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

- → Overview of CAD as a screening tool for TB
- → Understanding, interpreting, and using CAD output
- → Using CAD in TB screening programs
- → CAD products in the GDF catalog
- → Overview of different X-ray technologies and introduction to ultra-portable
- → Ultra-portable X-ray systems in the GDF catalog
- Summary

Learning Objectives

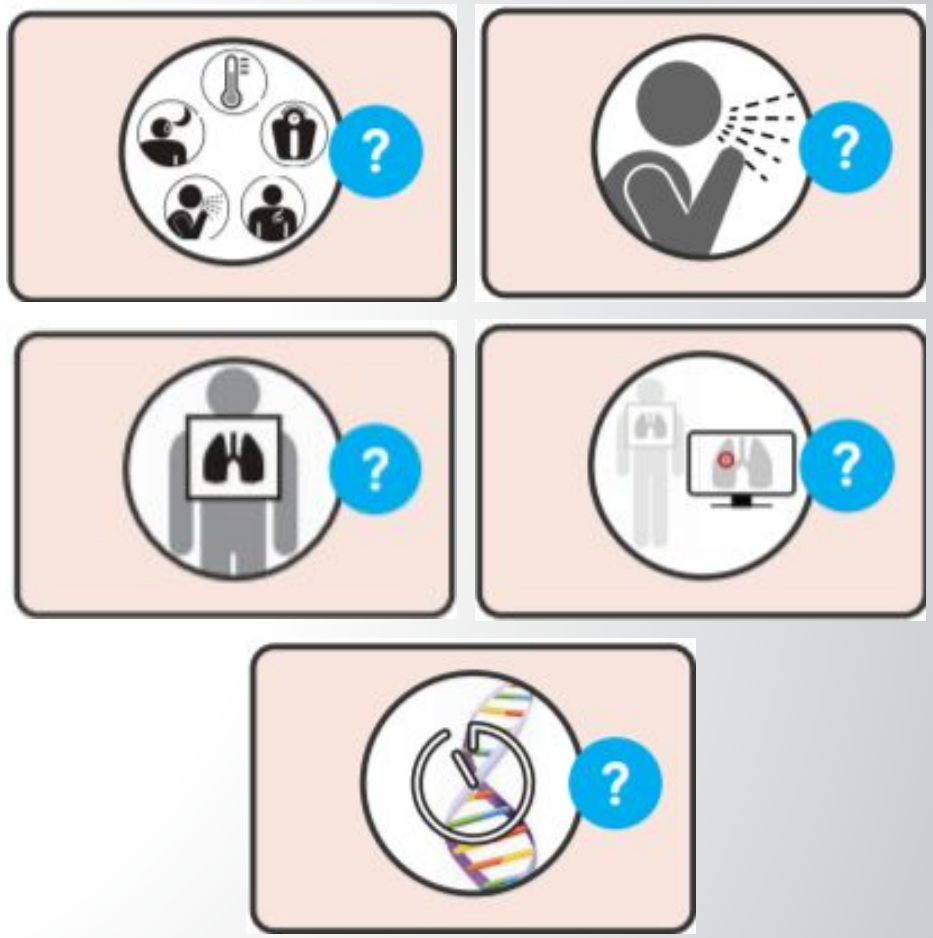
By the end of this module, participants should be able to:

- Describe what CAD technology is and how it can be applied in TB screening.
- Know the key features of the CAD products available from the GDF catalog.
- Understand what is meant by “ultra-portable X-ray” and the advantages and disadvantages of using it.
- Detail the components and pricing of the ultra-portable X-ray systems available in the GDF catalog.
- 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

