Introduction to Computer-Aided Detection (CAD) and Ultra-Portable X-Ray

MODULE 2

Stop TB Partnership

INTRODUCTION

This module explores new tools for TB screening: delving into detail on the use of computer-aided detection (CAD) and introducing ultra-portable X-ray (UP-XR) systems. The module also describes how the two systems may be integrated and their individual and combined utility for TB screening and triage.

Course Outline

- → Understanding, interpreting, and using CAD output
- → Using CAD in TB screening programs
- → Product features of CAD4TB
- → Recap of basic radiology and types of X-ray system
- → Introduction to ultra-portable X-ray and the Delft Light
- → How to use CAD and ultra-portable X-ray together
- Summary

Learning Objectives

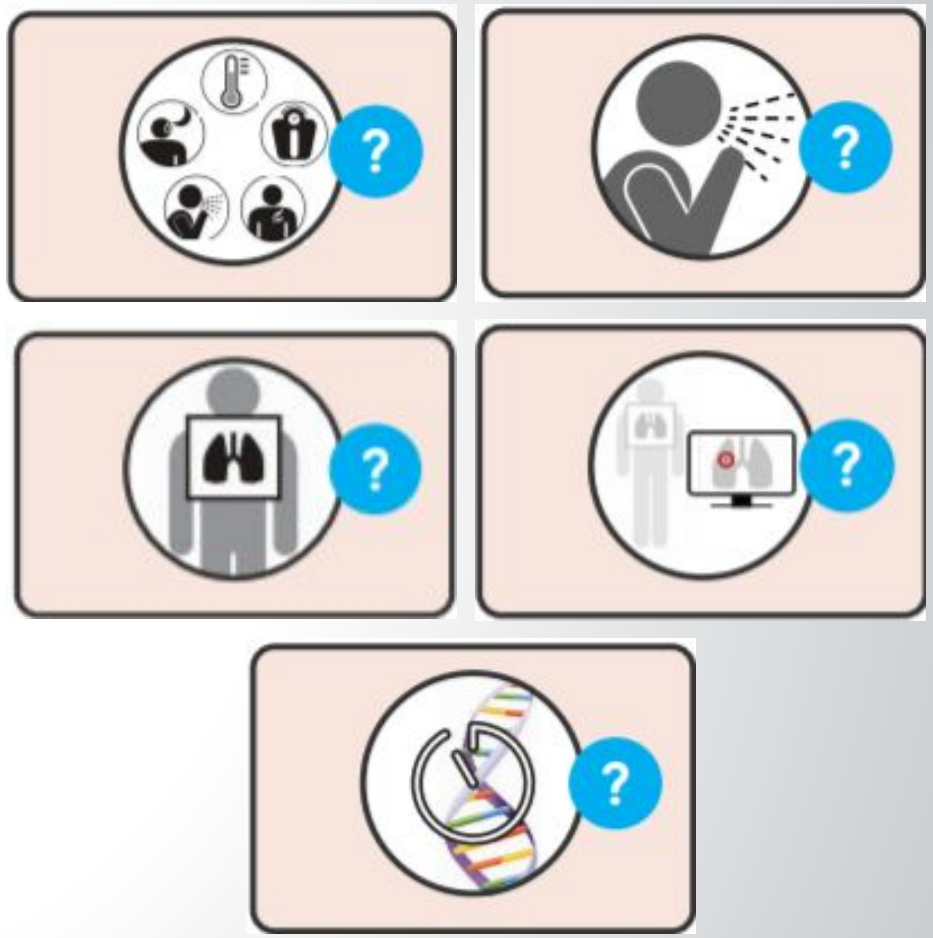
By the end of this module, participants should be able to:

- Describe what CAD technology is and how it can be applied in TB screening.
- Know the key features of CAD products, especially of CAD4TB.
- Understand what is meant by “ultra-portable X-ray” and the advantages and disadvantages of using it.
- Detail the components and pricing of the Delft Light ultra-portable X-ray system.
- Understand the different ways CAD and ultra-portable X-ray can be integrated for use in TB screening and triage.

Reminder: WHO Guidelines on Systematic Screening

In general populations without HIV aged 15 years and older in which TB screening is recommended:

- Systematic screening for TB disease may be conducted using a **symptom screen**, **chest X-ray with computer-aided detection (CAD) software,** or **molecular WHO-recommended rapid diagnostic tests,** alone or in combination.
- **CAD software** may be used in place of human readers for interpreting digital chest X-rays for screening and triage for TB disease.



Computer-Aided Detection (CAD) Software for Screening and Triage of TB

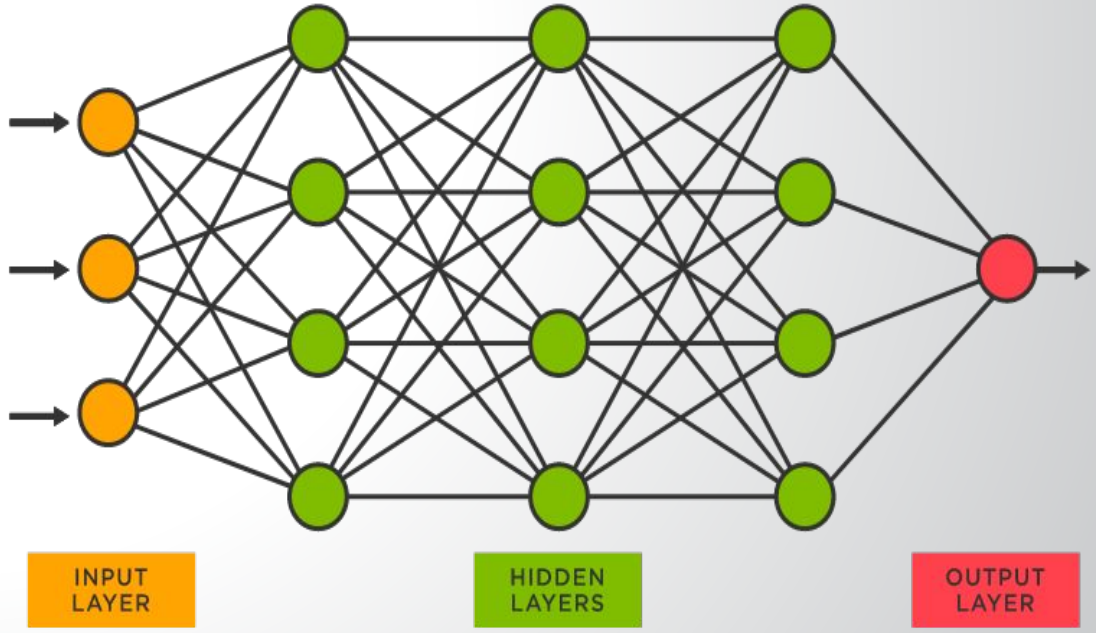
Overview of CAD as a Tool to Screen and Triage TB

Computer-aided detection (CAD) improves the detection of TB by circumventing inefficiencies in the interpretation of chest X-ray (CXR) images, automating and standardizing X-ray interpretation, and supplementing existing human health workers.

