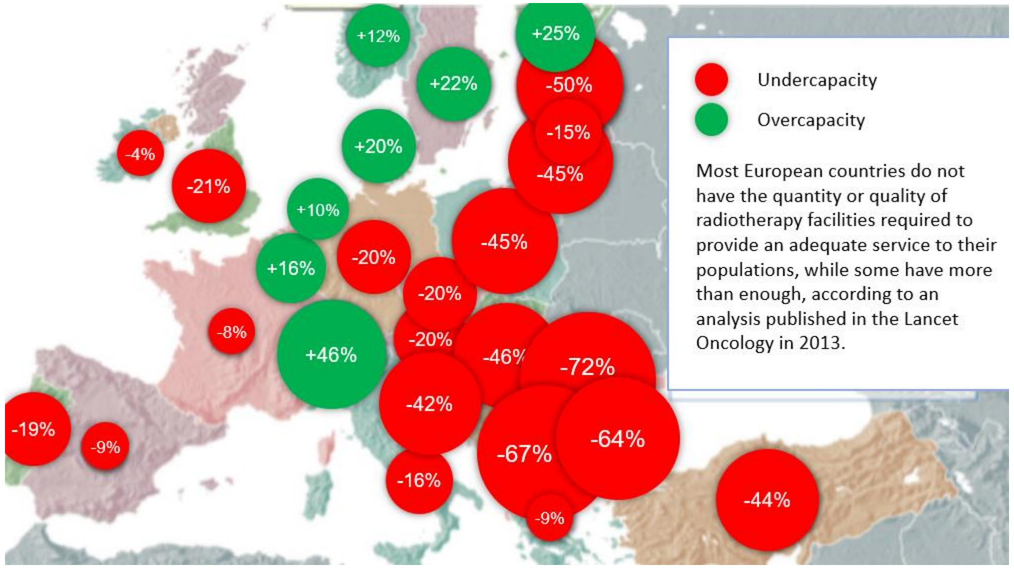
- The lack of infrastructure to ease the accessibility of treatment centres via well-maintained roads and safe and reliable transportation services also poses a huge issue.
- Power outages are quite detrimental and may shorten the lifetime of electrical equipment, eventually resulting in permanent damage.
- Moreover, the lack of certified and qualified personnel to operate and maintain the linacs and associated equipment is one of the biggest problems faced by most LMICs.
- These two last factors have indeed been repeatedly highlighted by professionals in LMICs, indicating the need for local investment in human resources.
- Ranging from the unavailability of accredited programmes to train professionals to the relatively low wages on the job, there is an ongoing brain drain to more attractive countries

GNP and Ratio of Inhabitants to Linacs and Cancer Mortality



Ige et al, *Surveying the Challenges to Improve Linear Accelerator-based Radiation Therapy in Africa: A Unique Collaborative Platform of All 28 African Countries Offering Such Treatment*. Clin Onco, 2021 33e521-e529 https://doi.org/10.1016/j.clon.2021.05.008

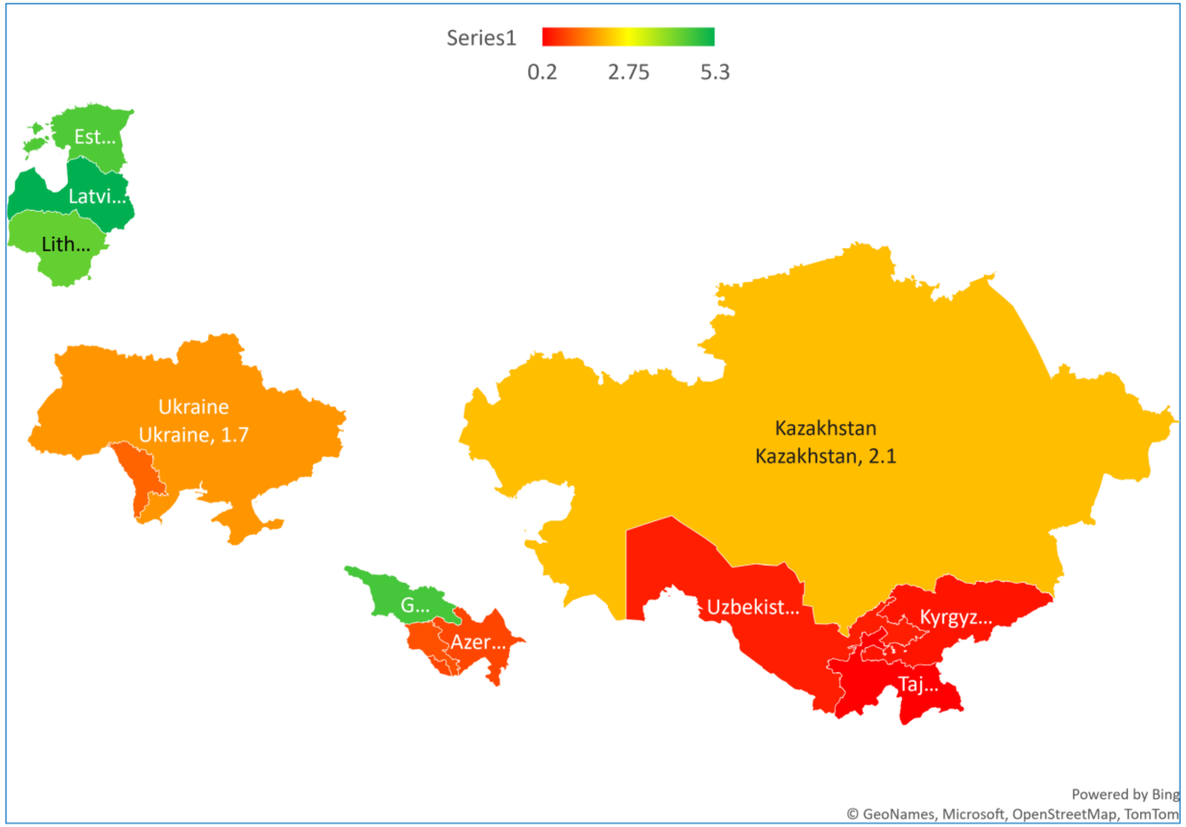
Shortage and challenges are not only in Africa