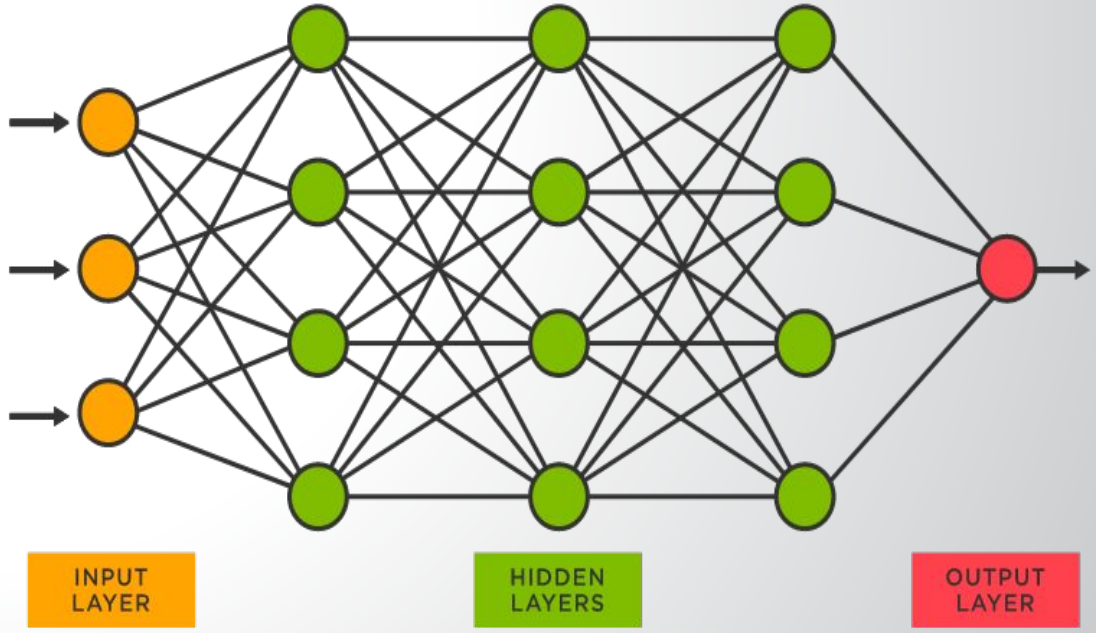
Overview of CAD as a Tool to Screen and Triage TB

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

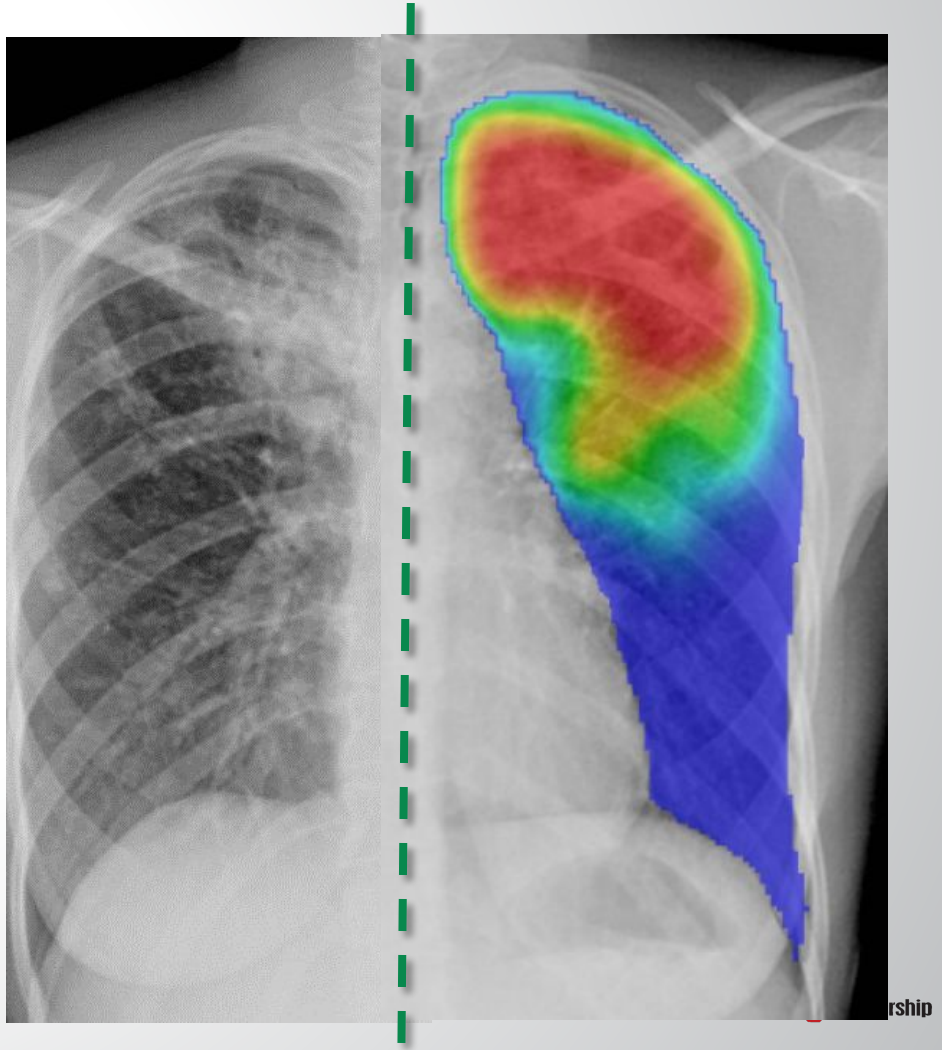
CAD receives digital X-ray or digitized analogue X-ray films and uses artificial intelligence to analyze them for signs of TB. This process can be done with or without an Internet connection.

