

LINACS to Narrow the Radiotherapy Gap

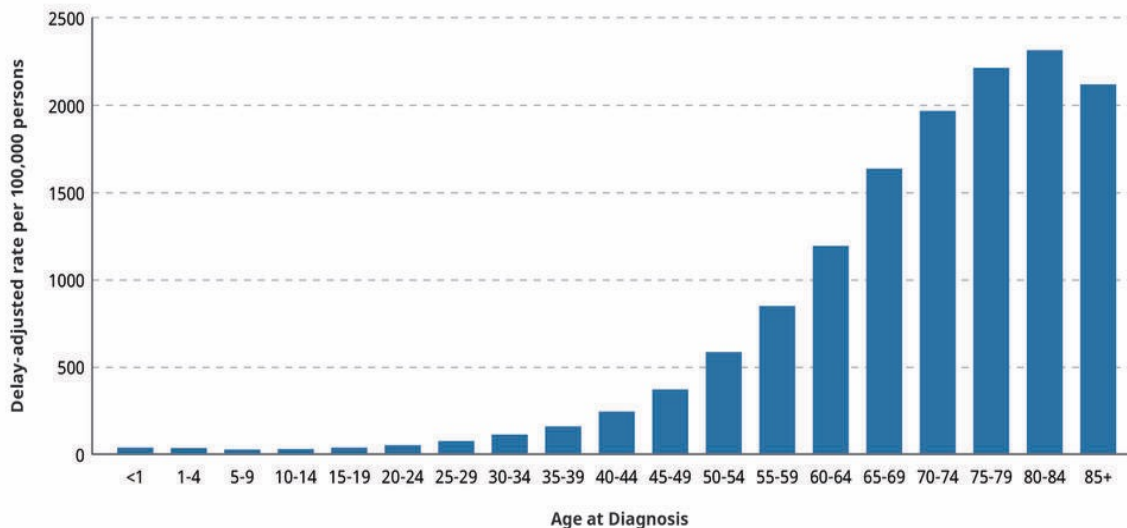
Manjit Dosanjh, CERN and JAI-Oxford
(on behalf of the STELLA collaboration)

UK Accelerator Institutes Seminar Series
16 February 2023



Cancer is a growing global challenge

- 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)
- The complete spectrum of care is needed: Prevention, screening, diagnosis, treatment
- Nearly 50-60% of all cancers can benefit from RT for cure or palliation



- **Age** is the biggest factor
 - More than nine out of 10 cancers are diagnosed in people **>45 and older**.
 - Older than **70** make up almost quarter of all new cases
 - **1 in 4 cancer deaths** are caused by **smoking**
- USA: 1.9 million new cancer cases diagnosed and 608,570 cancer deaths**

Radiation Therapy Today

Key external radiation therapy delivery systems

- Cobalt 60 machines
- **Linear accelerators (Linacs)**
- Image-guided radiotherapy (IGRT); MR-guided Linacs etc.
- Particle therapy (proton and carbon)
 - Compact Accelerators
 - Compact synchrotron
 - Proton therapy Linacs – LIGHT-ADAM (Daresbury)
- VHEE – compact high energy electron machine for deeper penetration
- FLASH therapy could be possible for all particles

The Problem:

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

- **For nearly 60% of cancers, RT is most useful tool** for cancer cure or pain-relief; inadequate supply of RT linear accelerators (Linacs).
 - Gap greatest in low-middle income countries (LMICs)
 - **70% of the cancer deaths** will occur in LMICs
 - **9 out of 10 deaths** from cervical cancer and **7 out of 10 from** breast cancer are in LMICs
 - **Only 10%** of patients in LMIC have access to RT
- Current Linac technology is **complex, labour intensive, and high cost** to acquire, install, operate and service.

There have been significant advances in cancer treatment

Triggered by the release of:

IAEA –DIRAC 2013 data showing huge disparities in global access

ESTRO-HERO published data showed huge variation in Western and Eastern Europe countries such as Bulgaria , Greece etc

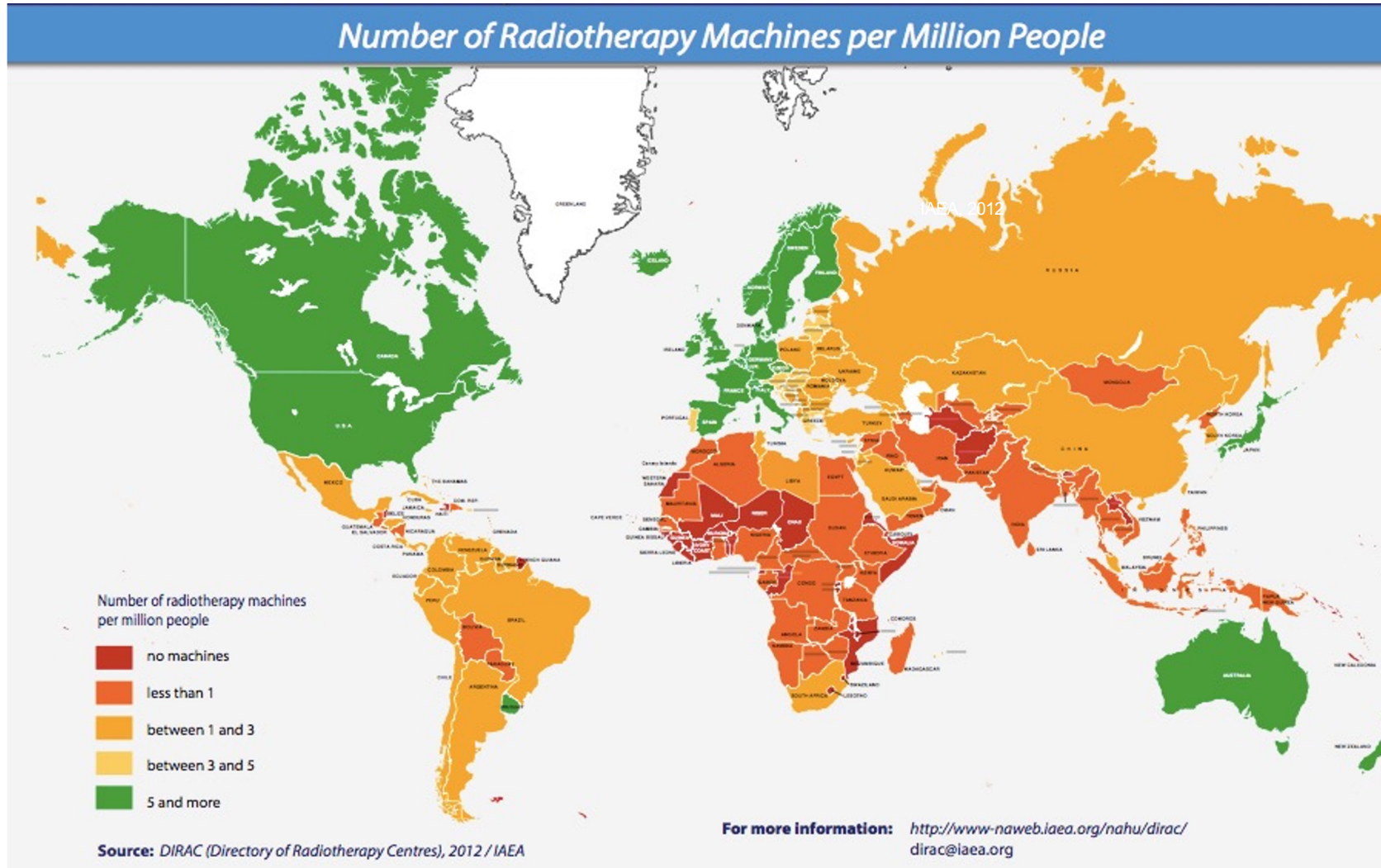
The importance of RT availability was further emphasized in the **2015 Global Taskforce on Radiotherapy for Cancer Control (GTFRCC) report**

Atun R, et al Expanding global access to radiotherapy. Lancet Oncol. 2015 Sep;16(10):1153-86

However, in spite of these advances there are still huge disparities and reliable data from the grass-roots helps to highlight the challenges and can trigger action:

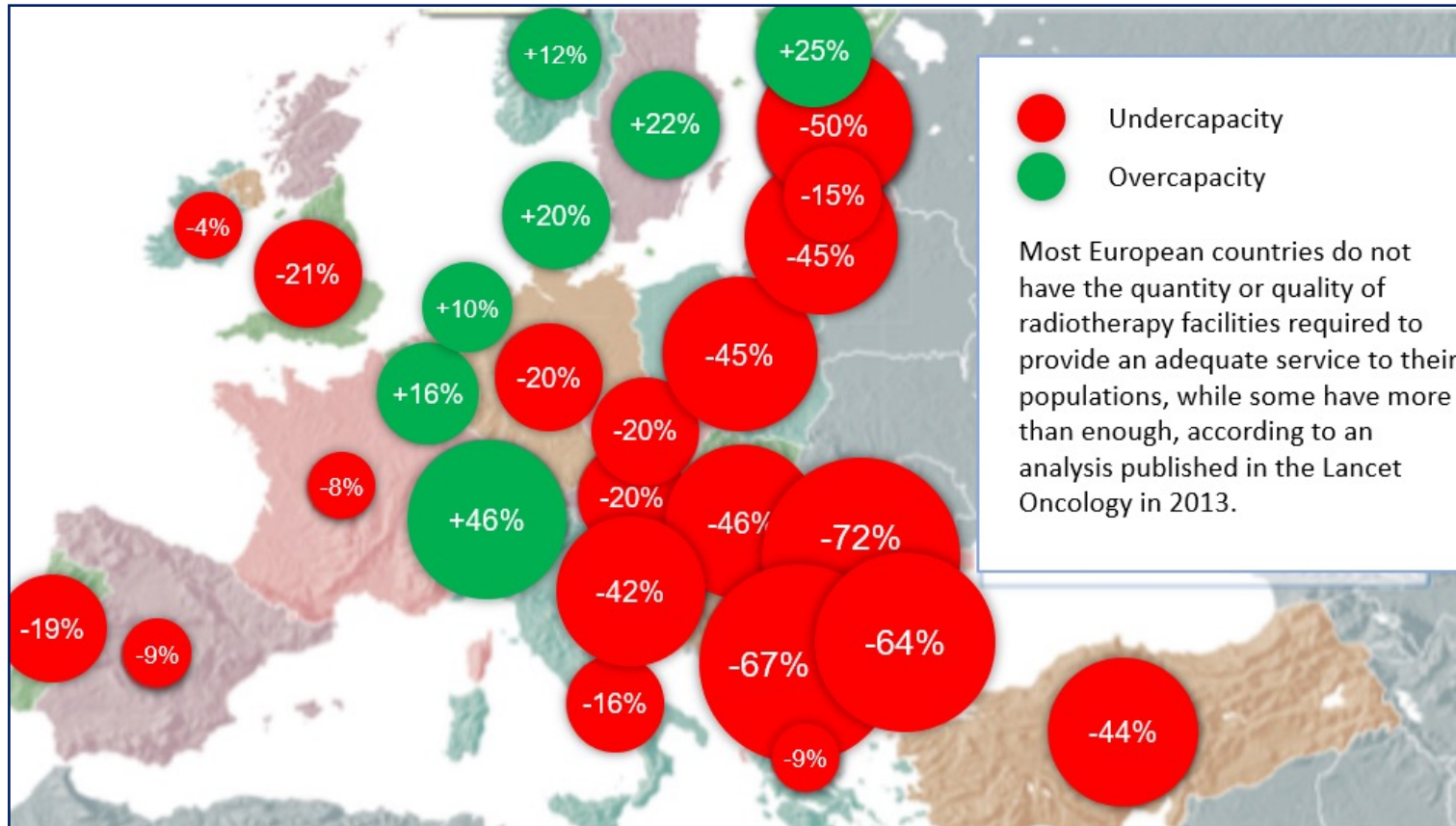
This is why ICEC/ STELLA started to look at Africa and other LMIC regions

Radiation Therapy is an essential part of cancer treatment



most of the 15,000 Linacs-RT units are in HIC (High Income Countries)

Access to RT technology in 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.