Radiation therapy capacities in Europe 2013

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

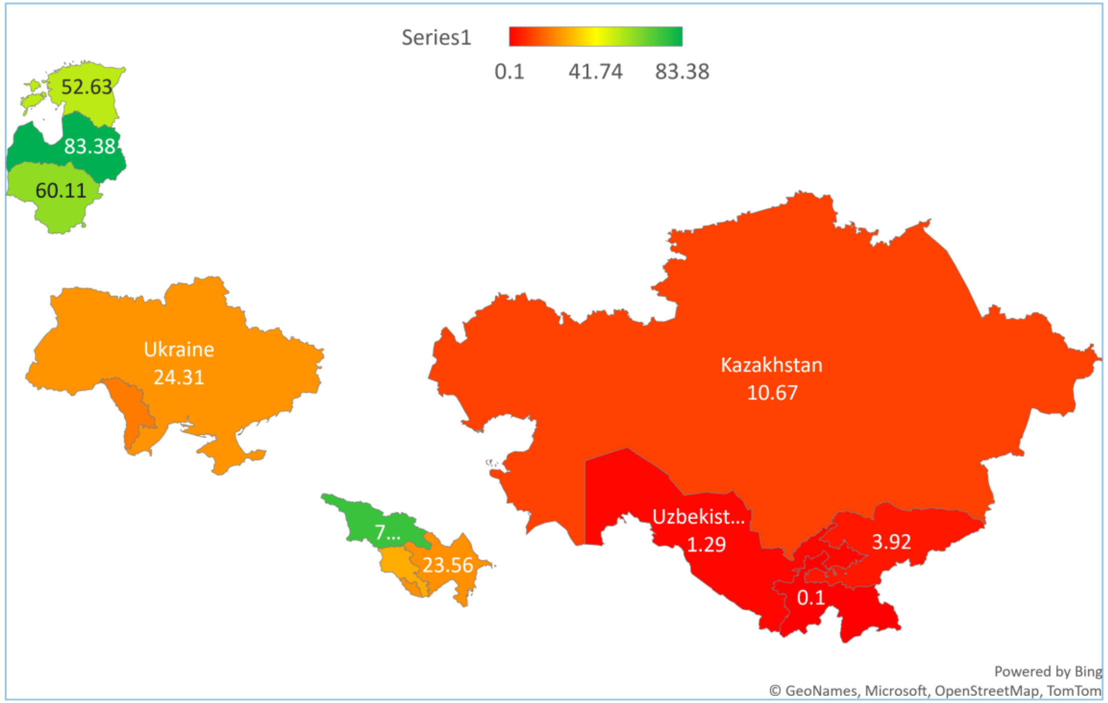
Total External Beam RT (cobalt +LINACS) units per 1,000,000 inhabitants



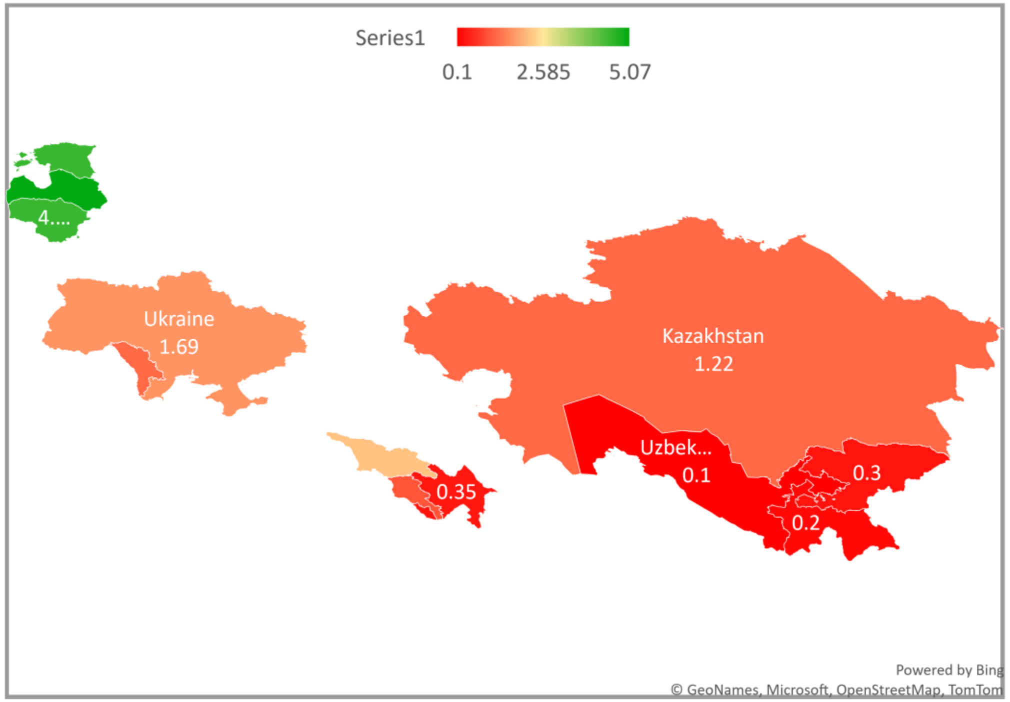
Access to Radiotherapy Technologies Study (ART) in the Baltics, Eastern Europe, Central Asia and the Caucasus

Shortages and challenges are not only in Linacs

Number of total imaging equipment per 1000 000 population



Experts per 100,000 inhabitants



Access to Radiotherapy Technologies Study (ART) in Former Soviet Union countries (Armenia, Azerbaijan, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Tajikistan, Ukraine and Uzbekistan)

Current status of RT

- Current Linacs provide very good treatment both in terms of technical capability and throughput.
- However current LINAC technology is **complex, labour intensive,** and **expensive** to acquire, install, operate and service
- Linac technology requires **strong, robust** and **reliable infrastructure** (power, clean water, supply chain etc.) to operate
- Many Linacs are purchased or deployed in Africa and LMICs without sufficient **training.** Many are never used or not close to their capacity
- Linac **servicing** can be slow and very expensive. Service contracts are expensive and not always purchased. Long down times (months or more).
- Can we use technology developments to address the current challenges and make RT more widely available?

Current Challenge: how to go from almost no radiotherapy to high quality radiotherapy globally in LMIC

Workshop on:

"Design Characteristics of a Novel Linear Accelerator for Challenging Environments"

Norman Coleman (ICEC) David Pistenmaa (ICEC) Manjit Dosanjh (CERN)

International Atomic Energy Agency (IAEA)

James Martin Center for Nonproliferation Studies (CNS)

National Aeronautics and Space Administration (NASA)

National Nuclear Security Administration (NNSA)

http://indico.cern.ch/event/560969/

1st Workshop addressed

1. the role of radiotherapy in treating cancer in challenging environments such as in many low- and middle-income countries (LMICs) and the related security concerns of medical radiological materials,
2. the design requirements of linear accelerators and related technologies for use in challenging environments,
3. the education, training and mentoring of the sustainable workforce needed to utilize novel radiation treatment systems
4. the costs of and financing for the implementation of the recommendations from the workshop.

STELLA SMART TECHNOLOGY TO EXTEND LIVES WITH LINEAR ACCELERATORS

1st Design Characteristics of a Novel Linear Accelerator for Challenging Environments
CERN, Nov 2016

Medical Linacs for challenging environments

- 1st Design Characteristics of a Novel Linear Accelerator for Challenging Environments, November 2016, CERN
- 2nd Bridging the Gap Workshop, October 2017, CERN

- 3rd Burying the Complexity Workshop, March 2018, Manchester
- 4th Accelerating the Future Workshop, March 2019, Gaborone

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CERN
International Cancer Expert Corps
Partnering to transform global cancer care
Science & Technology Facilities Council
UK Research and Innovation