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.**



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.

CAD Landscape Analysis

A recent landscape report identified **28 CAD** developers and **12 TB-specific** products already on the market. At least **7 of these have CE-marks.**

Common characteristics include:

- Mostly suitable for people >15 years old
- Read postero-anterior DICOM images
  - Antero-posterior images and other image formats (JPEG, PNG) also widely accepted
- Summarize results in a radiologist-style report
- Can be deployed online (cloud) and offline
- Integration with PACS and other clinical information systems
- Ability to be deployed with most mainstream X-ray systems

ai4hlth.org is a regularly updated online marketplace of CAD products for TB. 2021 update coming soon.

CAD Landscape Analysis

A recent landscape report identified **28 CAD** developers and **12 TB-specific** products already on the market. At least **7 of these have CE-marks**.

Products vary in that some:

- ➔ Can tailor their performance using local data (continuous learning)
- ➔ Require additional training using local data before deployment
- ➔ Can identify non-TB abnormalities

  (However, there is a lack of independent evaluation data on the performance of CAD for differential diagnosis and how accurately it localizes abnormalities).

ai4hlth.org is a regularly updated online marketplace of CAD products for TB. 2021 update coming soon.

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*

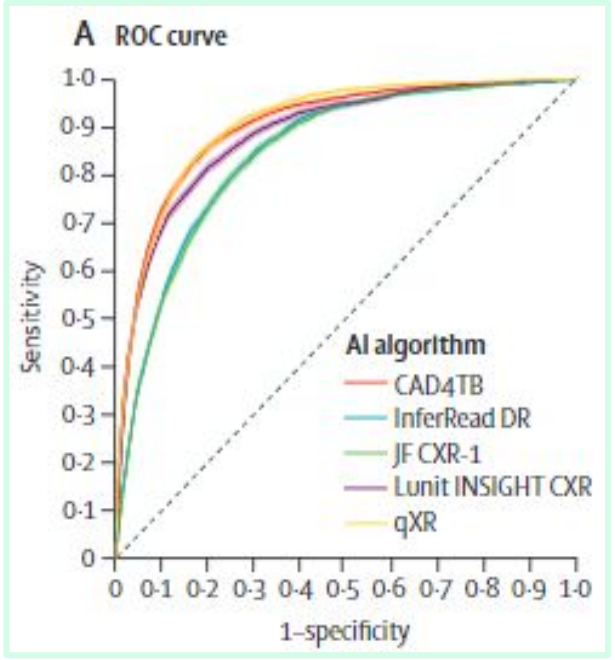
In the **latest head-to-head comparison** of the overall performance of the newest version of five commercial CAD software products, **all CAD products:**

- 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 to Place CAD 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 to Place CAD 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

CAD Products in the GDF Catalogue

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.