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

The Lancet Oncology Commission

Lancet Oncol, 2015, 16: 1153

Expanding global access to radiotherapy

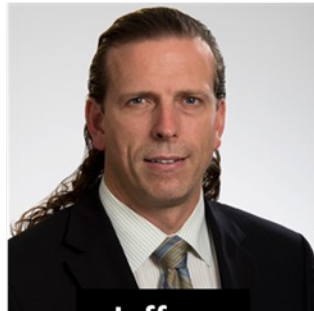
Rifat Atun, David A Jaffray, Michael B Barton, Freddie Bray, Michael Baumann, Bhadrasain Vikram, Timothy P Hanna, Felicia M Knaul, Yolande Lievens, Tracey Y M Lui, Michael Milosevic, Brian O'Sullivan, Danielle L Rodin, Eduardo Rosenblatt, Jacob Van Dyk, Mei Ling Yap, Eduardo Zubizarreta, Mary Gospodarowicz



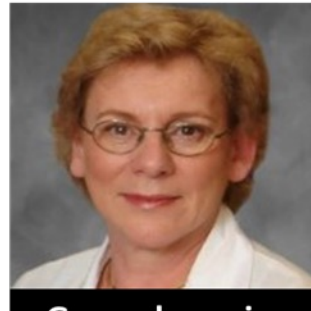
Our results provide compelling evidence that investment in radiotherapy not only enables treatment of large numbers of cancer cases to save lives, but also brings positive economic benefits.



Atun



Jaffray



Gospodarowicz

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.”



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

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However, in spite of these advances there are still huge disparities and reliable data from the grass-roots helps to highlight the challenges and can trigger action:

This is why ICEC/ STELLA started to look at Africa and other LMIC regions

Great strides have been made in the fight against cancer

But there are dramatic disparities in Access

Country	LINACs	Population	People per LINAC
Ethiopia	1	115 M	115,000,000
Nigeria	7	206 M	29,000,000
Tanzania	5	59.7 M	11,900,000
Kenya	11	53.9 M	4,890,000
Morocco	42	36.9 M	880,000
South Africa	97	59 M	608,000
UK	357	67 M	187,000
Switzerland	83	8.6 M	103,000
US	3727	331 M	88,000

Africa: 420 MV RT units for around 1.4 billion people

1 machine per 3.5 million people

UK: 359 MV RT units for around 68 million people

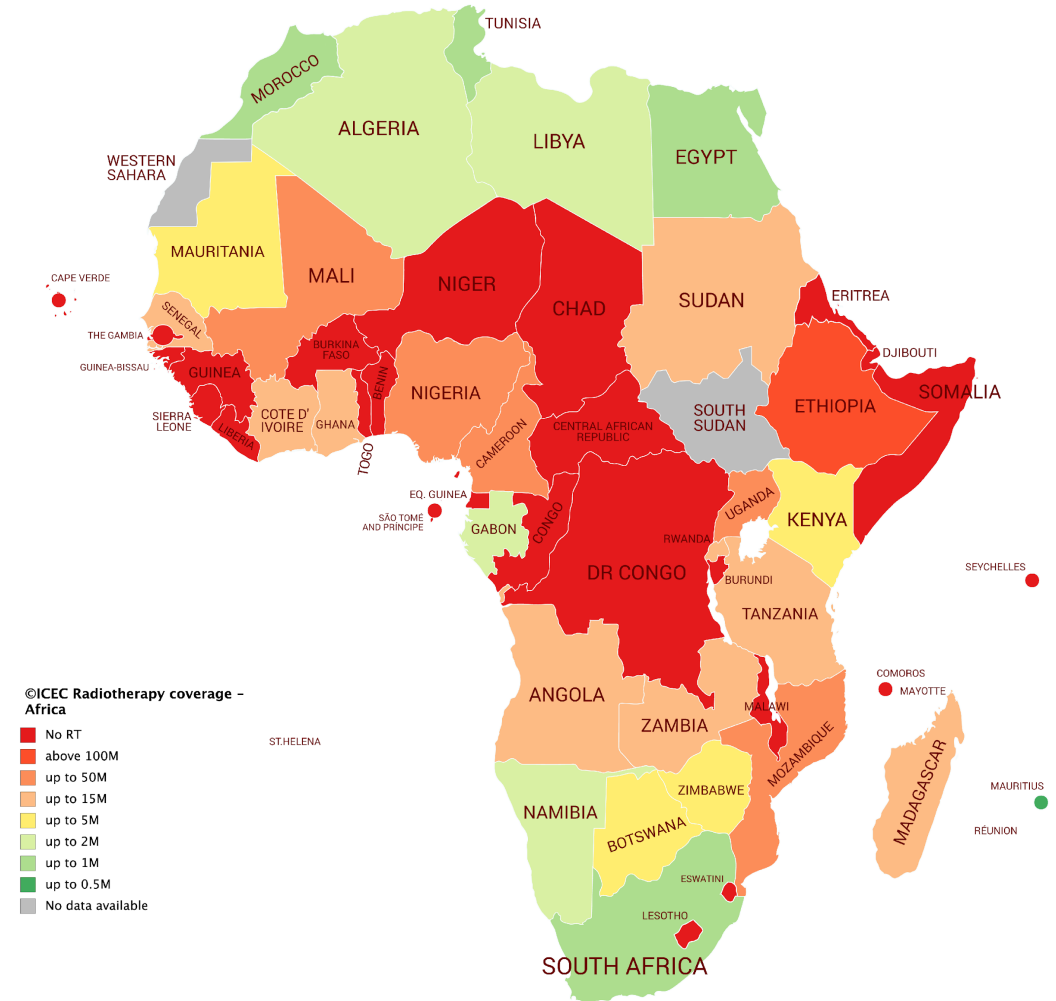
1 machine per 190,000

Switzerland: 84 MV for 8.7 million people

1 machine for 100,000

US: 3854 MV for around 330 million people

1 machine for 86,000



AFRICA'S RADIATION THERAPY STATUS

- **Acute shortage of RT** services both in quantity and quality
- **420 LINAC-RT** machines for nearly **1.4 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 cancer deaths in Africa
- Only **29** countries have RT facilities **25** 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-60 treatment machines
- Africa has around **88 cobalt-60** machines (half of which are over 20 years old) proportionally more than any other continent
- Some of the **25 African countries lacking a RT-Linac** will consider buying Co-60 machine because 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

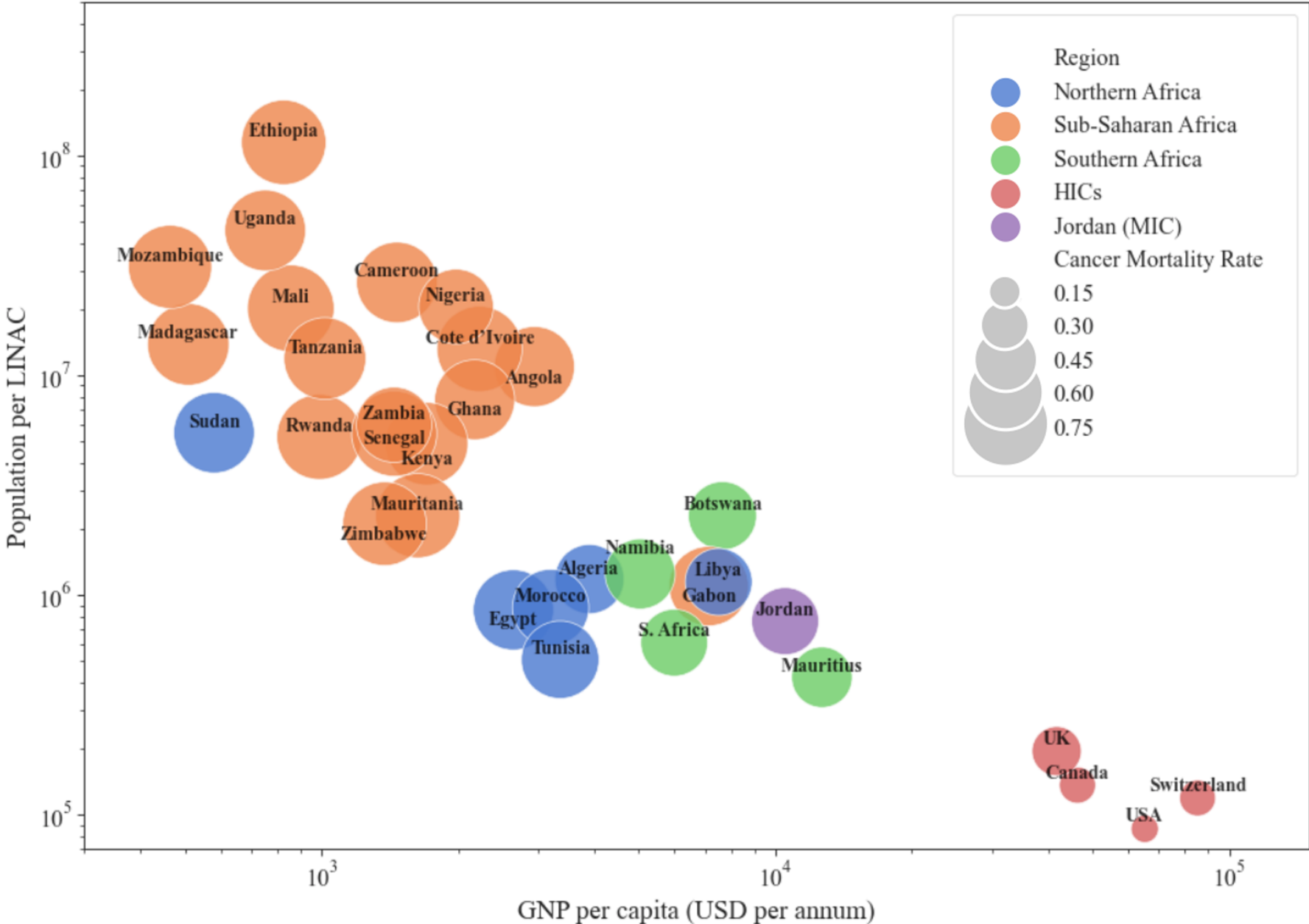
- Machines not adequate to meet demands
- High cost of care
- High mortality