OUR VISION: Project STELLA

Smart Technologies to Extend Lives with Linear Accelerators

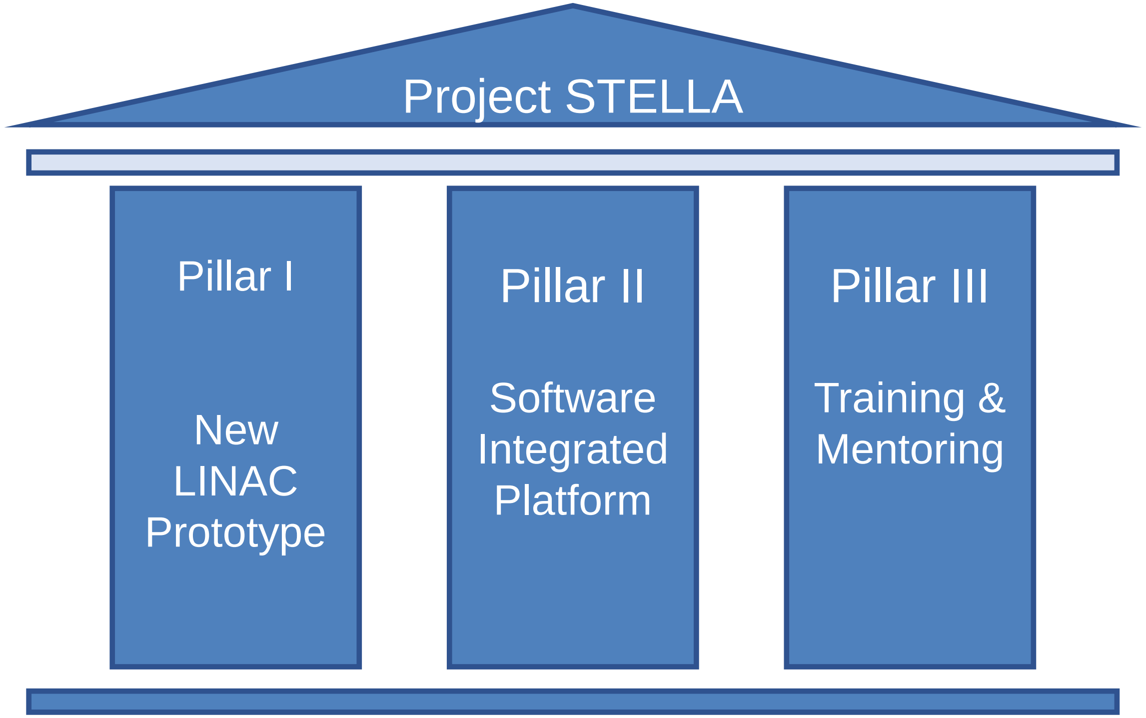
- A global partnership of the best clinicians, medical physicists and accelerator technologists globally
- A disruptive and innovative Radiation Therapy Treatment (RTT) system to improve access to quality cancer care
- Leveraging integrated software systems and use of AI
- An enhanced training, education and mentoring program that catalyzes RTT implementation in the global context
- Addresses a societal problem that is often considered too difficult to solve

Project STELLA (**S**mart **T**echnologies to **E**xtend **L**ives with **L**inear **A**ccelerators)

The Project STELLA is dedicated to:

- Expanding access to high quality cancer treatment globally
- Developing an innovative and transformative radiation therapy treatment system
- Driving down the cost out of RT and cancer care
- An enhanced training, education and mentoring program that catalyzes RTT implementation in the global context

STELLA: A Unique Collaboration



Innovative Technologies towards building Affordable and Equitable Global Radiotherapy (ITAR)

- **Define the problem**
- **Gather information** from African hospitals/facilities regarding challenges experienced 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
- Assess applications of **ML, AI and use of cloud-computing** in African and LMIC settings
- Create **conceptual design report** for the radiotherapy system to enable technical design and prototyping in next phase

STELLA questionnaire to define the problem

- We asked a **range of** questions
- Questions included the LINAC model, local environment, availability of services, subsystems, treatment and imaging.
- Which factors are responsible for machine downtime?

<u>Total LINACs surveyed</u>
HICs: 52
Africa: 59

STELLA/ITAR Questionnaire

Overview

- We asked 36 questions in 5 key areas shown in the table to at least one facility in all African countries with RT access.
- Also sent the survey to facilities in the UK, Canada and the USA, for comparison.
- We examined: the LINAC model, environment, services, subsystems, treatment and imaging.

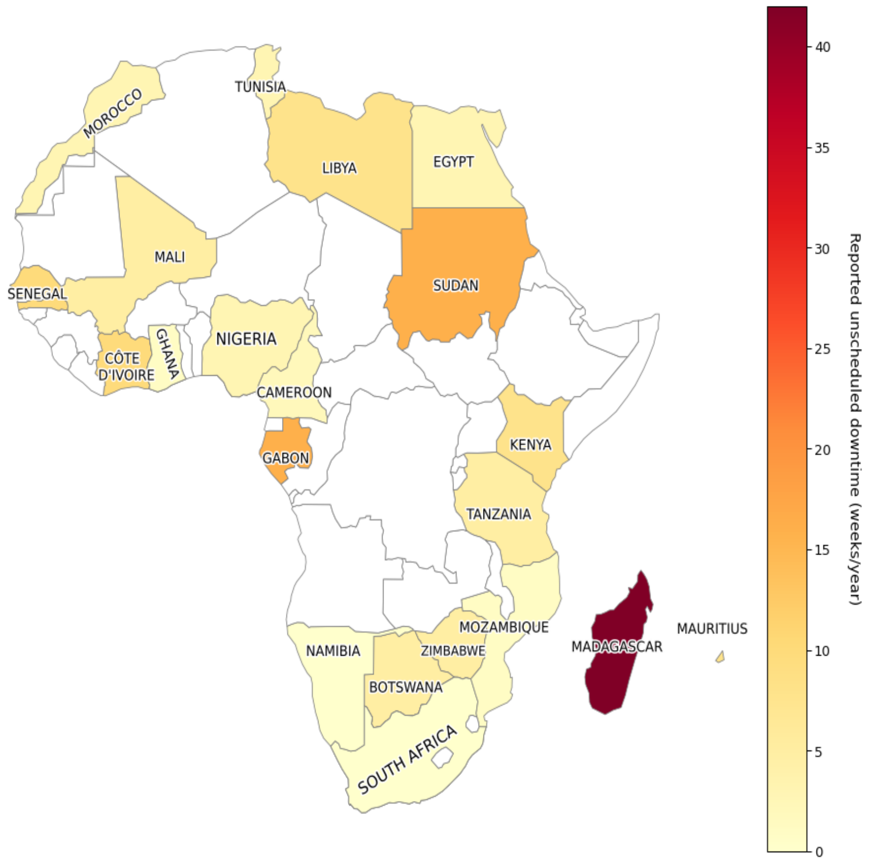
Focus	Questions
Model	What manufacturer and model? Year of installation?
	What number of treatments are performed per year on each machine?
Environment	What is the temperature and humidity in the area?
	What is the speed and availability of the internet connection?
	How reliable is the electricity supply?
	What is the floor area and ceiling height of the shielded area?
	What photon energy is your shielded area able to safely operate at?
Services	Do you have a service contract? Who provides it? What is the annual cost?
	How often does the machine have maintenance/tuning/calibration?
	What type of failures can you repair locally?
	Number of staff available for in-house repairs? Are staff formally trained?
Subsystems	How do you identify machine faults? Is it easy?
	Do you have problems with the vacuum system? How often?
	Do you have problems with the vacuum pump? Do you keep spares? Can you repair locally?
	Do you keep spare RF sources? Can you repair locally?
	Do you have problems with the MLC? Do you keep spares? Can you repair locally?
	Do you have problems with the electron gun? Do you keep spares? Can you repair locally?
	How much down-time do you experience?
	Do you have any software problems?
Treatment and Imaging	Does your hospital have diagnostic CT near the radiotherapy area?
	Do you use a tilting Couch? How important is this feature?
	How important is it for a LINAC to offer electron treatment mode?