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

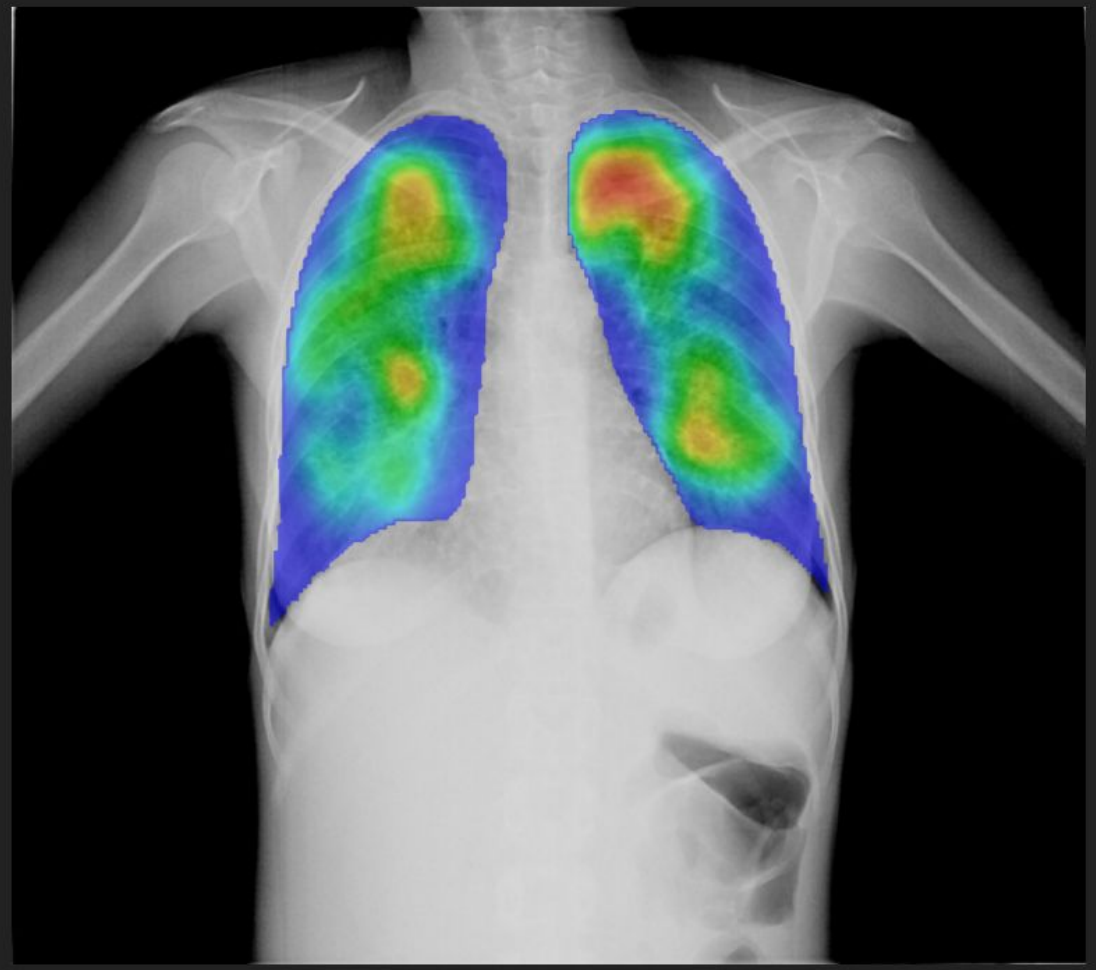
Cough:	Yes (3 days)
Fever:	Yes (7 days)
Shortness of breath	No
Household TB:	No