Capacity for Multi-disciplinary teams

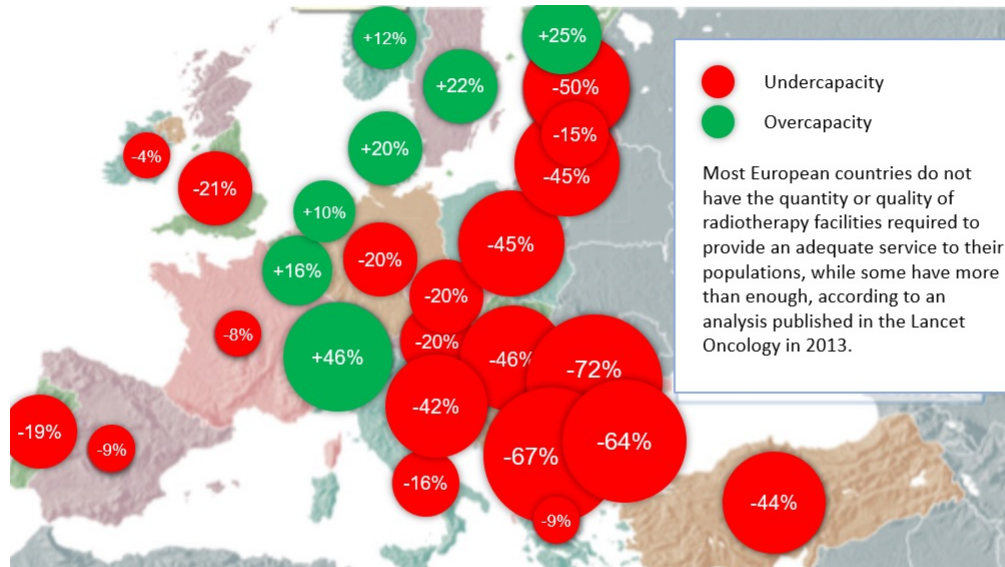
- Clinical skill gaps
- Need for training programs following global trends
- Lost time and high cost of short training time abroad



GNP and Ratio of Inhabitants to Linacs and Cancer Mortality



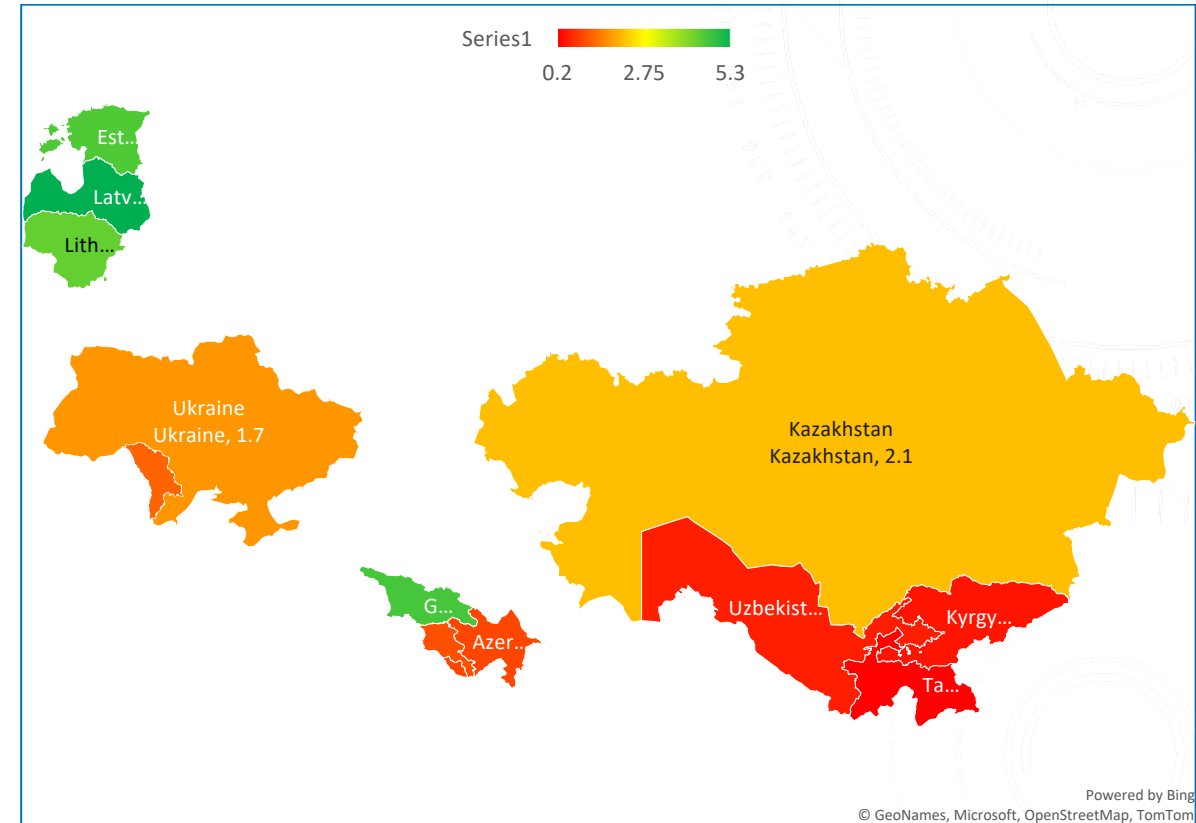
Shortage and challenges are not only in Africa



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

NOTE: Unpublished data please do not copy or distribute

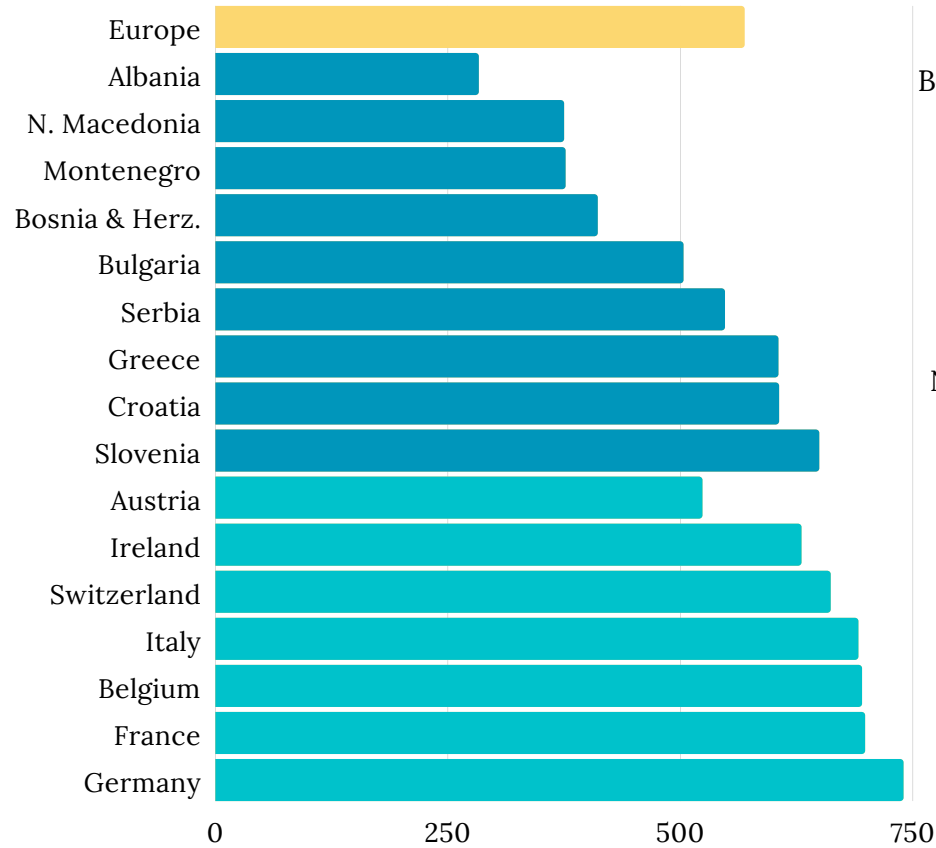
Study in the South-East- European (SEE) countries



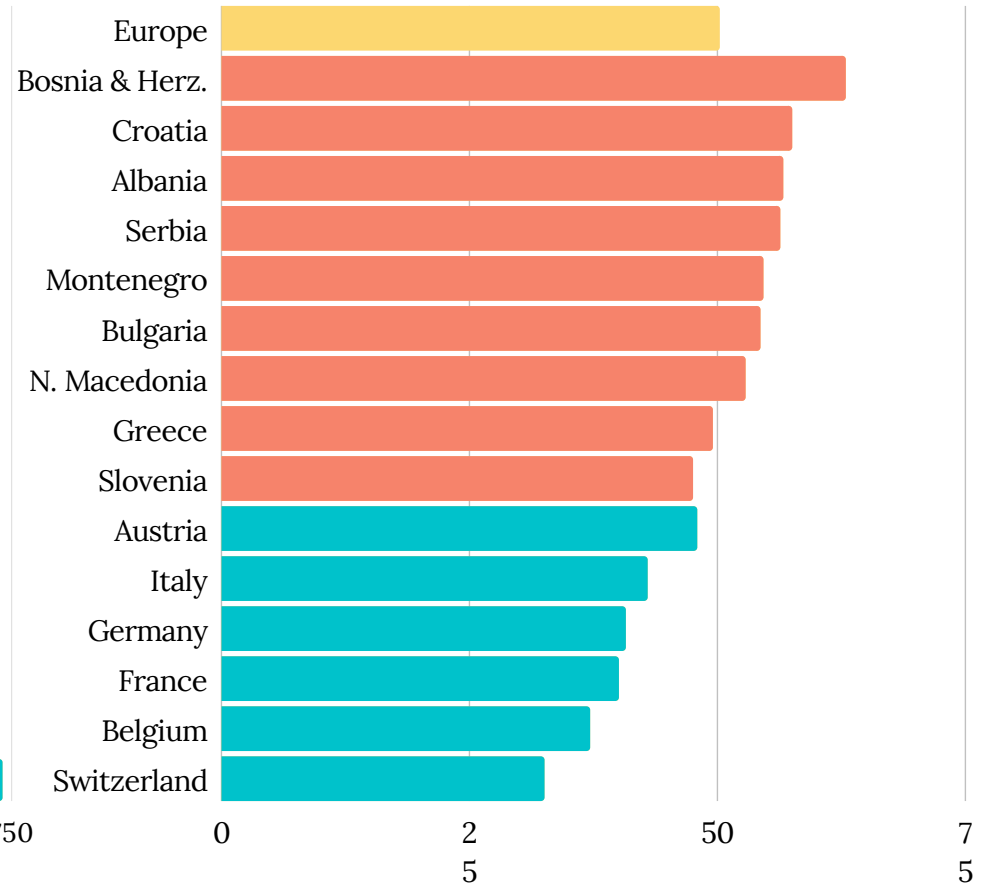
- Even at smaller regional level, there are huge disparities in access to RT

Cancer data for SEE (Balkan region)