A table highlighting the questions asked on the questionnaire

Map Showing Unscheduled Downtime

Figuring out what is Responsible for this Downtime?

- We investigated the impact of the various survey responses on machine downtime.
- Looked at univariate and multivariate analysis: observe how distributions of downtime vary for facilities grouped by question response.
- Also surveyed facilities in the UK, Canada, Switzerland and the USA, for comparison.



Survey to determine what causes downtime?

Focus	Questions
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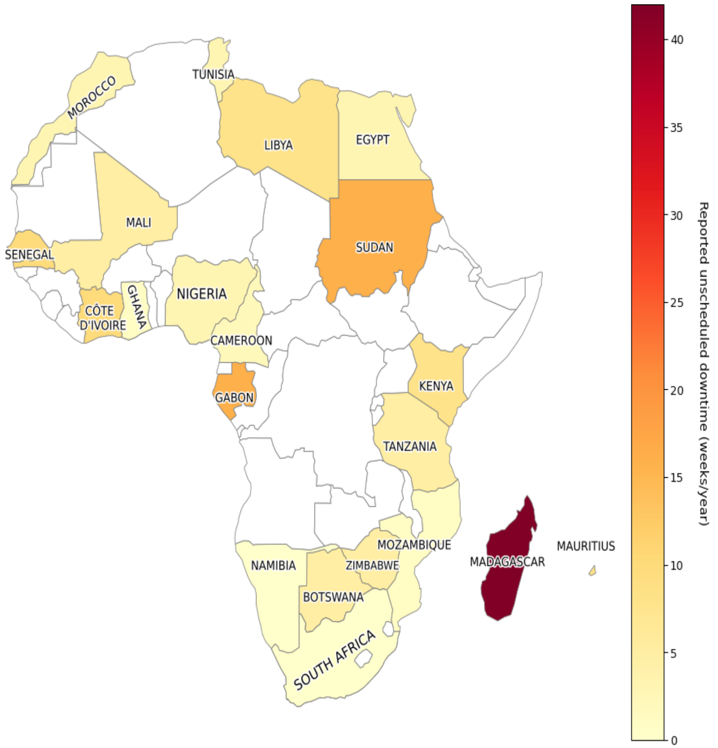


Established Initial data with the most vulnerable subsystems?

Subsystems

Observations

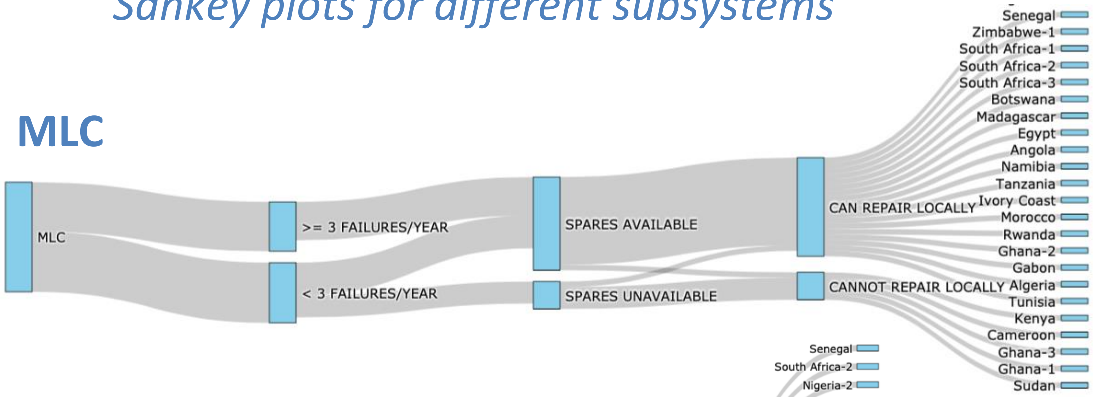
- **45%** of facilities experience **MLC** failures often. **77%** have spares. **78%** can repair locally.
- **44%** of facilities have experienced **electron gun** failure. **53%** keep spares. **33%** can repair locally.
- **53%** of facilities have experienced **vacuum pump** failure. **37%** keep spares. **48%** can repair locally.

Take-aways

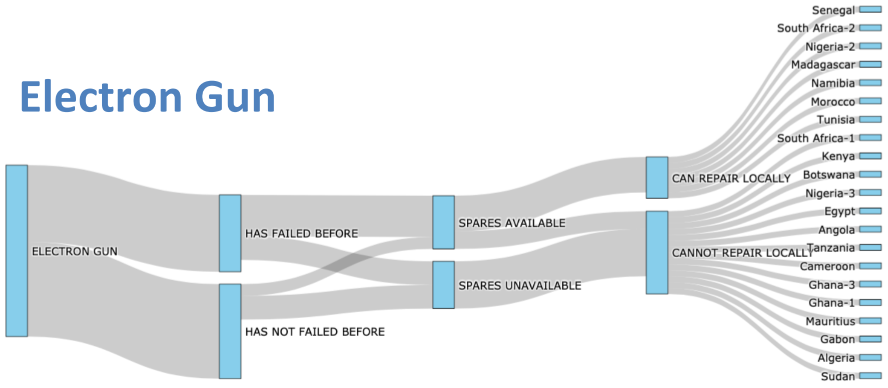
- If a facility experiences faults with a component, they are more likely to keep spare parts for it.
- If a facility keeps spare parts, they are more likely to have infrastructure in place to repair it.
- Ensure facilities have spares and can repair the part, before it has the chance to fail.
- Make fault diagnosis simple. A display/log on the machine will help staff easily identify faults.

Sankey plots for different subsystems

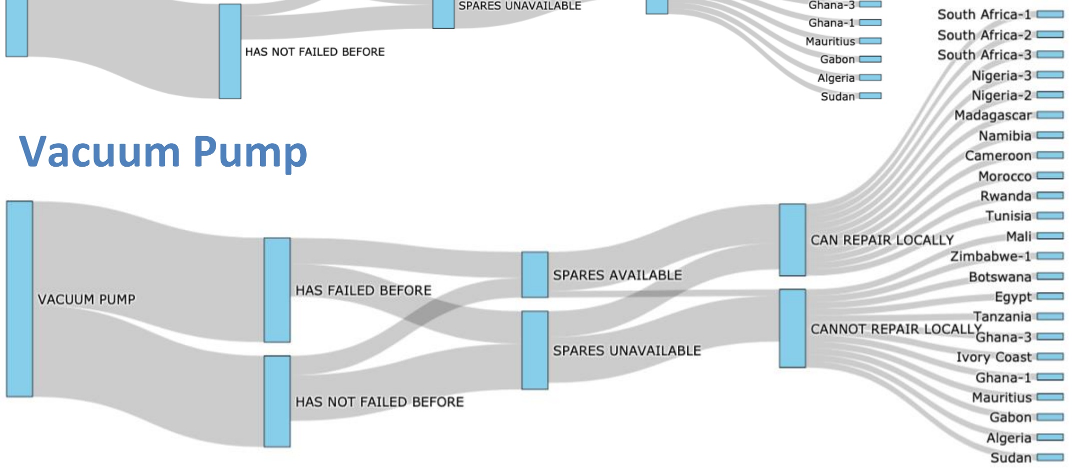
MLC



Electron Gun



Vacuum Pump



What have we established with from the Surveys?