CAD uses a type of artificial intelligence known as **deep learning neural networks** to read chest x-rays and identify signs of TB. Deep learning neural networks take inspiration from the human brain to allow machines to learn to perform specific tasks.

In March 2021, WHO recommended the use of CAD as an alternative to human readers to interpret CXR for screening and triage of TB in individuals aged 15 or over.

CAD is **not** recommended nor validated for use as a **diagnostic** tool.



CAD Output

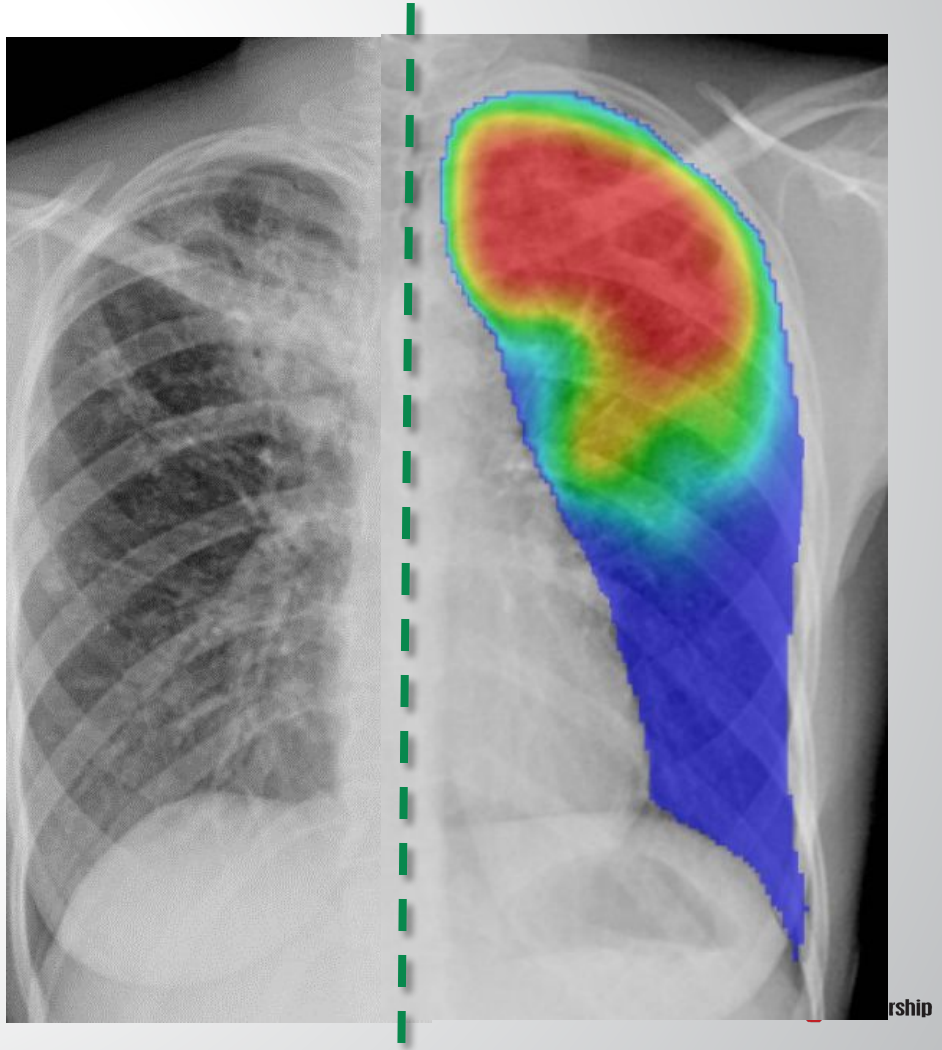
CAD receives digital X-ray or digitized analogue X-ray films and uses artificial intelligence to analyze them for signs of TB. This process can be done with or without an Internet connection.

In general, for **each** X-ray received, CAD provides:

- An **abnormality score** (between 0–1, or 0–100). High abnormality score = higher likelihood of TB.
- A **heatmap** showing where abnormalities are detected by CAD.
- Some CAD products provide a **binary classification** ("TB-related abnormalities present" or "TB-related abnormalities absent").

These can be summarized in a **customizable report** format.

CAD products increasingly also offer a number of **add-on features** such as **data dashboards.**



How to Understand the CAD Output

Abnormality score

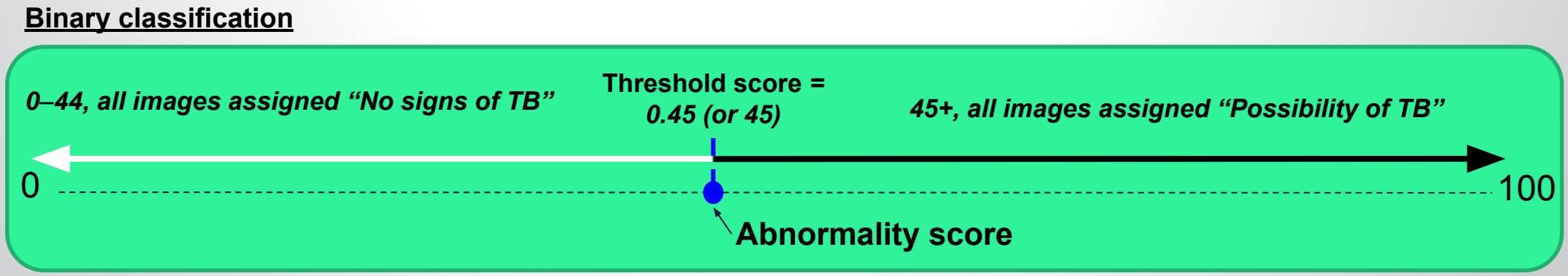
Abnormality scores are a **continuous output (between 0–1 or 0–100)** and represent the **likelihood** of TB being present in a particular X-ray.

However, abnormality scores are **not** probability and are not standardized across CAD software, so:

- An image with a score of 0.4 is **not** twice as likely to contain TB as an image with a score of 0.2
- A score of 0.5 from CAD product A does **not** mean the same as a score of 0.5 from CAD product B.

Binary classification

Selecting a **threshold score** translates this continuous output into a **binary classification: "Possibility of TB" // "No signs of TB."** All X-ray images higher than the threshold are assigned the "Possibility of TB" classification.



Detecting Non-TB Abnormalities by CAD

- Increasingly, more and more CAD products can function far more like a human radiologist than the simple TB-detecting tools from which they have evolved.
- Some TB-CAD software products can classify common CXR abnormalities, such as calcification, cardiomegaly, mass, nodule, and pleural effusion, as well as bone and heart abnormalities.
- However, there is a lack of independent evaluation data on the performance of CAD for differential diagnosis and how accurately it localizes abnormalities.