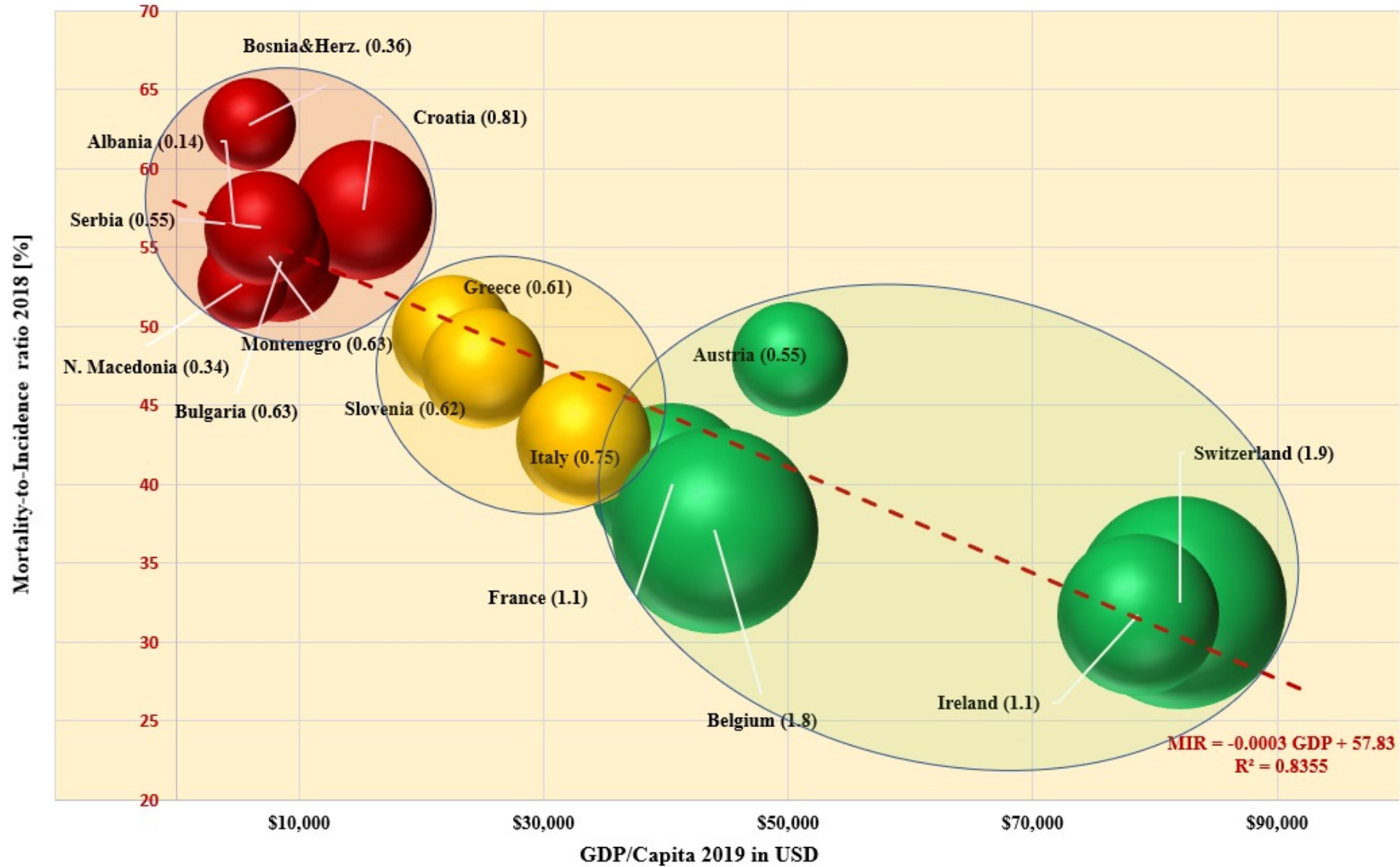
Cancer Incidence
Cases in 100'000, Both sexes



Mortality-to-Incidence [%],
All cancers, Both sexes 2018



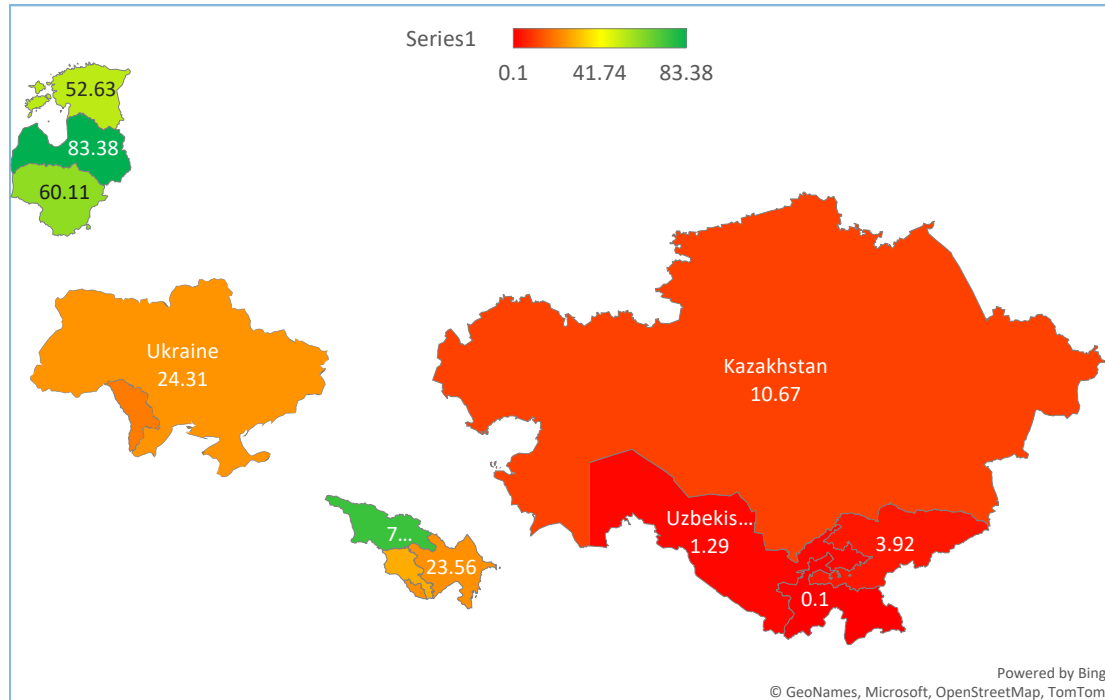
Linacs and Cancer Mortality in SEE Region (Balkan Peninsula)



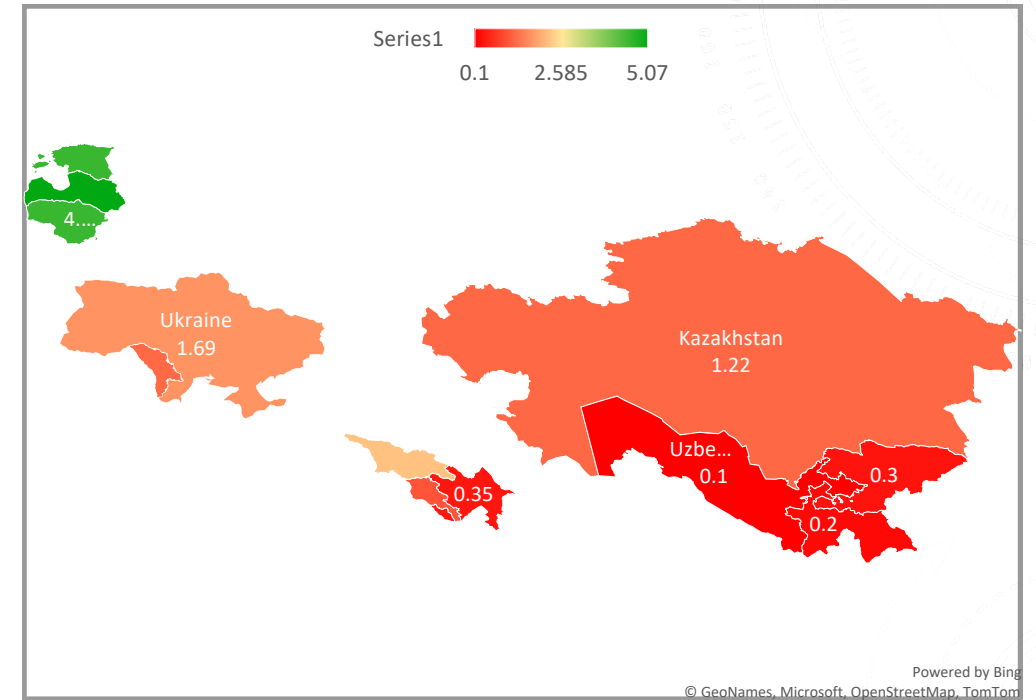
Dependence of the MIR on the GDP per capita and the density of conventional RT equipment. The radius of the spheres is proportional to the density of RT equipment per 100,000 population in the respective countries.

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 (Azerbaijan, Estonia, Georgia, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Moldova, Tajikistan, Turkmenistan, Ukraine and Uzbekistan)

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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 in both LMICs and HICs.
- 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).

1st workshop on: “Design Characteristics of a Novel Linear Accelerator for Challenging Environments”

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

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



International Atomic Energy Agency (IAEA)

James Martin Center for Nonproliferation Studies (CNS)

National Aeronautics and Space Administration (NASA)

National Nuclear Security Administration (NNSA)

Project STELLA

Smart Technologies to Extend Lives with Linear Accelerators

Project STELLA is a unique global collaboration involving some of the **best physics and medical talent, expertise** from leading laboratories in **accelerator design** and, importantly, **input and collaboration** from users in **Africa, other LMICs and HICs**.

The goal of this project is to **enable cancer care** through innovative technology that is disruptive and is centred in mentoring.

STELLA needs to be:

- Robust, modular, reliable and easier to use machine
- Affordable with the aim to **expand access to RT global**

Building the STELLA collaboration and defining a strategy

- 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



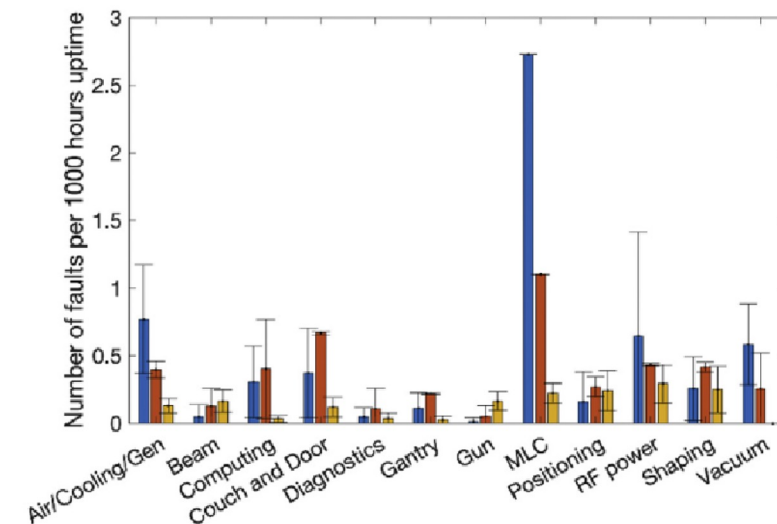
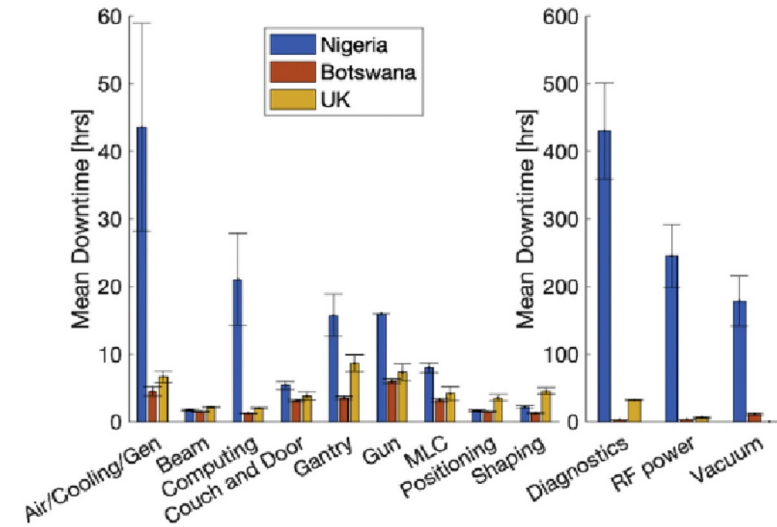
- 4th Accelerating the Future Workshop, March 2019, Gaborone