Subsystems

- 47% of facilities experience MLC failures often. 76% have spares. 77% can repair locally.
- 46% of facilities have experienced electron gun failure. 53% keep spares. 33% can repair locally.
- 55% of facilities have experienced vacuum pump failure. 33% keep spares. 45% can repair locally.
- If a facility experiences faults with a component, they are more likely to keep spare parts for it.
- If a facility keeps spare parts, they are more likely to have infrastructure in place to repair it.
- Ensure facilities have spares and can repair the part, before it has the chance to fail.
- Make fault diagnosis as simple. A display/log on the machine will help staff easily identify faults.

Downtime

- Downtime may depend strongly on vacuum pump failure. Make part very robust.
- Keep the mains supply as stable as possible, e.g. affordable UPS and backup generators.
- Complicated software? Aim for no software problems.
- A display/log on the machine may be easier to diagnose LINAC problems at the centre, but may not affect downtime compared to remote diagnosis by manufacturer.
- Aim to improve reliability of parts on new machines learning from the fault of old ones.

Environment

- All bunkers surveyed are protected to at least 6 MV.
- Median bunker dimensions: 3.5m and 42 m^2.
- Mean temperature in African bunkers: 22.6 °C.
- Temperatures may vary significantly throughout the day. Consider optimal operating temperatures of components.
- 87% of facilities have a humidity <= medium. Consider optimal operating humidities of components.

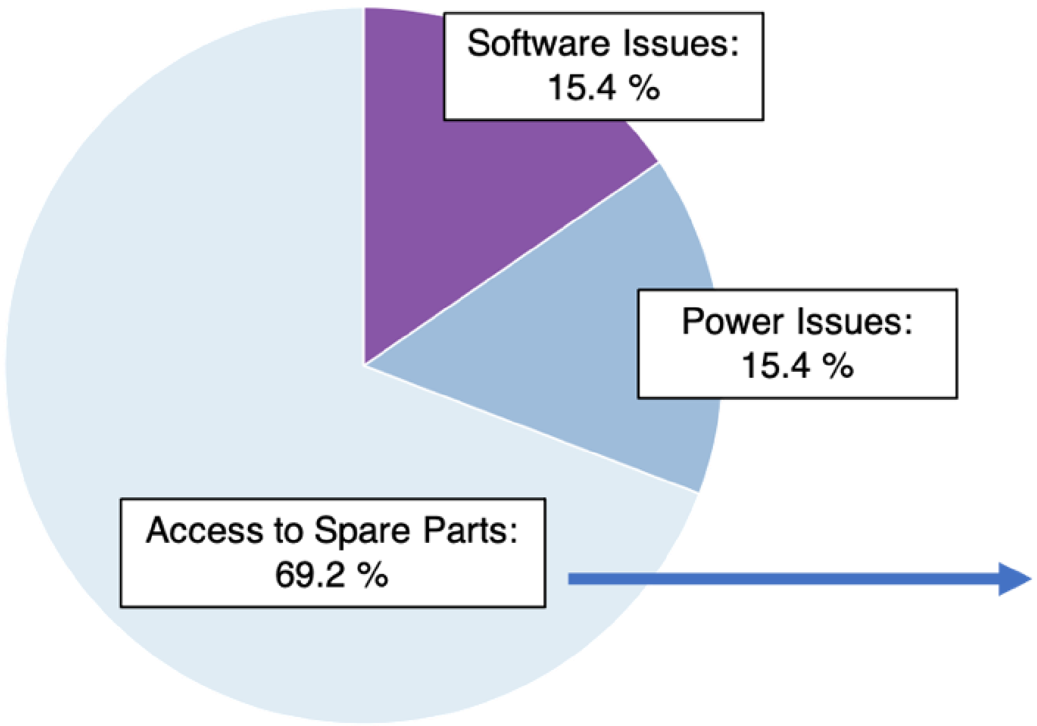
Possible Features

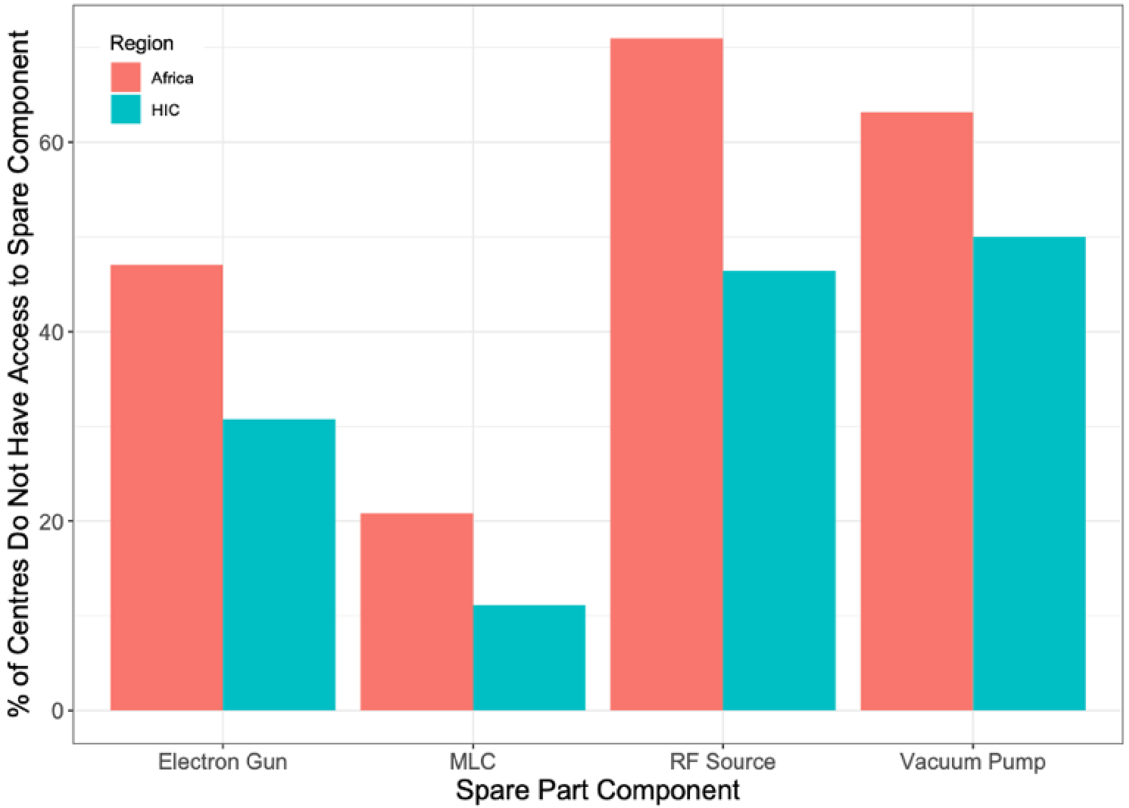
- 81% of facilities find the electron mode highly valuable.
- 26% of facilities currently have a tilting couch, many agree it would be a useful feature for advanced treatments.
- 94% of facilities have access to CT imaging close to RT machines. May need to provide this access in countries with currently no RT access.