Validation of CAD for Interpreting Digital X-ray

In 2020, the WHO Guidelines Development Group independently evaluated three independent evaluations of three different CAD software for detecting bacteriologically confirmed TB in a range of populations and settings.

The results show the variability of both human readers and CAD software programs across different settings and populations.

Type of case/reader	Sensitivity	Specificity
WHO target product profile	**> 0.90**	**> 0.70**
Screening use case		
CAD software	0.90–0.92	0.23–0.66
CXR with human reader	0.82–0.93	0.14–0.63
Triage use case		
CAD software	0.90–0.91	0.25–0.79
CXR with human reader	0.89–0.96	0.36–0.63

Source: WHO Consolidated Guidelines on Tuberculosis

Conclusion: There is **substantial overlap** in the sensitivity and specificity of human readers and CAD software, suggesting that there is **little difference** between the two.

Further:

- In many settings, health providers **without training in radiology** are tasked with interpreting chest X-rays.
- These readers may not be as highly skilled as the "gold-standard" readers used for comparison in the evaluations.
- So, CAD may perform even more favorably in comparison.

Validation of CAD for Interpreting Digital X-ray

Tuberculosis detection from chest x-rays for triaging in a high tuberculosis-burden setting: an evaluation of five artificial intelligence algorithms

Zhi Zhen Qin, Shahriar Ahmed, Mohammad Shahnewaz Sarker, Kishor Paul, Ahammad Shafiq Sikder Adel, Tasneem Naheyan, Rachael Barrett, Sayera Banu*, Jacob Creswell*

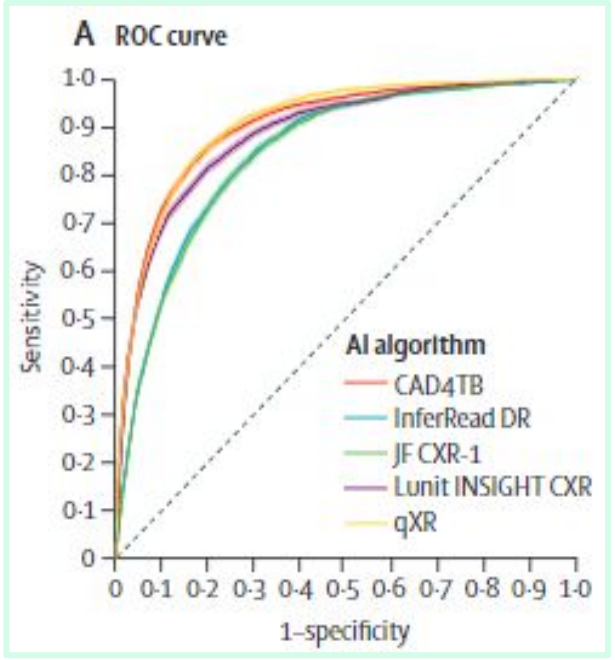
In the **latest head-to-head comparison** of the overall performance of the newest version of five commercial CAD software products, **all CAD products:**

- Significantly outperformed local radiologists
- Were able to halve the number of Xpert tests required, while maintaining high sensitivity (>90%)
- Performed worse in older age groups and those with a history of TB

Comparing different CAD products

The performance of different CAD products can be compared by constructing a **Receiver Operating Characteristic (ROC) curve** and calculating the **area under the curve (AUC).**

CAD performance ranking from high to low:



CAD product	AUC
qXR	90.81%
CAD4TB	90.34%
Lunit INSIGHT CXR	88.61%
InferRead DR Chest	84.90%
JF CXR-1	84.89%

Where does CAD fit in the TB Screen Algorithm?

CAD can be used **with** trained human readers as a decision support tool or **in place of** trained human readers.

Alongside human readers

CAD can also work **with** human readers:

- Helping radiologists to optimize their workflow
- Alerting human readers to abnormal images requiring prioritization
- Providing reporting assistance
- Providing quality control
- Performing pre-reading assistance

In place of human readers

WHO recommends CAD to **replace** human readers in two broad situations in individuals aged 15 and older:

Screening: CAD can be a valuable tool for screening asymptomatic individuals without significant risk factors (e.g., active case finding).

Triage: CAD can be useful in identifying TB in individuals with TB symptoms, risk markers, or other positive test results (e.g., in health care facilities).

The CAD software used must be to the same standard as those evaluated by the WHO Guidelines Development Group.

In either situation, there is insufficient evidence to support the use of CAD with CXR alone for TB diagnosis.

Where does CAD fit in the TB Screen Algorithm?

There are a number of **advantages** to either technique.

Alongside human readers

The entire output of CAD, or parts of the output, may be used to inform triage decisions by trained human readers alongside clinical information.

Advantages:

- CAD can be used to supplement decision-making, potentially improving on human reader performance.
- While human readers' judgement can be used:
  - Where a CAD reading is not conclusive/near the threshold score
  - In populations where CAD is not approved (e.g., in children <15 years)
  - Alongside CAD for reading X-rays that show a non-TB abnormality

In place of human readers

The CAD output may be used by trained non-radiologist personnel to decide the triage outcome. A threshold score is set, and everyone assigned a CAD score higher than this receives confirmatory diagnostic testing.

Advantages:

- Increased access to chest X-ray where there is a scarcity of trained human readers or no human readers
- May be used to rapidly triage people by non-radiological personnel in high throughput settings
- CAD does not become exhausted when reading large quantities of images
- No intra- and inter-reader variability

Where is CAD used in the project TB screening algorithm? – for NTP to customize

- Suggested information:
  - Will CAD be used alongside or instead of human reader?
  - Who will receive and review the output?
  - What approach will be taken to screening children <15 years?

PRODUCT FEATURES OF CAD4TB

CAD4TB

Latest version: Version 7
Certification: CE marked, class IIb

DELFT IMAGING

Input

- Postero-anterior (PA) digital chest X-rays
- Can be used to read images from any kind of chest X-ray machine
- Chest X-ray image format: DICOM, PNG, JPEG
- Using an app (SNAP4CAD), analog X-ray images can be used as well

Output

For each X-ray read, CAD4TB provides:

- Abnormality score for TB
- Binary classification “TB” or “Not TB”
  - Customizable default threshold score: 60
- Heat map

For the screening program, CAD4TB provides a full report with screening results. Advanced management dashboard to monitor screening progress also available.