Initial Failure Report Gaborone (Botswana)-Abuja (Nigeria)-Oxford (UK)

Wroe et al (S. Sheehy Melbourne/Oxford)

- Nigeria has far longer repair times than in the UK, the repair hub is normally in a different continent or South Africa and maintenance is often not to the same standard
- Interestingly Botswana which is a fairly affluent country and pays for manufacturer's warranty, service and repair has similar downtime with more faults to LMICs
- MLC (multi-leaf collimator) has the most faults but diagnostics, RF and vacuum contribute to the longest downtime



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

ITAR Study and the STELLA project CDR

ITAR study funded by STFC and coordinated by Graeme Burt



STELLA/ITAR Questionnaire

Overview

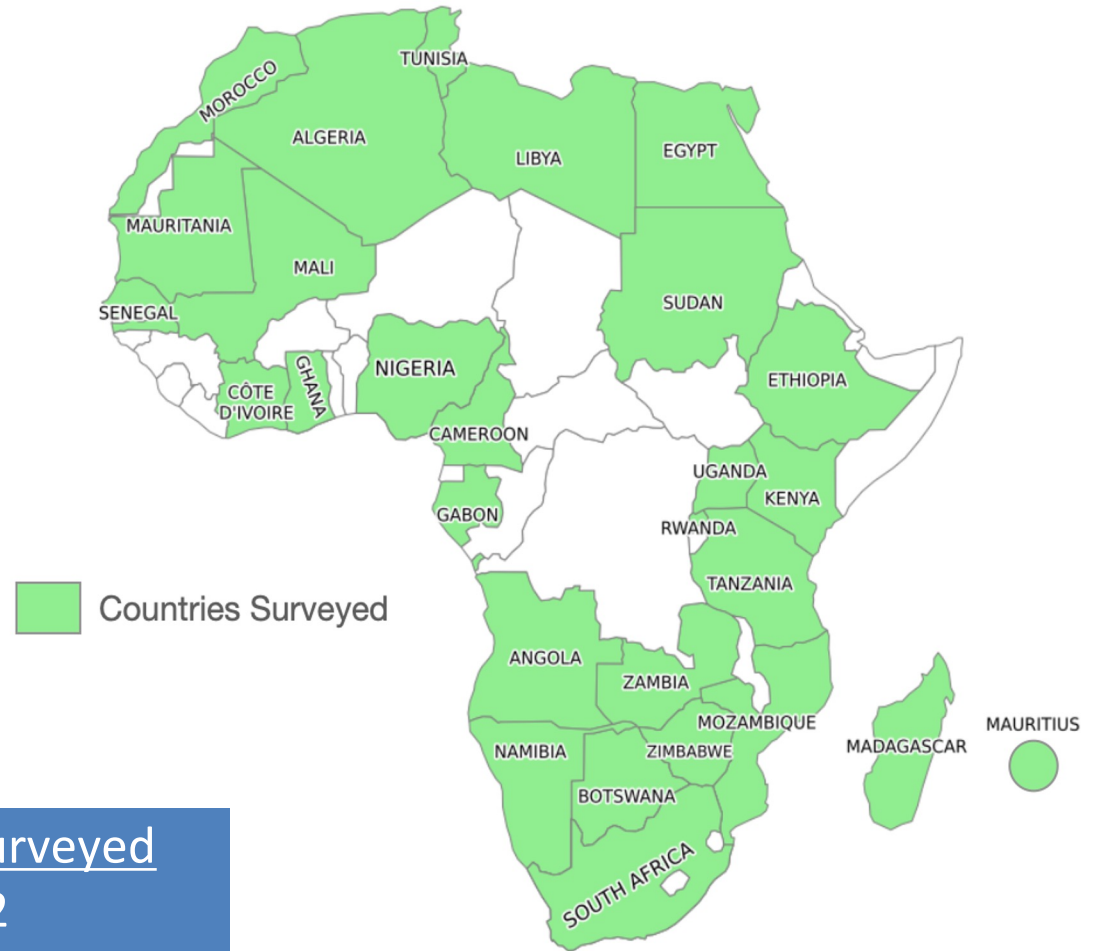
- We asked 36 questions in 5 key areas shown in the table to at least one facility in all African countries with RT access.
- Also sent the survey to facilities in the UK, Canada and the USA, for comparison.
- We examined: the LINAC model, environment, services, subsystems, treatment and imaging.

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

Data Obtained from African Countries That Have LINAC-based RT and from HICs

Country	Total number of LINACs surveyed
UK	25
USA	14
Canada	11
Switzerland	2
Jordan	1

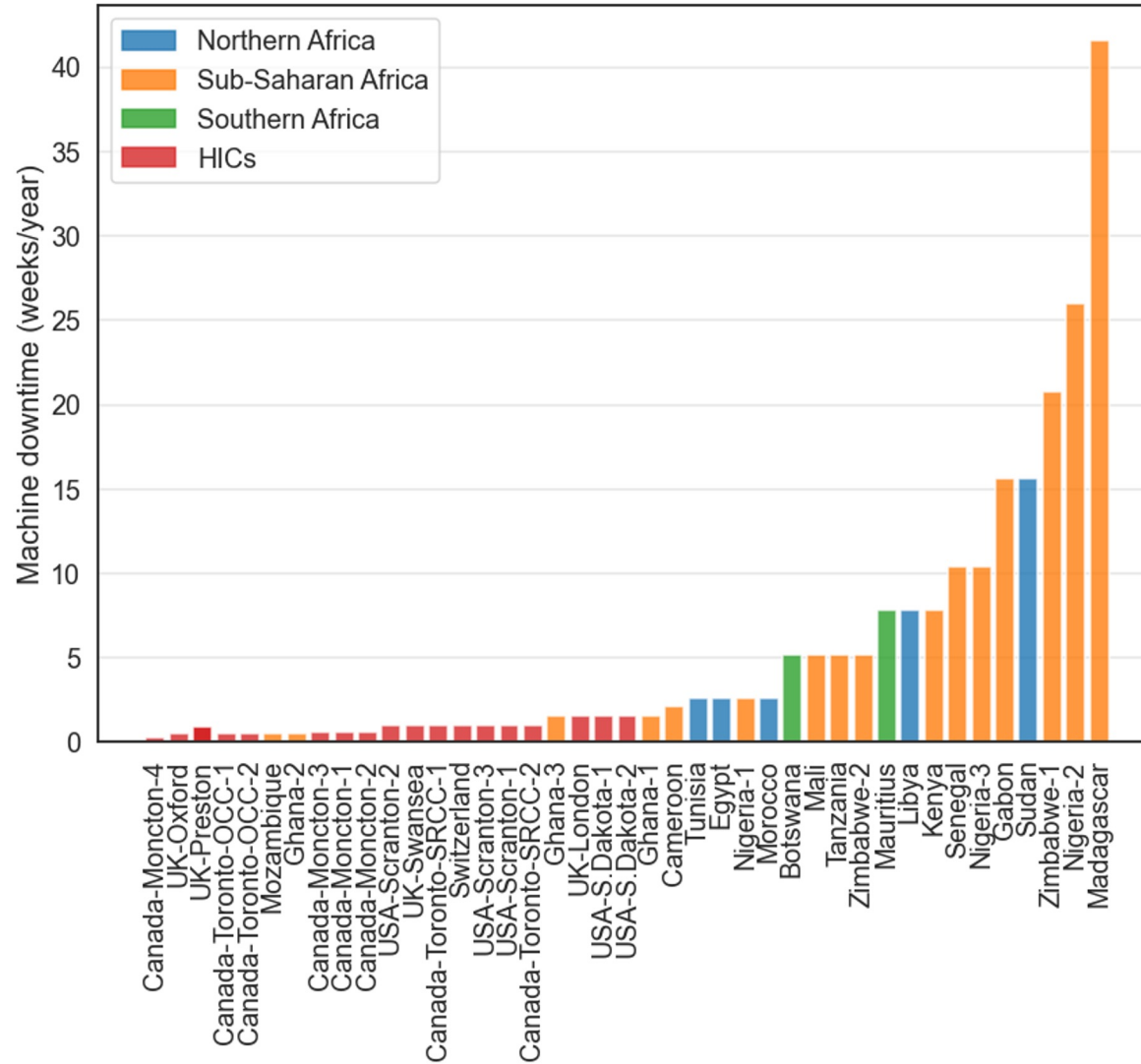


Total LINACs surveyed

HICs: 52

Africa: 59

Downtime: General Comparison Between African Regions and HICs

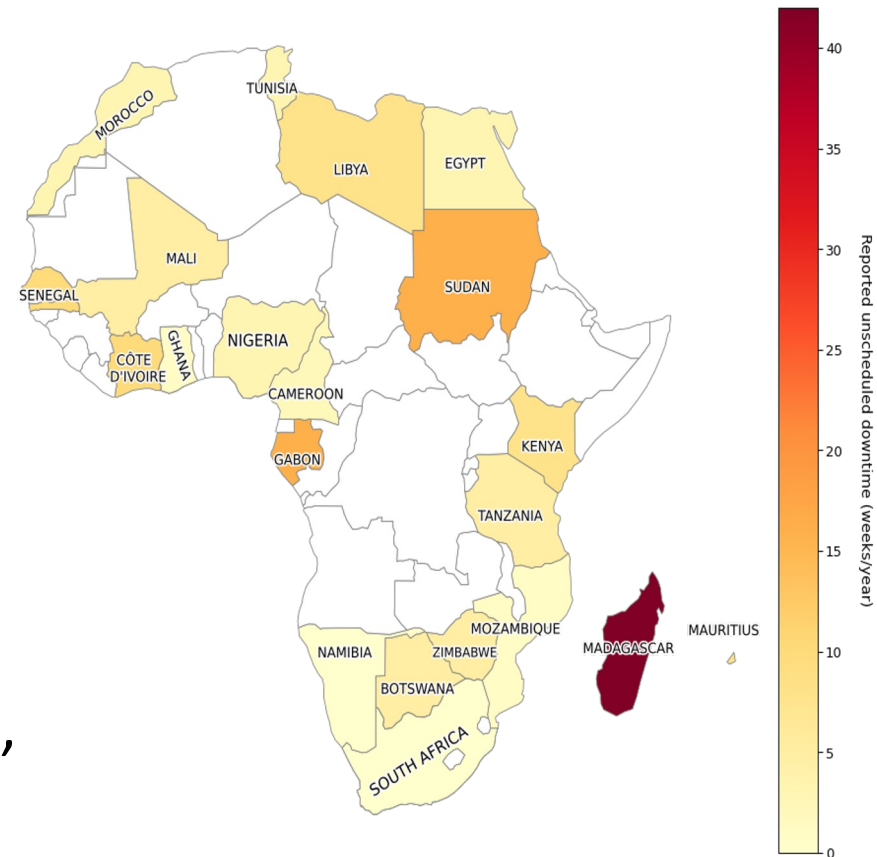


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Map Showing Unscheduled Downtime