Services and Education

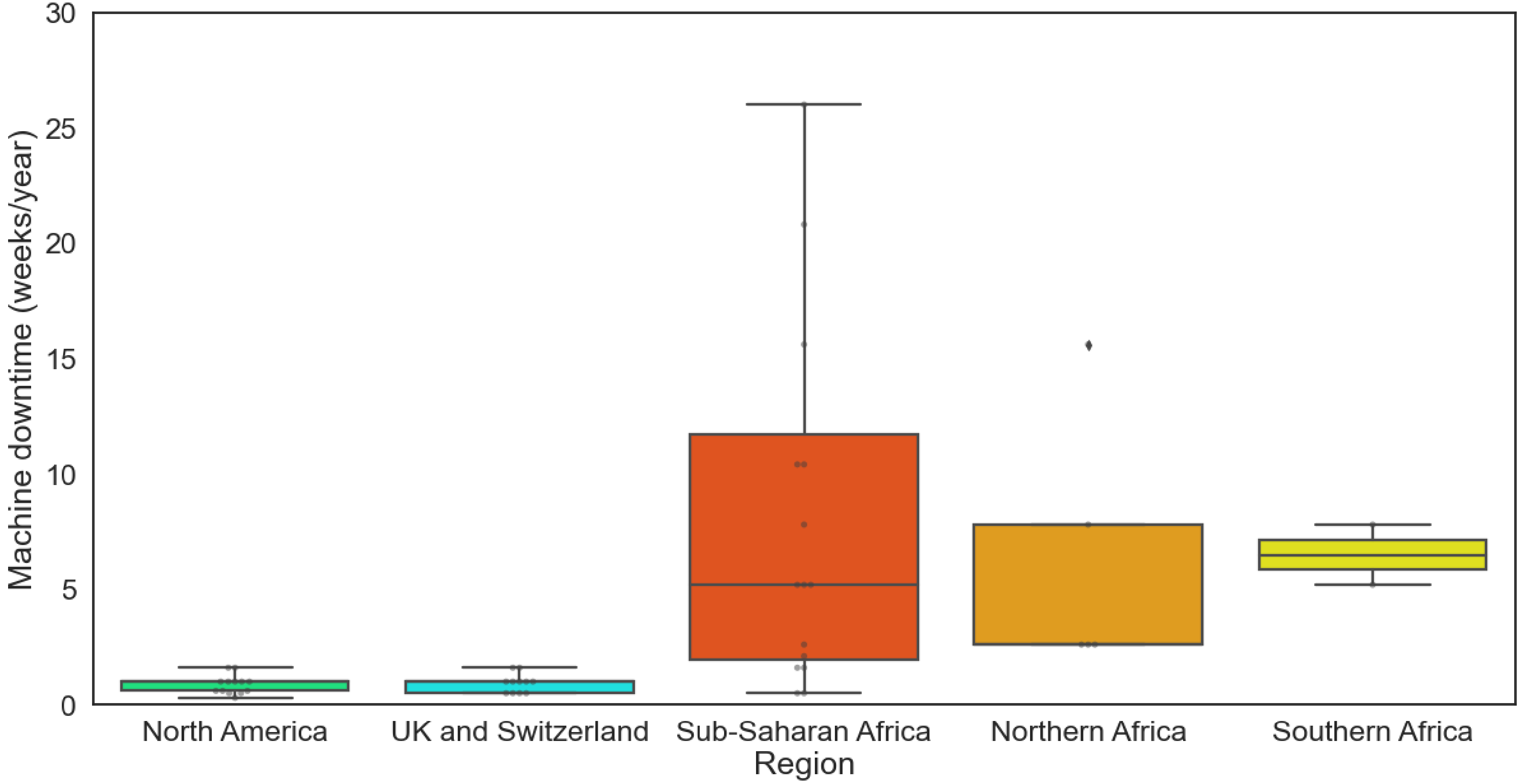
- 91% of facilities have a service contract.
- 63% of facilities can troubleshoot problems with machine.
- 71% of facilities have staff attend a formal training course.
- 90% of facilities have medium or high speed internet. Consider bandwidth availability before opting for a full online training programme.