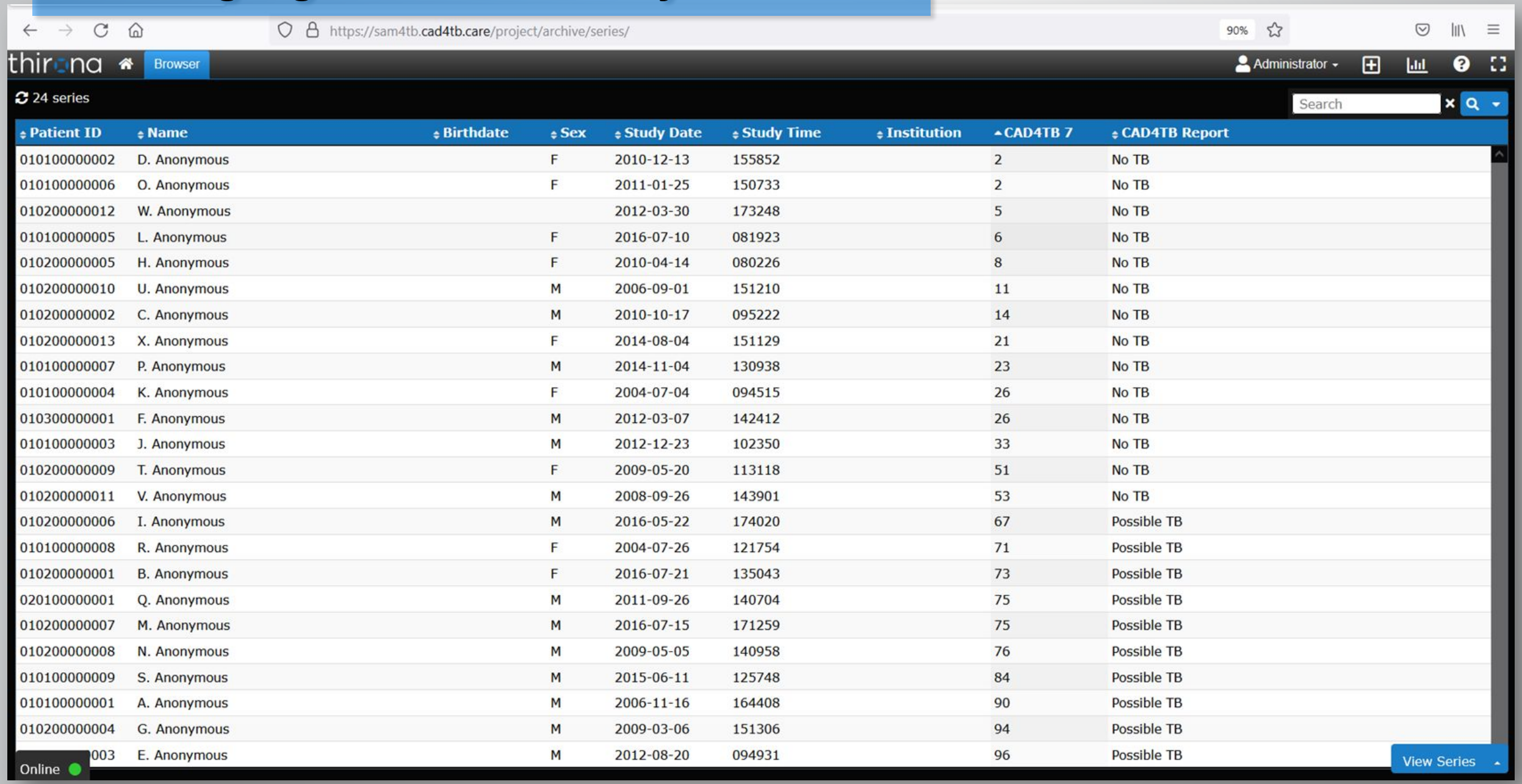
Deployment

Online, offline, hybrid (offline use with online synchronization)

PACS: CAD4TB is a mini PACS system that can store up to 30,000 x-ray images.

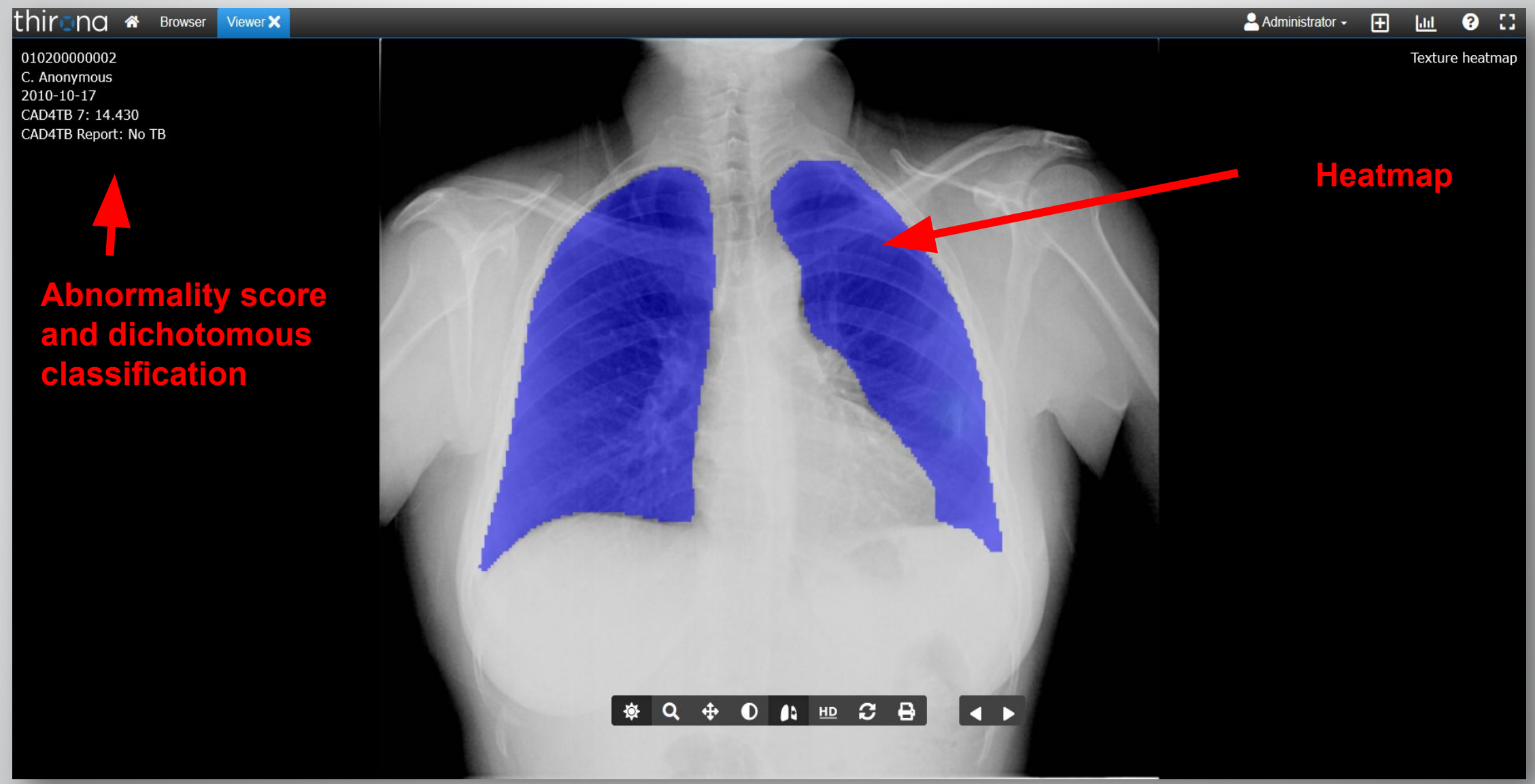
If the user has their own PACS system, CAD4TB output (score, report and heat map) can be send to the PACS system.