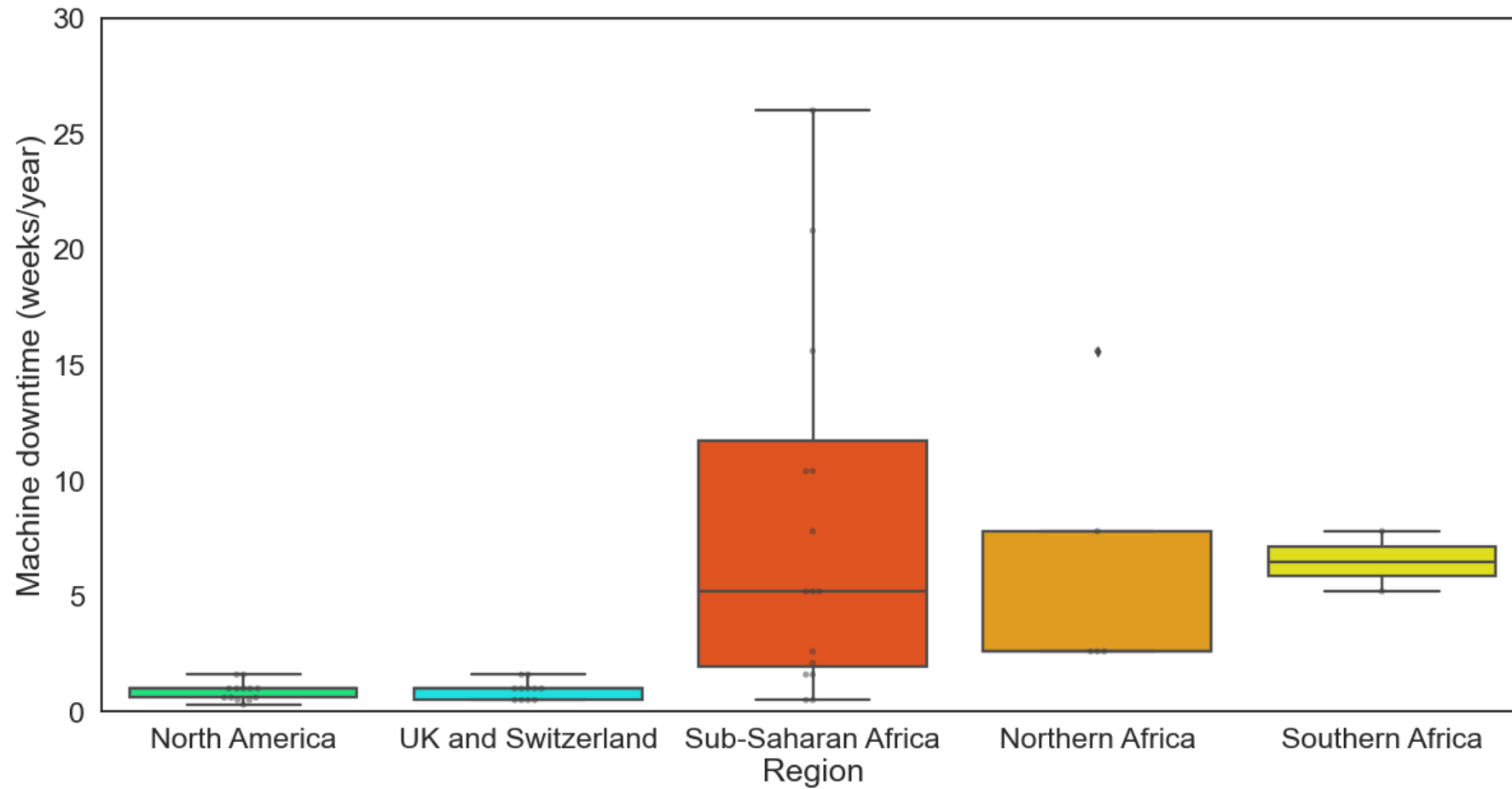
What Is Responsible for This Downtime?

- 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.



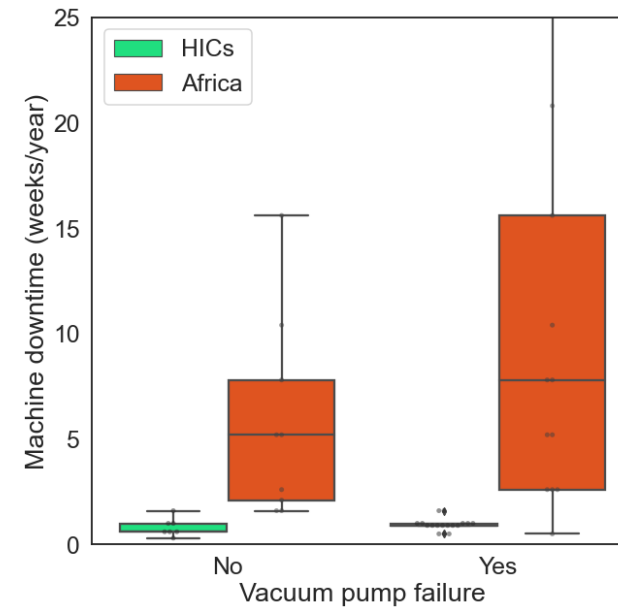
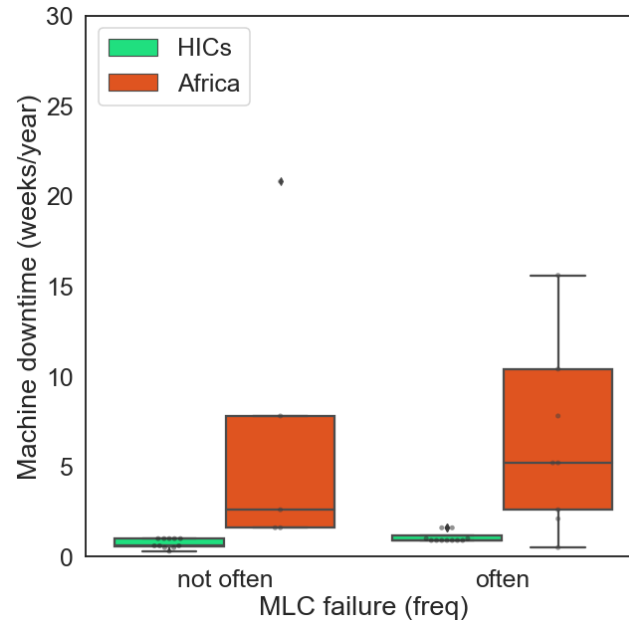
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Downtime: General Comparison Between African Regions and HICs



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Downtime and System Failures



Significant differences in downtime for access to spares only observed for the **MLC** and the **vacuum pump**.

MLC:

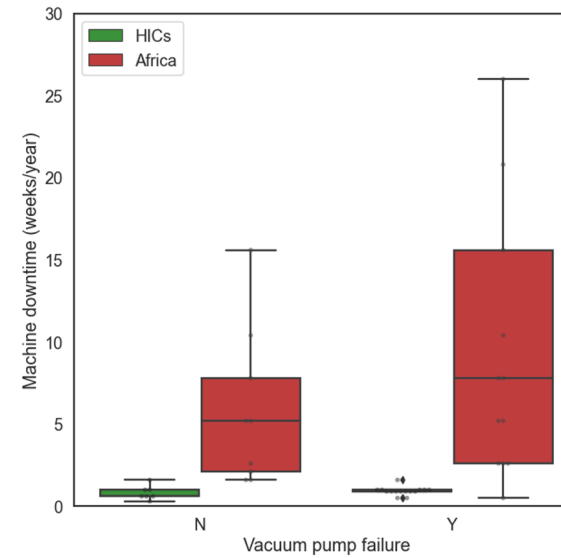
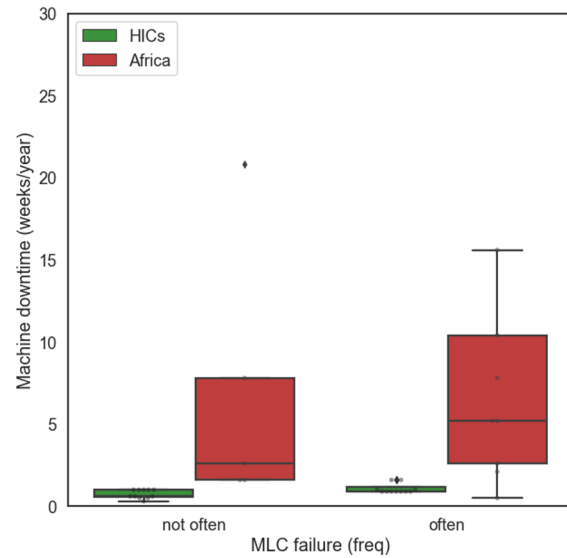
- Average downtime was significantly greater in HIC facilities where the MLC failed often. $p=0.007$. No evidence to suggest the same in African facilities.

Vacuum Pump:

- Larger downtime in African facilities that experience vacuum pump failure. Evidence to suggest difference $p=0.14$. No evidence to suggest the same in HICs.

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Downtime and System Failures



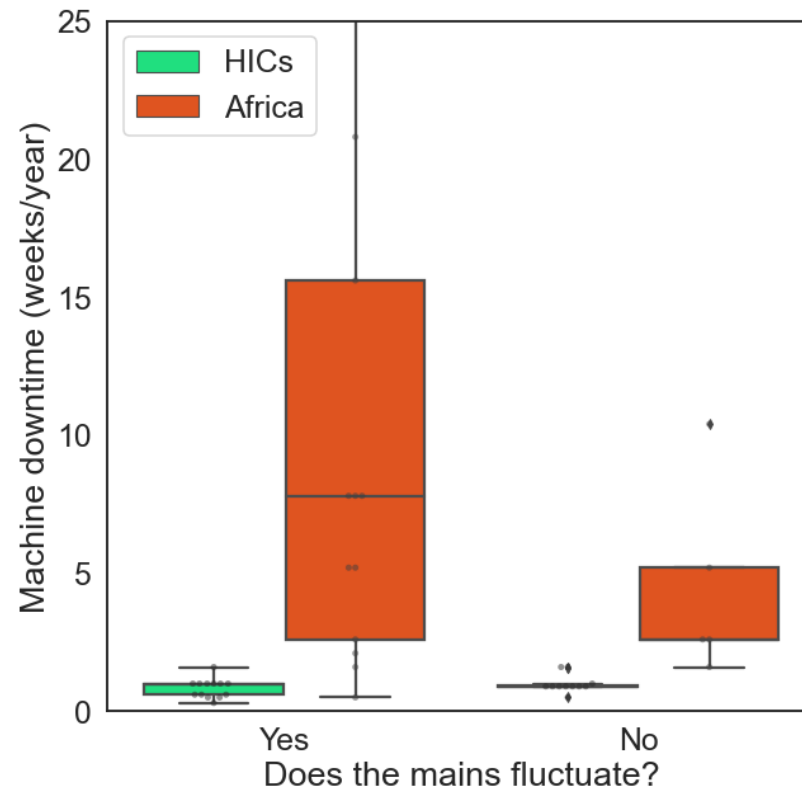
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Downtime and Mains Fluctuations