Main Reason for LINAC Downtime: Access to Spare Parts

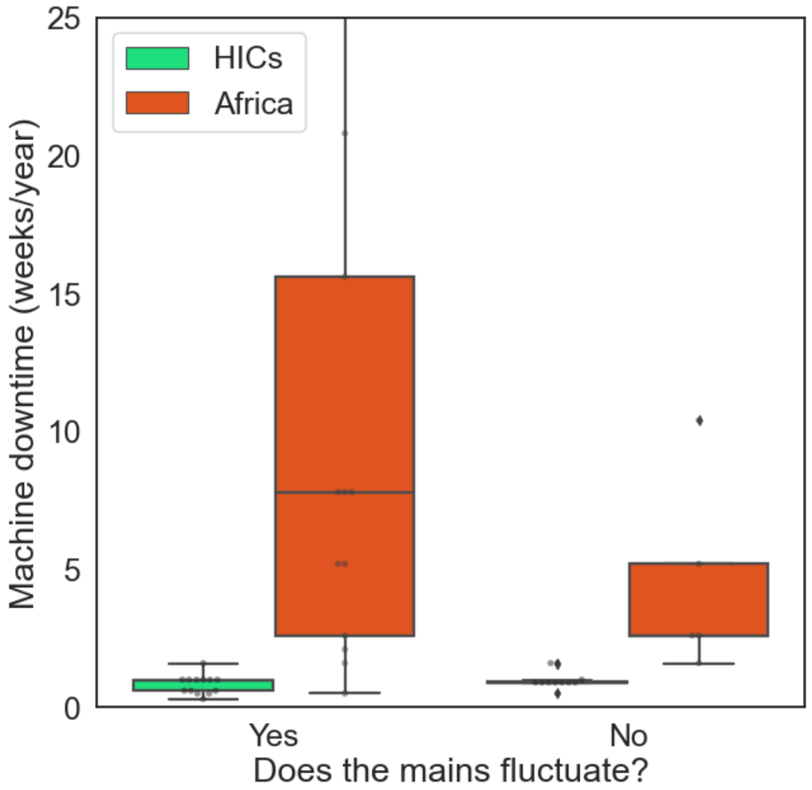




Downtime: General Comparison Between African Regions and HICs

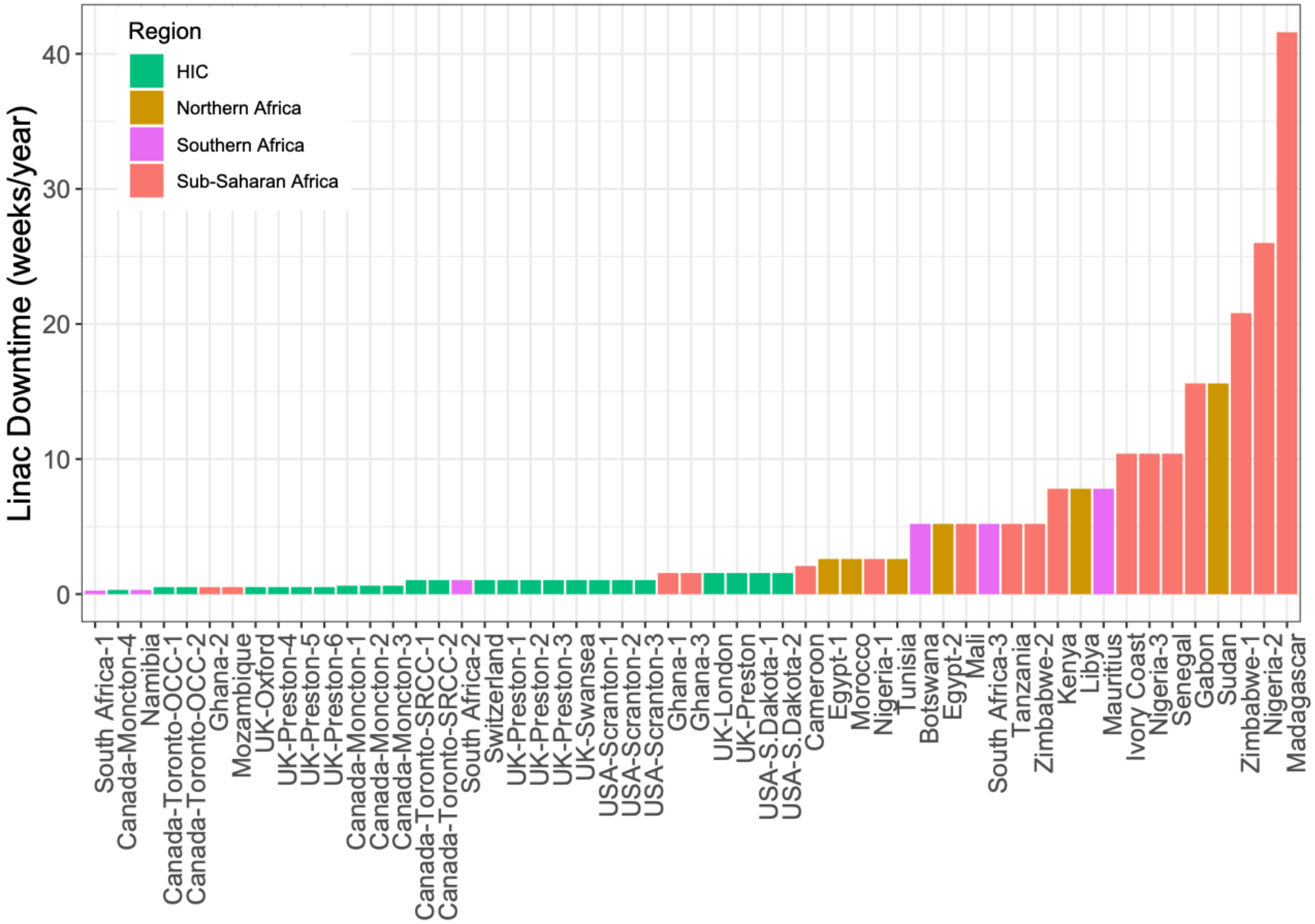


Downtime and Mains Fluctuations



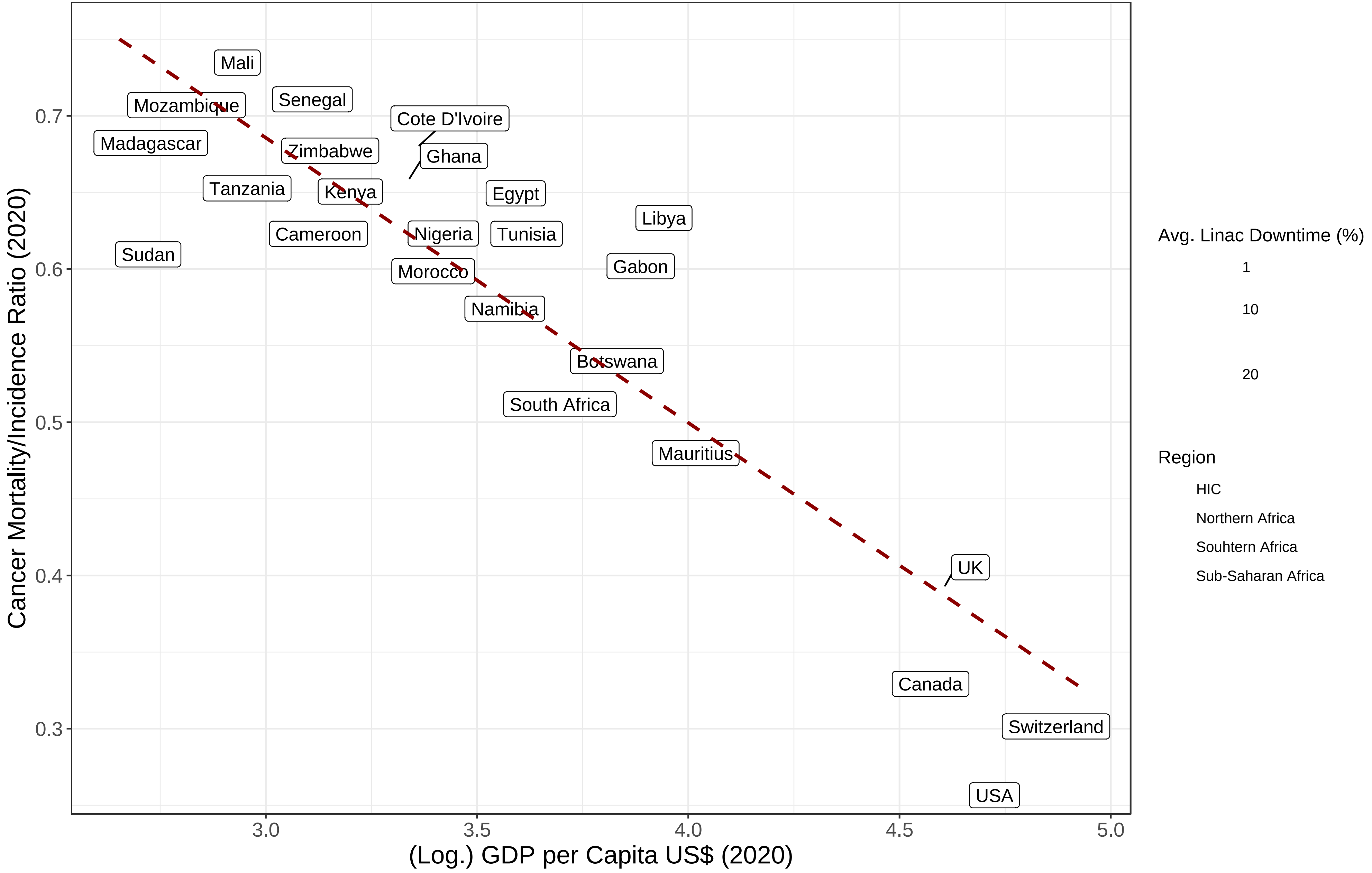
- Downtime in African facilities with mains fluctuation was 11.1 ± 12.0 weeks/year. The group of African facilities that did not experience mains fluctuation had downtime of 4.5 ± 3.6 weeks/year. A two-sample T-test yields p=0.09, **suggesting evidence to that downtime is dependent on mains fluctuations in Africa.**
- **No evidence to suggest that mains fluctuations affect downtime in HICs**.