Screening register in CAD4TB system



Patient ID	Name	Birthdate	Sex	Study Date	Study Time	Institution	CAD4TB 7	CAD4TB Report
010100000002	D. Anonymous		F	2010-12-13	155852		2	No TB
010100000006	O. Anonymous		F	2011-01-25	150733		2	No TB
010200000012	W. Anonymous			2012-03-30	173248		5	No TB
010100000005	L. Anonymous		F	2016-07-10	081923		6	No TB
010200000005	H. Anonymous		F	2010-04-14	080226		8	No TB
010200000010	U. Anonymous		M	2006-09-01	151210		11	No TB
010200000002	C. Anonymous		M	2010-10-17	095222		14	No TB
010200000013	X. Anonymous		F	2014-08-04	151129		21	No TB
010100000007	P. Anonymous		M	2014-11-04	130938		23	No TB
010100000004	K. Anonymous		F	2004-07-04	094515		26	No TB
010300000001	F. Anonymous		M	2012-03-07	142412		26	No TB
010100000003	J. Anonymous		M	2012-12-23	102350		33	No TB
010200000009	T. Anonymous		F	2009-05-20	113118		51	No TB
010200000011	V. Anonymous		M	2008-09-26	143901		53	No TB
010200000006	I. Anonymous		M	2016-05-22	174020		67	Possible TB
010100000008	R. Anonymous		F	2004-07-26	121754		71	Possible TB
010200000001	B. Anonymous		F	2016-07-21	135043		73	Possible TB
020100000001	Q. Anonymous		M	2011-09-26	140704		75	Possible TB
010200000007	M. Anonymous		M	2016-07-15	171259		75	Possible TB
010200000008	N. Anonymous		M	2009-05-05	140958		76	Possible TB
010100000009	S. Anonymous		M	2015-06-11	125748		84	Possible TB
010100000001	A. Anonymous		M	2006-11-16	164408		90	Possible TB
010200000004	G. Anonymous		M	2009-03-06	151306		94	Possible TB
[illegible]003	E. Anonymous		M	2012-08-20	094931		96	Possible TB

CAD4TB viewer window showing heatmap and score– no TB



CAD4TB viewer window showing heatmap and score– possible TB

CAD4TB symptom and GXP report

Patient Information

PatientID	010100000001
Name	A. Anonymous
Gender	Male
Date of birth	1971-10-12

010100000001

Patient Symptom Information

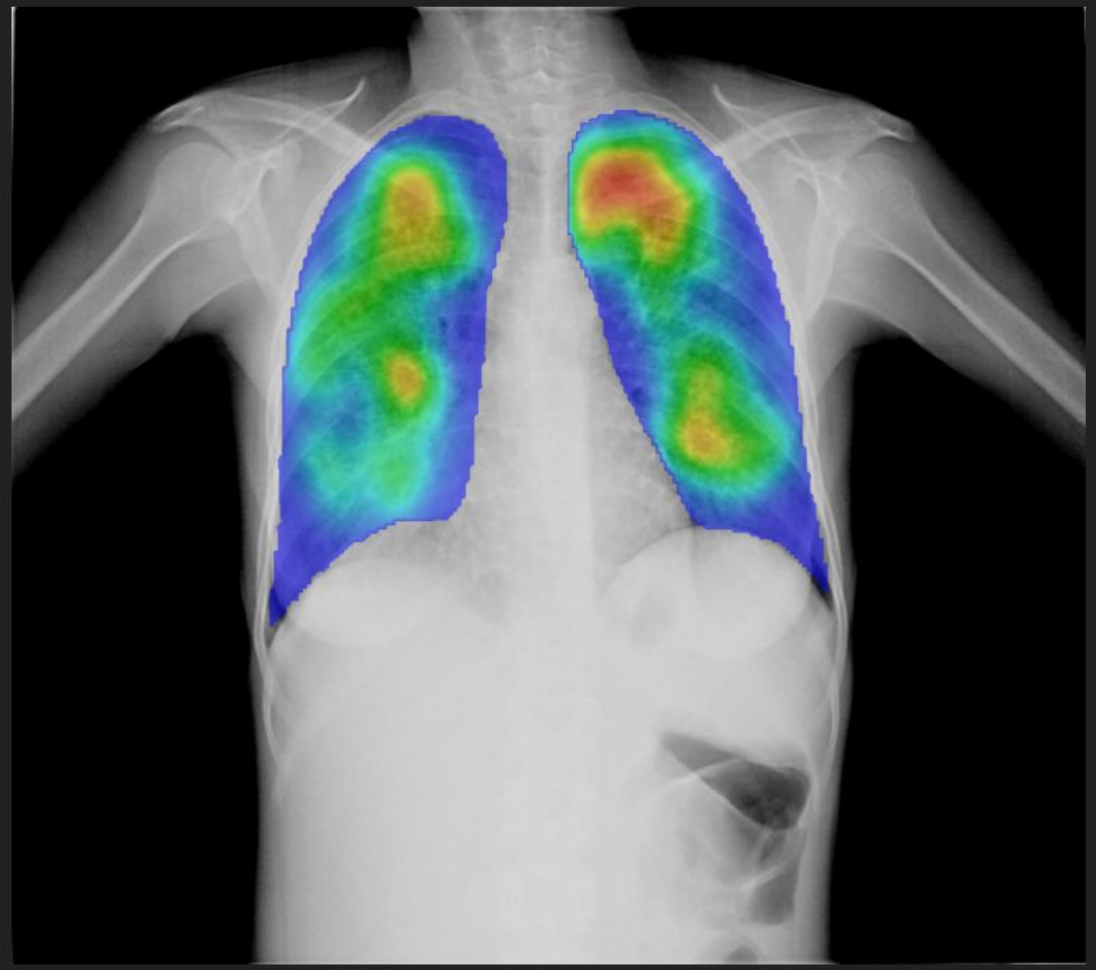
Cough:	Yes (3 days)
Fever:	Yes (7 days)
Shortness of breath	No
Household TB:	No

Patient lab results

GeneXpert:	MTB Detected
RIF resistance:	Not detected

CAD4TB Assessment

CAD4TB 7	90
CAD4TB Report	Possible TB



Online

CAD4TB insights module showing gender, age and score distribution

RECAP ON BASIC RADIOLOGY

Types of X-ray Technology

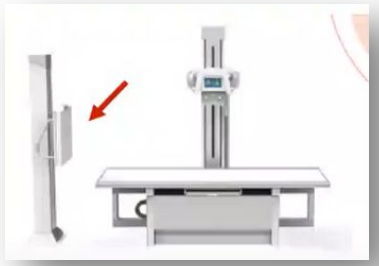
Digital radiography (DR)