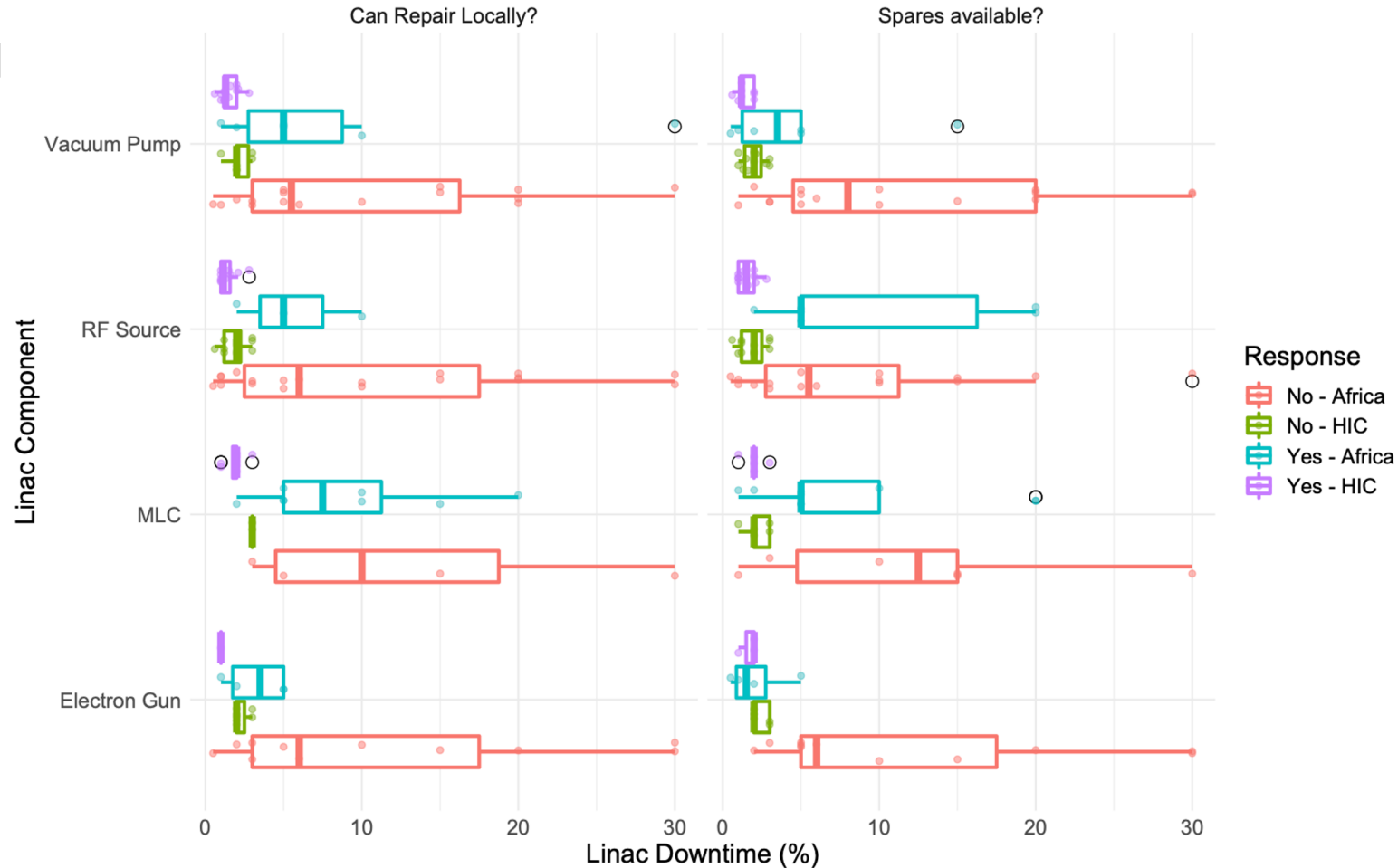


- Downtime in African facilities with mains fluctuation was 11.1 ± 12.0 weeks/year. The group of African facilities that did not experience mains fluctuation had downtime of 4.5 ± 3.6 weeks/year. A two-sample T-test yields $p=0.09$, **suggesting evidence to that downtime is dependent on mains fluctuations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

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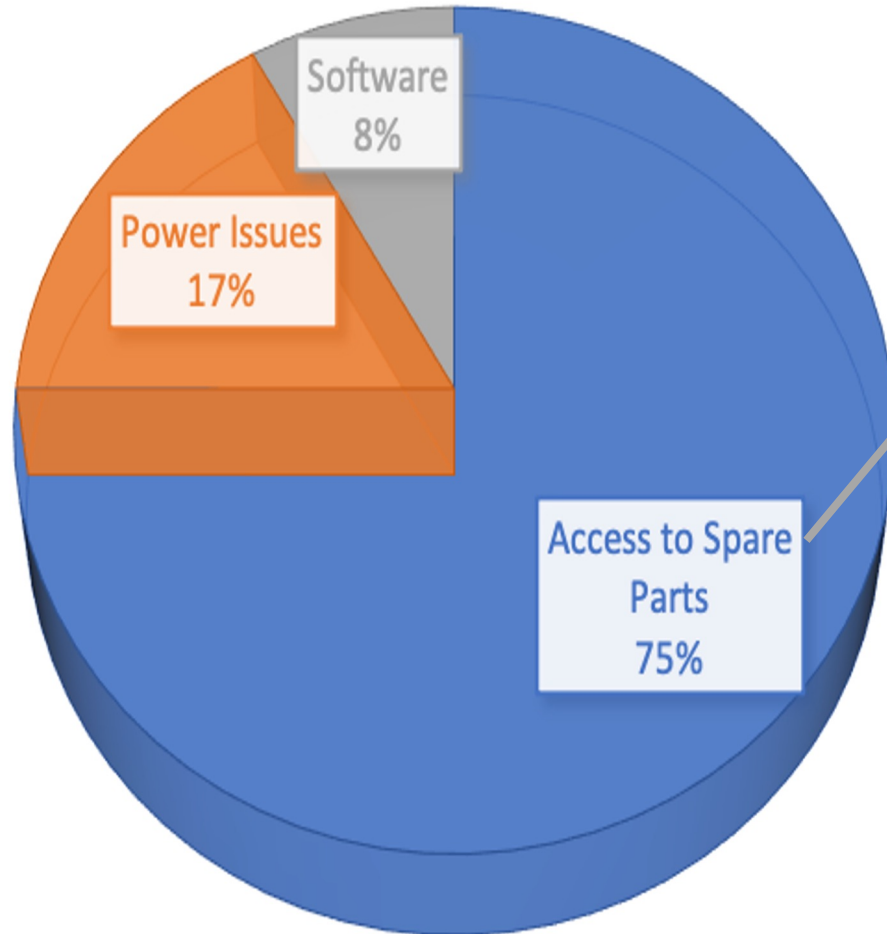
Failure statistics

- Not all failures and repairs are created equal.
- Africa has far longer repair times than in the UK, USA, the repair hub is normally in a different continent or South Africa and maintenance is often not to the same standard
- MLC, Vacuum system, RF Source and the electron gun are the largest contributor to machine downtime
- ITAR focussed on solving the downtime issues in these components.



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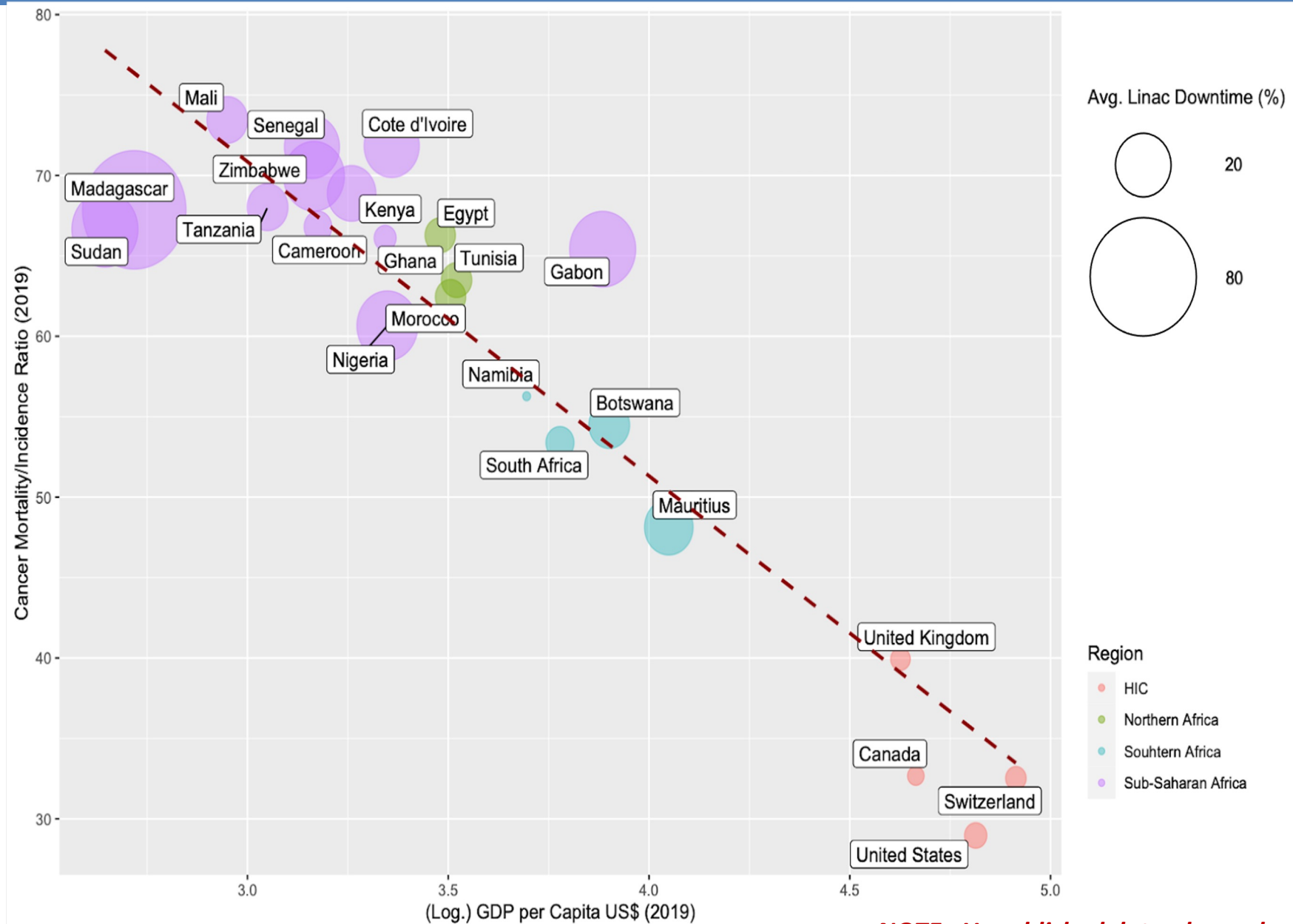
Overall Reasons For LINAC Downtime from Survey



- **69%** don't have access to spare **RF Sources**.
- **65%** don't have access to spare **Vacuum Pumps**.
- **63%** don't have access to spare **Electron Guns**.
- **32%** don't have access to spare **MLCs**.