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

CAD4TB V7 Package and Price

One CAD4TB software perpetual license with 12-month support and maintenance $12,750

- Five **viewing licenses** (five additional computers can view images on the CAD4TB server)
- The client can **choose**:
  - Where to **store X-rays**: on local server, local cloud, or supplier's server.
    - Up to 300 images per license per day can be stored on Delft server (using Amazon Web Services).
  - To automatically **de-identify** data
- One year of support and maintenance, **starting on the day of successful installation** and user acceptance

One CAD4TB box + 10" tablet $2,750

- Storage capacity approx. **20,000 images**
- Supplied with a **USB disk (1TB)** for offline backup
- One-year warranty, starting on the day of successful installation and user acceptance
  - Total warranty period **cannot exceed four years** from the day of initial successful user acceptance

A **volume-based pricing discount** when procuring multiple CAD4TB perpetual licenses

Number of CAD4TB perpetual licenses purchased	Price (per license) in USD
1–9	12,750.00
10–19	11,475.00
20–49	10,837.50
50+	10,200.00

CAD4TB V7 Package and Price

Installation and training — $1,150

- Software operating environment and server configuration
- Installation (software and hardware) and
- **Threshold score calibration** study in the setting of intended use based on WHO protocol and toolkit

One-year extension of support and maintenance — $5,100

- Free software patches, upgrades, and update
- **Remote support for issue resolution** within one working day from the date of reporting
- **Corrective maintenance**
  - Covering replacement hardware, shipment to site, disposal of faulty hardware, cost of replacement work, personnel transport, and arrangements
- One-day remote **theoretical and practical training** of up to 10 operators
  - Hard and digital copies of training materials for each trainee
  - Access to Delft eLearning online platform for each trainee

- **Note:** Should be procured at the time of procuring one CAD4TB software perpetual license or one CAD4TB box or while the initial warranty period of item to be covered is still running. It extends the initial warranty period of one CAD4TB system (license and box) for 12 months.

Three-year extension of support and maintenance — $11,475

InferRead DR Chest

Latest version: Version 1
Certification: CE marked class IIa

InferVision

Input

- Postero-anterior (PA), antero-posterior (AP) 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

Output

For each X-ray read, InferRead DR Chest provides:

- Heat map
- Dichotomous output for TB
- Abnormality score for TB
- Dichotomous output for non-TB abnormalities
- Abnormality score for non-TB abnormalities

These are summarized in a structured report.

Deployment

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

INTRODUCING ULTRA-PORTABLE X-RAY

Types of X-ray Technology

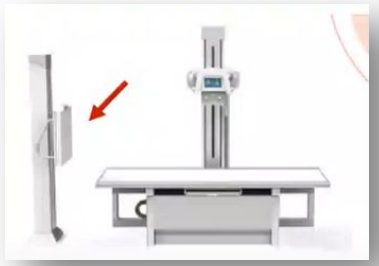
Digital radiography (DR)

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)

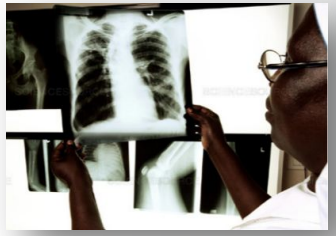
Existing analog generator and digital detector or CR reader



- **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



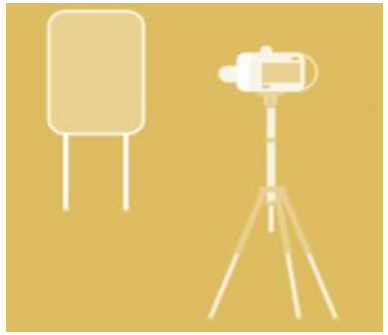
- Traditional method of X-ray imaging
- **Image receptor**: Analog film
- **Wet processing** using trained human resources to generate final image
- **Need trained human reader** to interpret film, **difficult to use in the field**
- **Output** is the X-ray film
- **Integration** with PACS not possible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