Digital generator and detector package

- Latest development in X-ray technology
- **Image receptor:** Solid state detector
- **Automatic image processing** using provided software
- Digital output (DICOM, JPEG)
- **Integration** with PACS possible due to digital image format
- **Reading by CAD** is automatic
- **High image quality** and better radiation dose efficiency
- **Portable** systems available
- **Rapid image** generation

Retrofit and computed radiography (CR)

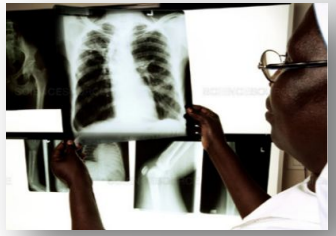
Existing analog generator and digital detector or CR reader



- **Image receptor:** New digital detector (retrofit) or digitizer/CR reader (CR)
- **Image processing** can be automatic using software (retrofit) or need digitization using CR reader (CR)
- **Output** is digital (DICOM,JPEG)
- **Integration** with PACS possible due to digital image format
- **Reading by CAD** only possible after digitization
- **Lower** radiation dose efficiency than DR systems

Analog radiography

Analog generator and manual image processing



- Traditional method of X-ray imaging
- **Image receptor**: Analog film
- **Wet processing** using trained human resources to generate final image
- **Need trained human reader** to interpret film, **difficult to use in the field**
- **Output** is the X-ray film
- **Integration** with PACS not possible
- **Reading by CAD** only possible after digitization
- **Lower** throughput possible due to complex image processing
- **Poor** radiation dose efficiency

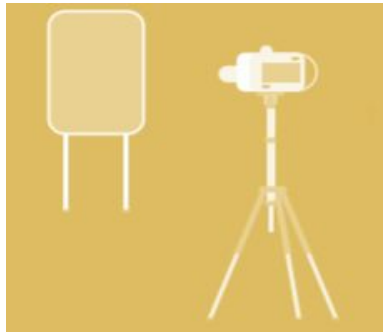
INTRODUCING ULTRA-PORTABLE X-RAY

Introducing Ultra-portable X-ray (UP-XR)

Types of radiographic systems:

Stationary:
High workload, stable electricity, general radiology, delivers high image quality

Mobile:
Moderate workload, intermittent power supply, can be moved/rolled around, high image quality



Ultra-portable:
Low to moderate workload, battery powered, acceptable image quality, low radiation, field friendly

Advantages of UP-XR:

- De-centralize X-ray screening and expand access
- Built in battery operated
- Low weight—reduced physical strain on staff carrying or setting up the system
- Reduced radiation exposure
- Image quality reportedly comparable to stationary X-ray

Disadvantages of UP-XR:

- Limited battery life when operating devices without connection to electrical mains
- Low to medium throughput
- More portable detector and generator stands may be more manual to operate

Stop TB Partnership

DELFT LIGHT

Core System

- CE-marked for Medical Device Systems and Procedure Packs
- The **generator, detector, and console** all have **built-in Li-ion** batteries, allowing use in the field without electricity for limited periods of time.
- The **generator** is provided with a **handswitch** to allow the remote operation of the system from a distance of 3 meters.
- The aluminum **generator stand** is capable of 360-degree rotation and can be dismantled for transport in its own bag (also supplied).
- The **detector panel hanger** (VersariX) can be used to hang the detector from improvised mounts (walls or doors) and can be adjusted vertically (40 cm–200 cm range).
- The **console** has image processing and manipulation software installed and also provides the link to CAD4TB.

The **core system** consists of an **X-ray generator TR 90/20 (manufactured by Mikasa), X-ray detector CXDI 702-C with accompanying application software (Canon NE) and HP laptop**, and accompanying software package.

Detector

Generator

Console

Generator stand

Detector panel hanger

Accessories

- **Backpack,** which is able to transport all Delft Light components except the generator stand (which comes with its own bag)

Radiation protection equipment

- Including 1 **protective lead apron,** 10 **shock detection stickers,** and 5 water-resistant, durable and portable **radiation warning signs**, mentioning radiation hazard and pregnancy

Supplementary and external power sources

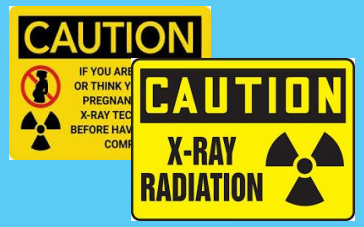
- **Replacement detector batteries (x2) and chargers** are provided with the system. The charger recharges two batteries simultaneously.

- **Solar panel and power bank** to recharge all electrical components in screening situations without access to electricity

Alongside the **core system,** accessory equipment is provided to ensure the smooth and safe operation of the system in the field, including;

Backpack

Radiation protection equipment



Radiation hazard signs


Lead apron

Shock stickers

Supplementary and external power sources


MobiSun solar panel with built-in power bank


Exchangeable generator and detector batteries with battery charger

Summary: GDF's Ultra-portable Package

Generator

Included:

- X-ray generator with handswitch and detector
- Generator stand and detector panel hanger
- X-ray console laptop
- CAD4TB software, offline box, tablet
- Backpack
- Lead apron, shock stickers, radiation hazard signs
- Replacement detector batteries, battery charger, solar panel