LINAC Downtime by Country



STELLA
SMART TECHNOLOGY TO EXTEND LIVES WITH LINEAR ACCELERATORS

Impact of GDP per Capita and Linac Downtime and Cancer Mortality/Incidence



Summary of Current Findings

- Local repair and access to parts a significant factor determining downtime
- Software problems are a major contributor to downtime
- Frequency and voltage fluctuations also appear important
- Current data suggests - component importance on downtime: **Electron Gun**, **Vacuum Pump, MLC, RF source, Software, Power Fluctuation**

Current Project Goals for STELLA LINAC

- **Key issues** from reviewing **the various surveys, data gathering exercises, failure mode data and discussions at workshops**
- It was clear that a single machine cannot be realised to encompass all aspects. Categorisation Priorities:

High Priority	• Staff training and skill requirements to run a RT machine • Severities and cost of repairing technical failures • Frequency of failures (i.e. component lifetime)
Medium Priority	• Making the electrical system robust to fluctuations and minimising the power requirements • Robustness to temperature fluctuations and dust • Delivering higher dose • Initial capital cost and the cost of spare parts
Lower Priority	• Size of the machine • Total machine lifetime (as opposed to component lifetime) • Easy upgradability

Key Design Choices

- **Key design goal is to offer Higher Availability and Reliability**
- **Repairs are difficult & reduce availability**
- Choice of design and components to improve lifetime
- Choose components that can be replaced in house with less-expensive spares
- Use of machine learning to predict faults in advance to protect the machine and order spares
- Use of AI to identify the cause of faults and early detection/prevention strategy
- Simplify the MLCs
- Choice of 6 MeV energy to lower energy consumption and easier to use in limited resource environments

Linacs alone are not the solution: which are other key factors?

What is the current situation in the following:

1. Radiotherapy infrastructure and physical environment
2. Funding and procurement
3. Education and training
4. The major challenges looking ahead

Colour shaded countries represent 26 participated in survey from 28

Challenges highlighted from the second survey

Despite geographical, financial, and cultural differences among all 26 countries, what unites them is their need for an **organised**, **integrated approach**. Improving **awareness of radiotherapy** and **encouraging governmental buy-in** as to its importance for improving cancer treatment outcomes is a common goal.

In summary

- requiring a simplified procurement and funding process,
- planning for future services by increasing training opportunities in all radiotherapy disciplines,
- incentivising staff retention.
- respondents from all 26 countries reported optimism about the future and a growing awareness of the need for safe and effective cancer care amongst their healthcare providers.

Where are we now?

- Gathered information from African hospitals/facilities regarding challenges faced in providing radiotherapy in Africa
- Identified the challenges with those who live with them day-to-day
- Created design specifications for a radiotherapy machine to meet these challenges for an improved design
- Assessing applications of ML, AI and use of cloud-computing in African and LMIC settings
- Created conceptual design report (Graham Burt and ITAR) for the radiotherapy system to enable technical design and prototyping in next phase
- **ICEC secured $1.75M funding from DOE**

Next Phase: this week just had ICEC-CERN STELLA Kick-off meeting: *"Re-engineering the Next Generation of Medical Linear Accelerators for Use in Challenging Environments"*

CERN and ICEC have agreed to leverage the DOE funding granted to ICEC for collaboration for the STELLA Project

Kick-off meeting involved the collaborations partners which included Cambridge, Lancaster, Oxford University, key leaders from LMICs (Botswana, Egypt, Ghana, Jordan, Kenya, Morocco, Nigeria, Senegal), IAEA experts, DOE-NNSA, other radiation oncologists.

STELLA Project Leader is Manjit Dosanjh,
3 Pillar Coordinators: LINAC: Steinar Stapnes (CERN); Software: Raj Jena (University of Cambridge); Training & Mentoring Nina Wendling (ICEC)

Meeting provided an update on the progress of STELLA, overview and challenges, expected deliverables for this phase of the project, brainstorming and coordination of the efforts going forward

Ultimate Goal for STELLA Project

- Linacs must be: Robust, modular, reliable and simple to use machines

- Are affordable
  - ✓ Reduce Capital cost
  - ✓ Reduce Operating costs
  - ✓ Reduce Service and Maintenance costs
  - ✓ Reduce number of experts needed
  - ✓ Increase number of treated patients per year

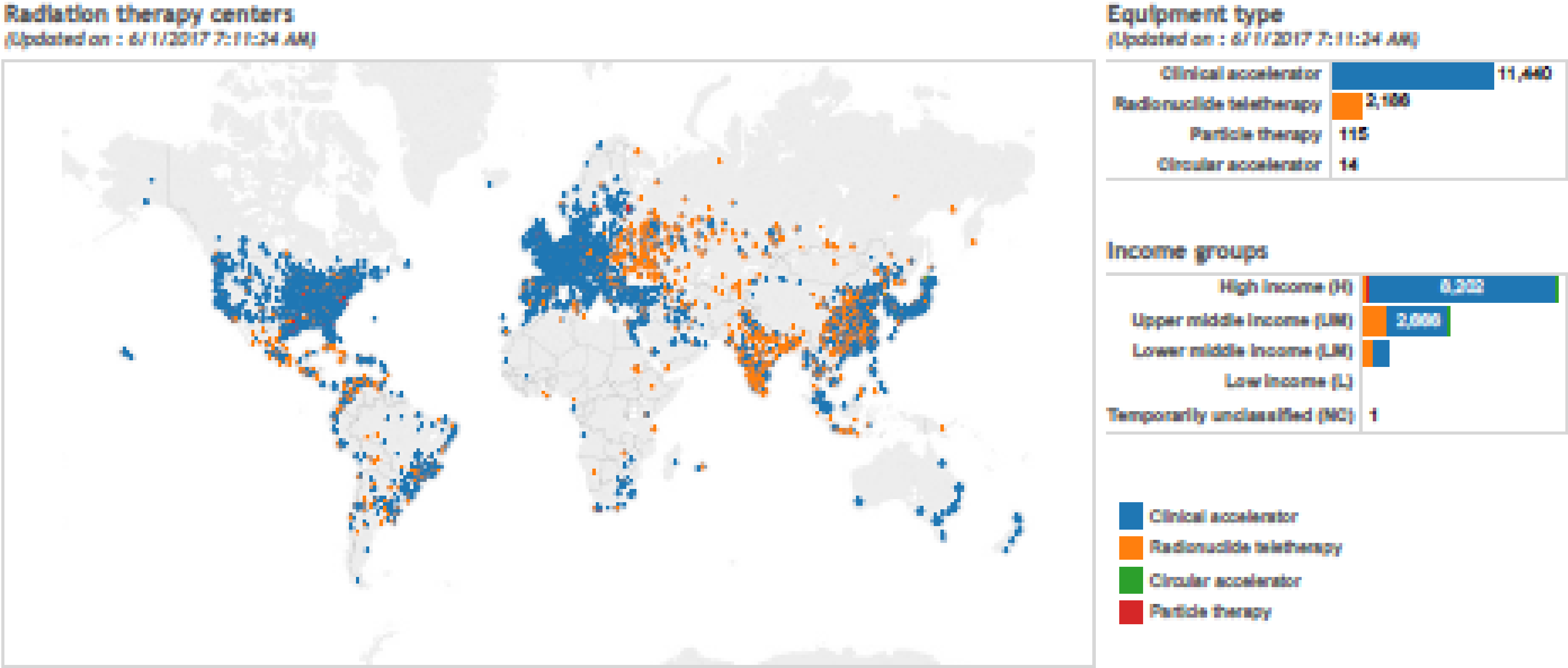
- Build expertise and capacitance

Improving access for all cancer patients globally

Thank You for Listening

- Power of seeing and understanding the challenges together and making STELLA a reality

World-wide radiotherapy coverage



Countries	RT centers	Equipment	Linac	Radionuclide Therapy	Circular Accelerator	Particle Therapy
139	7041	13755	11440	2186	14	115