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

Types of radiographic systems:

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

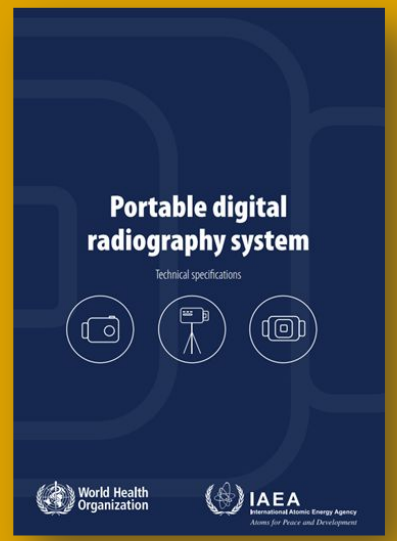
Mobile:
Moderate workload, intermittent power supply, can be moved/rolled around, high image quality



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

Advances in X-ray technology have resulted in increasingly portable “ultra-portable” digital X-ray systems.

WHO-IAEA working group jointly developed minimum technical requirements for X-ray digital portable systems (published in August 2021).



Recommended to support decision-making regarding the selection, incorporation, allocation and use of portable X-ray systems.

Intended for health care providers, managers of imaging departments, procurement and regulatory agencies, policymakers, and planning officers in ministries of health.

Stop TB Partnership

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

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

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

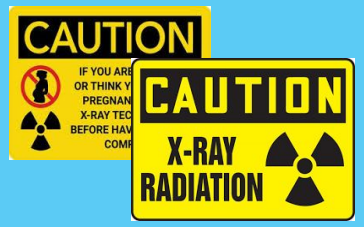
- **Replacement detector batteries (x2) and chargers** are provided with the system. The charger recharges two batteries simultaneously.

- **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

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

Generator

Console

Generator stand

Detector panel hanger

Detector

NOT included:

- Thyroid shield
- Lead shield

Delft Light Full Kit—Pricing

From the GDF catalog, the price of the Delft Light full kit is **$66,750.**

Volume-based discount is available:

# Kits	Price (per item)
01 – 04	$66,750.00
05 – 10	$66,057.50
11 – 19	$65,365.00
20 – 49	$64,672.50
50 +	$63,980.00

If purchasing this item together with one CAD4TB software perpetual license, one CAD4TB box is provided **free of charge,** and the support and maintenance on the CAD4TB software perpetual license is **valid for 15 months instead of 12 months.**

The **full kit** of Delft Light includes:

Component	Weight (kg)
X-ray generator	7.0
X-ray generator Stand	8.0
X-ray detector (incl. batteries)	3.8
X-ray detector stand	0.4
Console laptop/workstation	1.5
Lead apron	3.0
Battery chargers	1.0
Solar panel/power bank	6.0
Carrying case (empty)	2.5
Total	**33.2**

One-year warranty is included with purchase. Installation, training and warranty **extensions** are available at **added cost.**

Delft Light Full Kit—Pricing

Warranty

One-year warranty is included (including batteries) starting on the day of successful installation and user acceptance or 15 months from the date of invoice.

Warranty includes:

- **One remote session** for preventive maintenance, including the provision of a maintenance report
- **Software patches, upgrades, and updates**
- **Delft Imaging Helpdesk** 24/7 availability for service calls, ensuring an issue resolution within five working days maximum from the date of issue reporting
- **Replacement/repair** of faulty components (**excluding batteries**), including associated transport costs

Installation and training

- One session of theoretical and practical training of up to two operators on safety, use, transportation, and maintenance per instrument
- Provision of hard and digital copies of training materials and access to Delft eLearning online platform for each trainee
- Installation performed at the same time as training