Console

Generator stand

Detector panel hanger

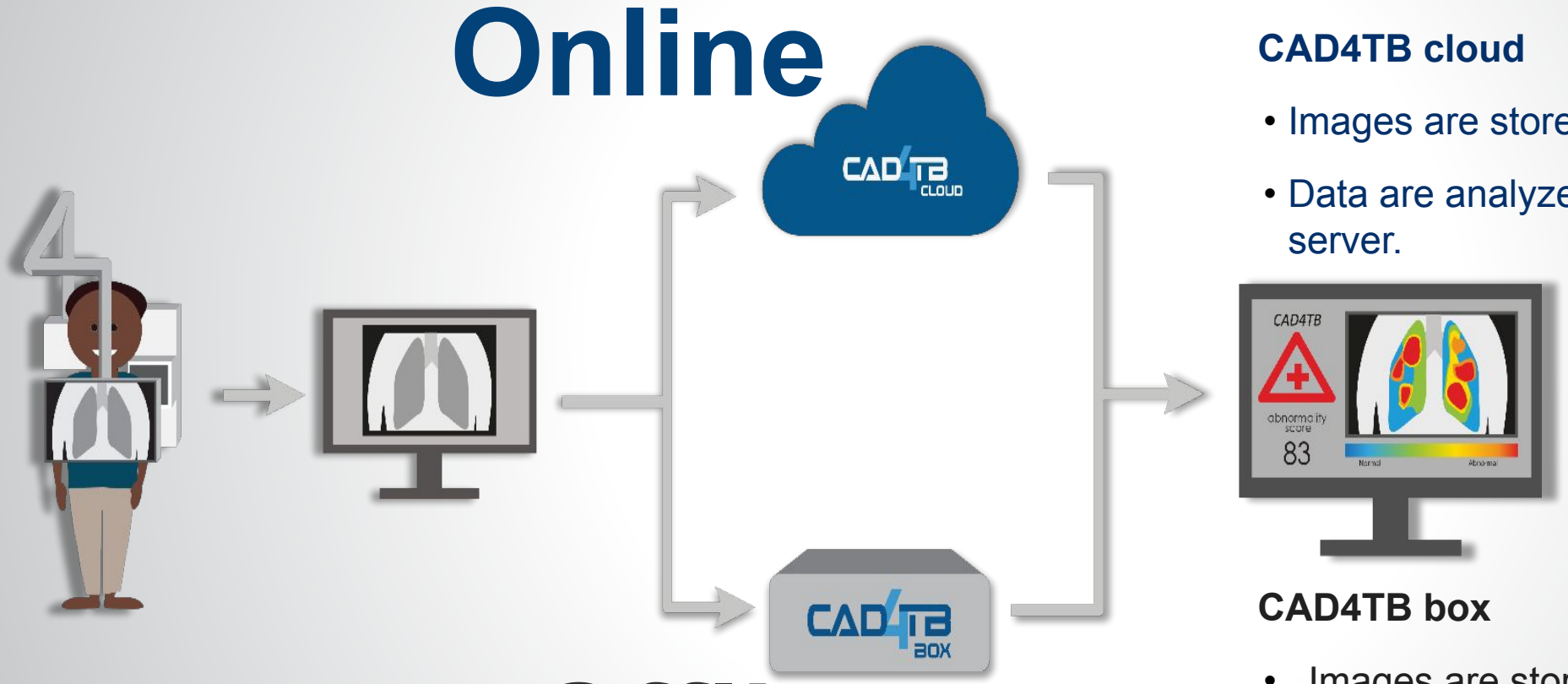
NOT included:

- Thyroid shield
- Lead shield

Detector

Connection with CAD4TB

How Delft Light connects to CAD4TB depends on whether the system is used online or offline.



CAD4TB cloud

- Images are stored online.
- Data are analyzed through a secured data server.

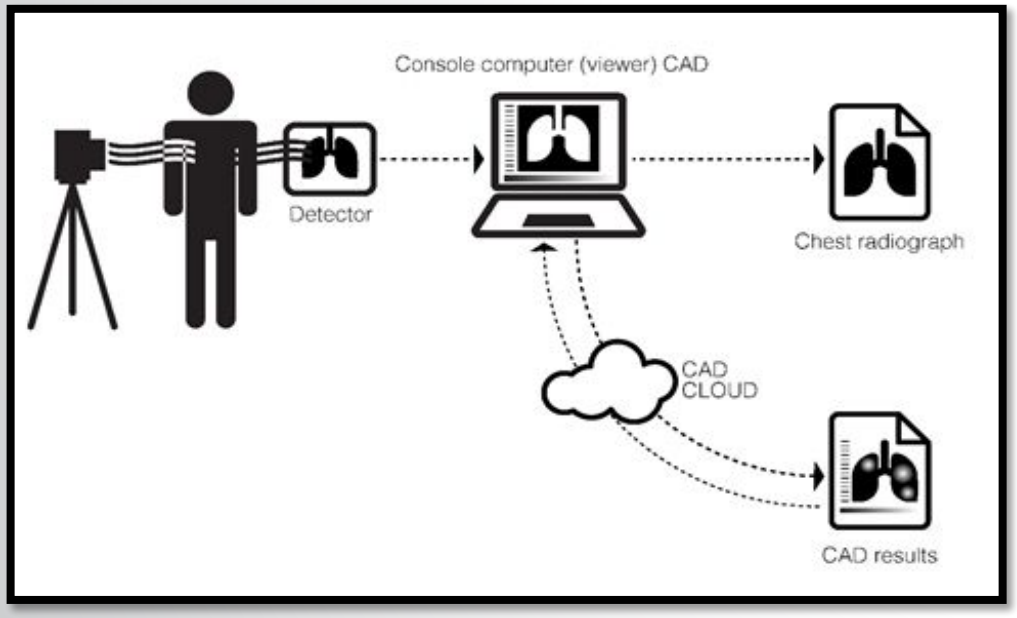
CAD4TB box

- Images are stored locally.
- Images are synchronized with CAD4TB cloud when Internet is available.

Connection with CAD4TB

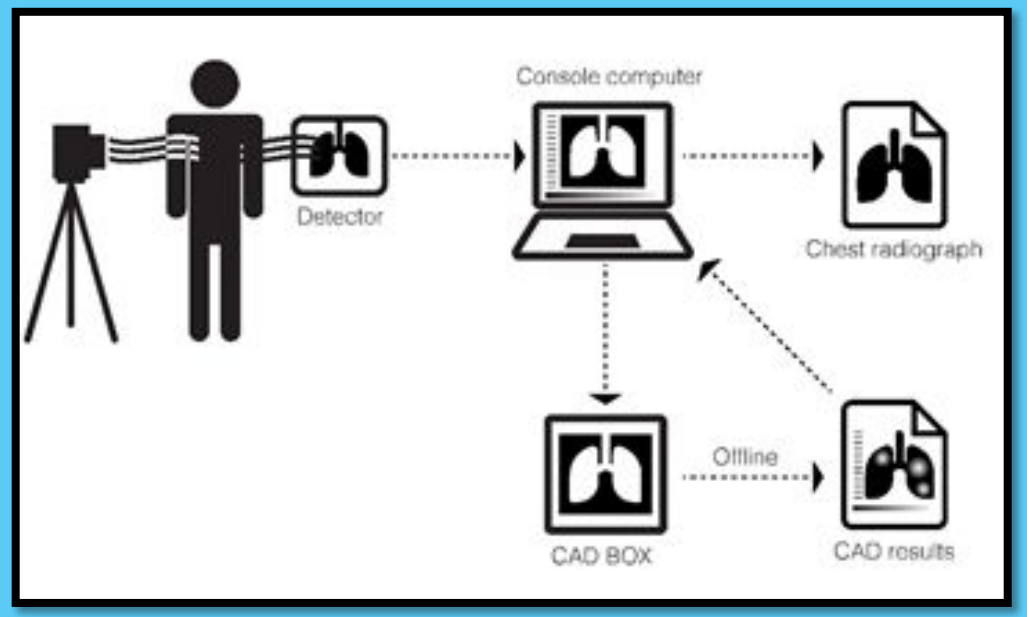
Online

- The Delft Light console receives CXR images from the detector and is used to upload them to the CAD cloud containing the artificial intelligence.
- Results from CAD4TB are shown on the CAD4TB web platform, accessed from Internet browsers.