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



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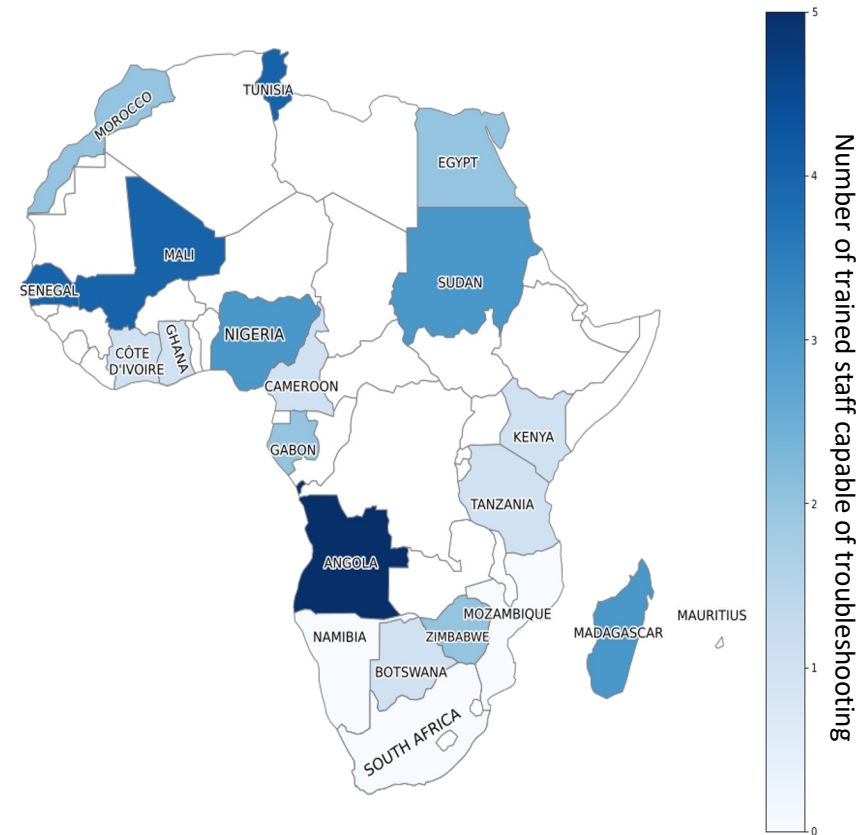
Education and Internet Connectivity

Are staff trained to troubleshoot the LINAC?

- **20/27** (74%) African facilities have staff who have attended a formal training course.
- **18/19** (95%) are supplied by the manufacturer, either on-site or online.

How fast is the internet connection?

- **28/30** (93%) African facilities have a medium or high internet speed (kb/s - Mb/s).
- Bandwidth may vary dramatically between facilities.



A choropleth map of the number of trained staff capable of troubleshooting

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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 m².
- 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.

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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

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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	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 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	<ul style="list-style-type: none">• 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 that have happened
 - Can we simplify the MLCs

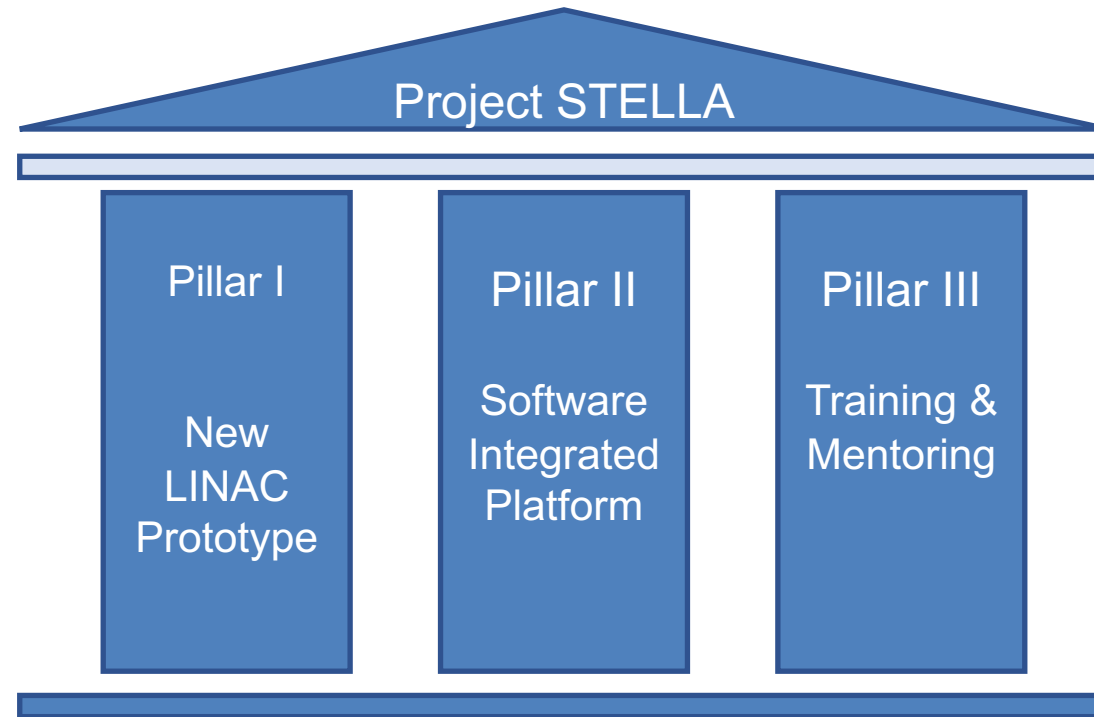
Where are we now?

- **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** for the radiotherapy system to enable technical design and prototyping in next phase
- **Currently securing funding for building and testing prototype**

STELLA-CDR 2021

- A suitable Low-energy Linear **electron accelerator** is being developed which matches identified needs, incorporating **modern optimization processes** and technologies able to provide **robust operation and modularized implementation**:
 - **Electron beam source**
 - **Linear accelerator**
 - **RF power source**
 - **Beam delivery system**
- Developing a prototype solution for a **cost-effective treatment**:
 - **Simpler installation**
 - **Robust operation**
 - **Easier to maintain**
 - **Reduced cost**
 - **Intelligent Control: Remote diagnostics and fault/breakdown detection**

STELLA: A Unique Collaboration



Project STELLA is **re-imagining** all aspects of the **delivery of RT**, its **associated systems**, **advancing science and informatics** as part of the overall delivery of cancer care including consideration of **capacity building** and the **unique challenges in LMICs**



International
Cancer
Expert Corps



Science and
Technology
Facilities Council



UNIVERSITY OF
OXFORD



Parallel survey in Africa since Linacs alone are not the answer

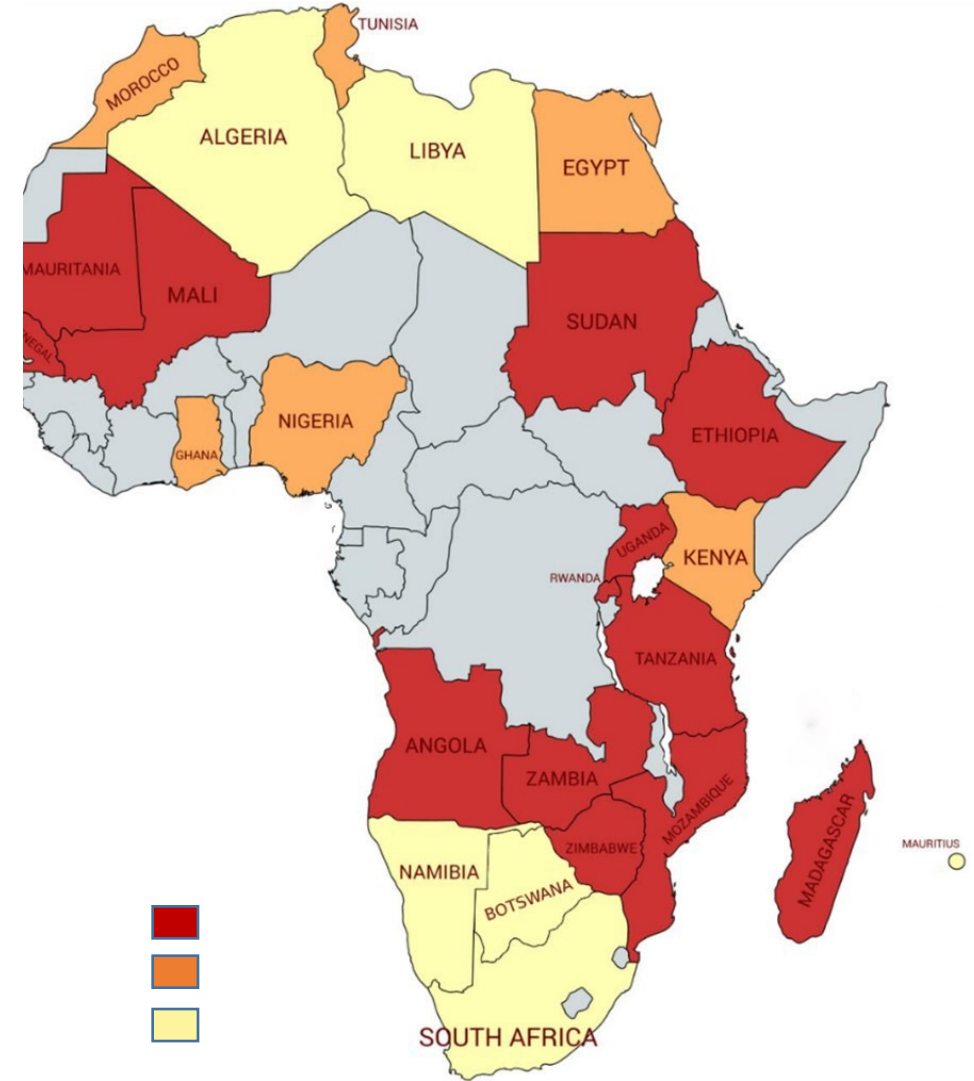
- From your current perspective, what are the three most important problems/challenges that you and others in radiation therapy in your country are facing?
- How do you see the physical infrastructure in your country changing over the next 5-10 years?
- What radiation therapy system(s) do you have at this time?
- What additional radiation therapy technologies would you like to have at your facility?
- Infrastructure and environment
- Adequacy of your workforce (staffing)
- Education and training
- Procurement and Funding

RT Services Survey: responses from 26 Countries

We are aware that increase in RT equipment means there is need to have capacitance building to operate these new facilities

We are assessing what is needed and what seems to work well and what needs to be done to meet the increasing personnel?

We are looking at the level of education and training that is available and what is needed



Challenges highlighted from the second survey

- 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.
- Need to improve power: Power outages are quite detrimental and may shorten the lifetime of electrical equipment, eventually resulting in permanent damage.
- 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 have indeed been repeatedly highlighted by professionals in LMICs, indicating the need for local investment in human resources.
- Lack of experts: 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

ICEC : trusted network, mentorship, training

...PEOPLE, technologies, knowledge, methods



Surbhi
Grover



Botswana 2019 Project STELLA
A Partnership to Transform Global Cancer Care



Norm
Coleman



Manjit
Dosanjh

Taofeeq
Ige

Ultimate Goal

- Robust, modular, reliable and easier 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
- With the aim to
 - ✓ Improve patient through-put
 - ✓ Increase effectiveness
 - ✓ Decrease running cost, staff cost, machine cost
 - ✓ Expand access to RT

ICEC in parallel is working on solutions for Expertise, Capacity, Capability

This work was possible only with the collaboration of
ICEC, ITAR, STELLA, SEEIIST and ART teams

Especially to:

- Deepa Angal-Kalinin and Peter MacIntosh - UKRI STFC and their team
- Graeme Burt - Lancaster University and team
- Norm Coleman, Donna O'Brien, and David Pistenmaa and Eugenia Wendling - International Cancer Expert Corps Team
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- Ugo Amaldi, Paul Collier and Walter Wuensch
- Suzie Sheehy, Oxford and Melbourne
- SEEIIST and ART Study collaborators

Thank you for listening