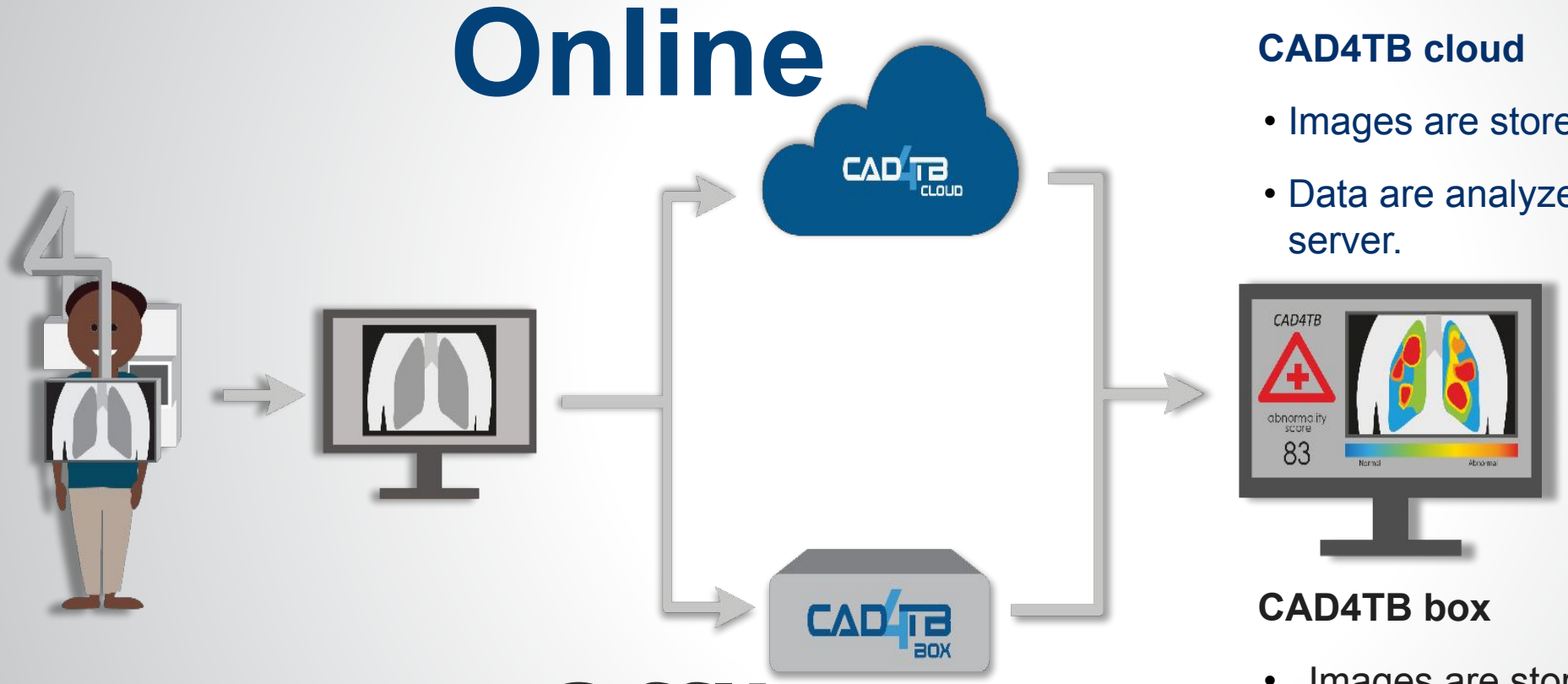
Warranty extension

- One-year extension: $4,460
- Three-year extension: $27,834

Warranty extension should be procured when purchasing the Delft Light full kit or while the initial warranty period is still running.

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.