Offline

- The CADTB box (pictured) containing the artificial intelligence is connected to the console laptop and analyzes the CXRs it receives from the laptop.
- Results from CAD4TB are shown on the console laptop.



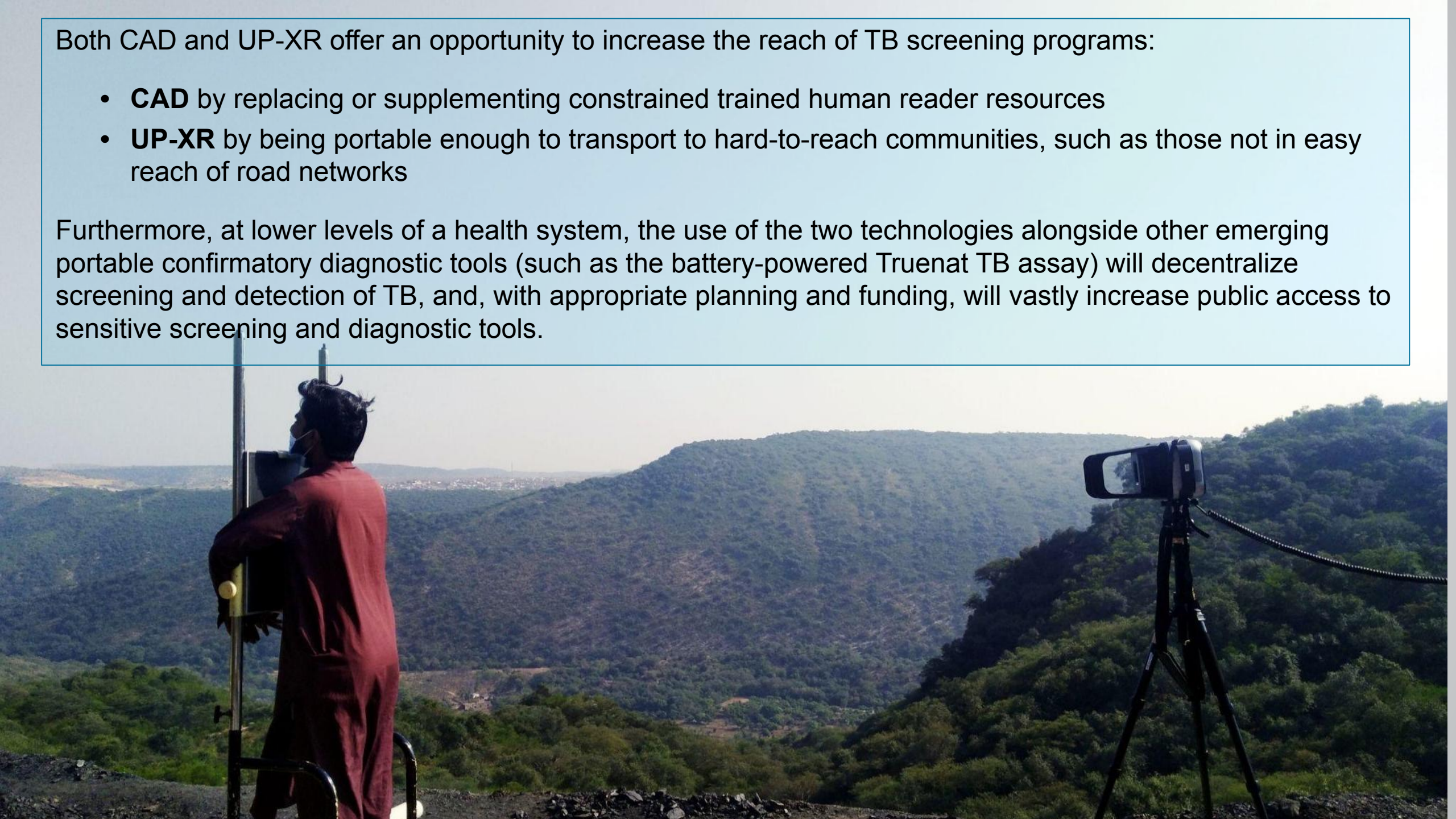
Hybrid

Hybrid setup uses the offline equipment configuration but with pre-configured synchronization of data to a server when the Internet connection is restored after periods of operating offline.

Both CAD and UP-XR offer an opportunity to increase the reach of TB screening programs:

- **CAD** by replacing or supplementing constrained trained human reader resources
- **UP-XR** by being portable enough to transport to hard-to-reach communities, such as those not in easy reach of road networks

Furthermore, at lower levels of a health system, the use of the two technologies alongside other emerging portable confirmatory diagnostic tools (such as the battery-powered Truenat TB assay) will decentralize screening and detection of TB, and, with appropriate planning and funding, will vastly increase public access to sensitive screening and diagnostic tools.



Summary

- CAD software is an interpretation tool that uses artificial intelligence to detect TB on chest X-rays.
- CAD software has accuracy comparable to, or even better than, human readers.
- WHO recommends CAD to be used with human readers or in place of human readers when screening the general population (>15 years old).
- UP-XR is recognized by WHO as a subtype of the portable digital X-ray.
- UP-XR systems are field friendly. They can be operated on battery alone, emit less radiation, and produce images comparable to stationary machines.
- When procured, UP-XR systems come with a complete core system and set of accessories.
- UP-XR and CAD are integrated in different ways, depending on whether use is online, offline, or a hybrid of the two.
- Together, UP-XR and CAD are an opportunity to decentralize TB screening and care.

Knowledge Check—Question 1

Two chest X-rays are taken from individuals by CAD. One is assigned a score of 80 and the other a score of 60.

Does this mean the second person is 25 percent less likely to have TB than the first?

ANSWER

No, because the CAD output is not linearly related to the probability of having TB. There is no relationship between the two scores.

Knowledge Check—Question 2

Can CAD results alone be used to diagnose TB?

ANSWER

No, CAD is not validated to diagnose TB and is not recommended by WHO to do so. Anyone with a high score on CAD should receive confirmatory diagnostic testing, for example, using Xpert or Truenat.

Knowledge Check—Question 3

What does CAD output usually include?
(Select all that apply)

- ❑ Numerical abnormality score
- ❑ Classification “Active TB,” “Healed TB”
- ❑ Heatmap

Knowledge Check—Question 4

There are four types of X-ray technology.

Can you name them?

ANSWER

Digital (DR), computed (CR), retrofit, analog

Knowledge Check—Question 5

What are some of the benefits of using ultra-portable X-ray? (Select all that apply)

- ❑ Ability to screen high-risk groups in areas difficult to reach by road
- ❑ Higher throughput compared to stationary
- ❑ Reduced radiation exposure
- ❑ Reduced physical strain on staff operating the machine