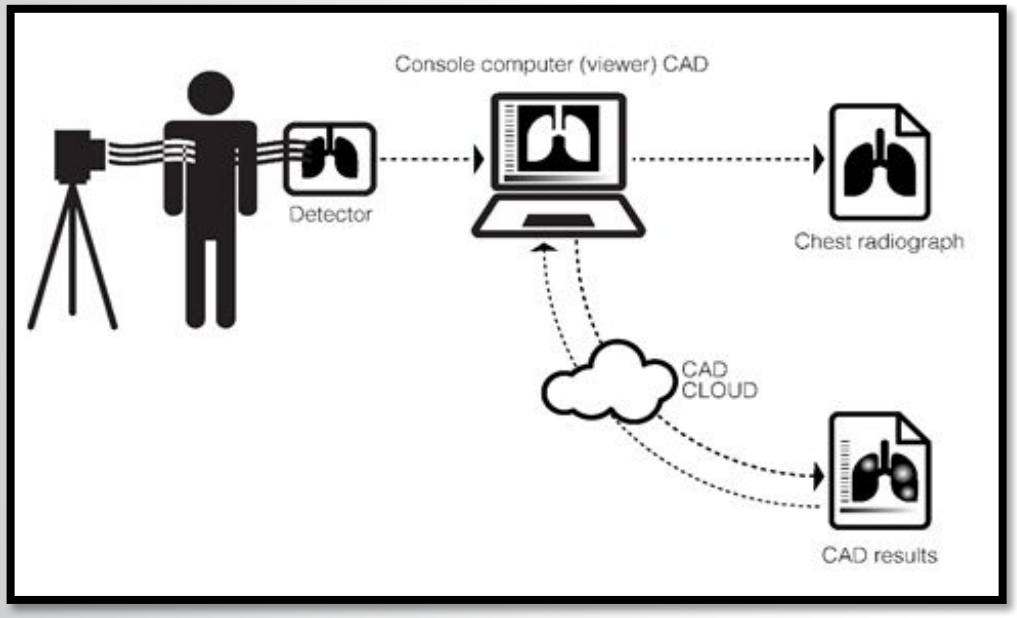
CAD4TB box

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

Connection with CAD4TB

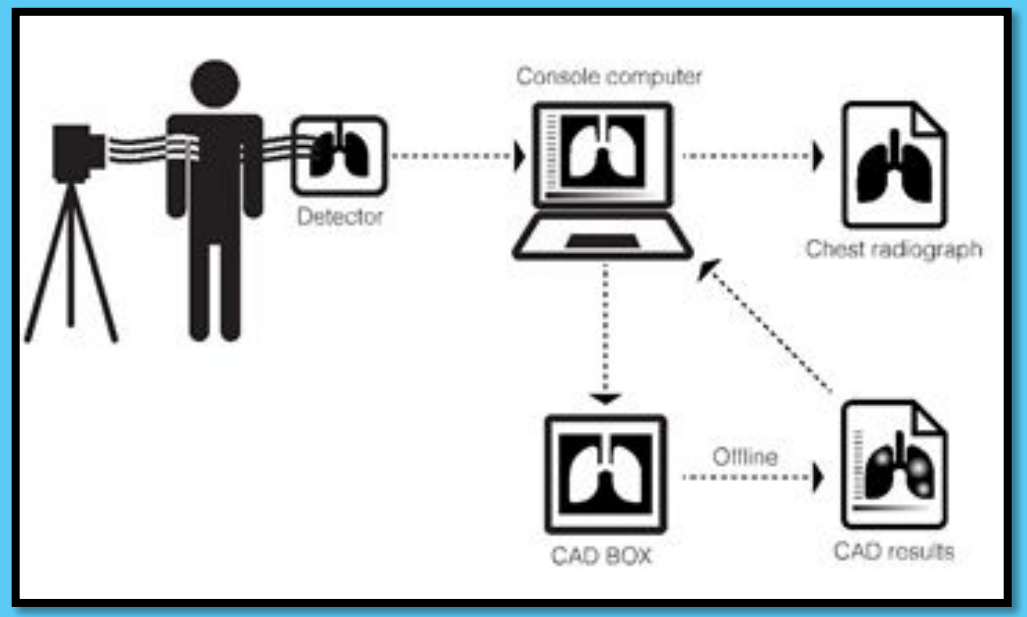
Online

- 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.



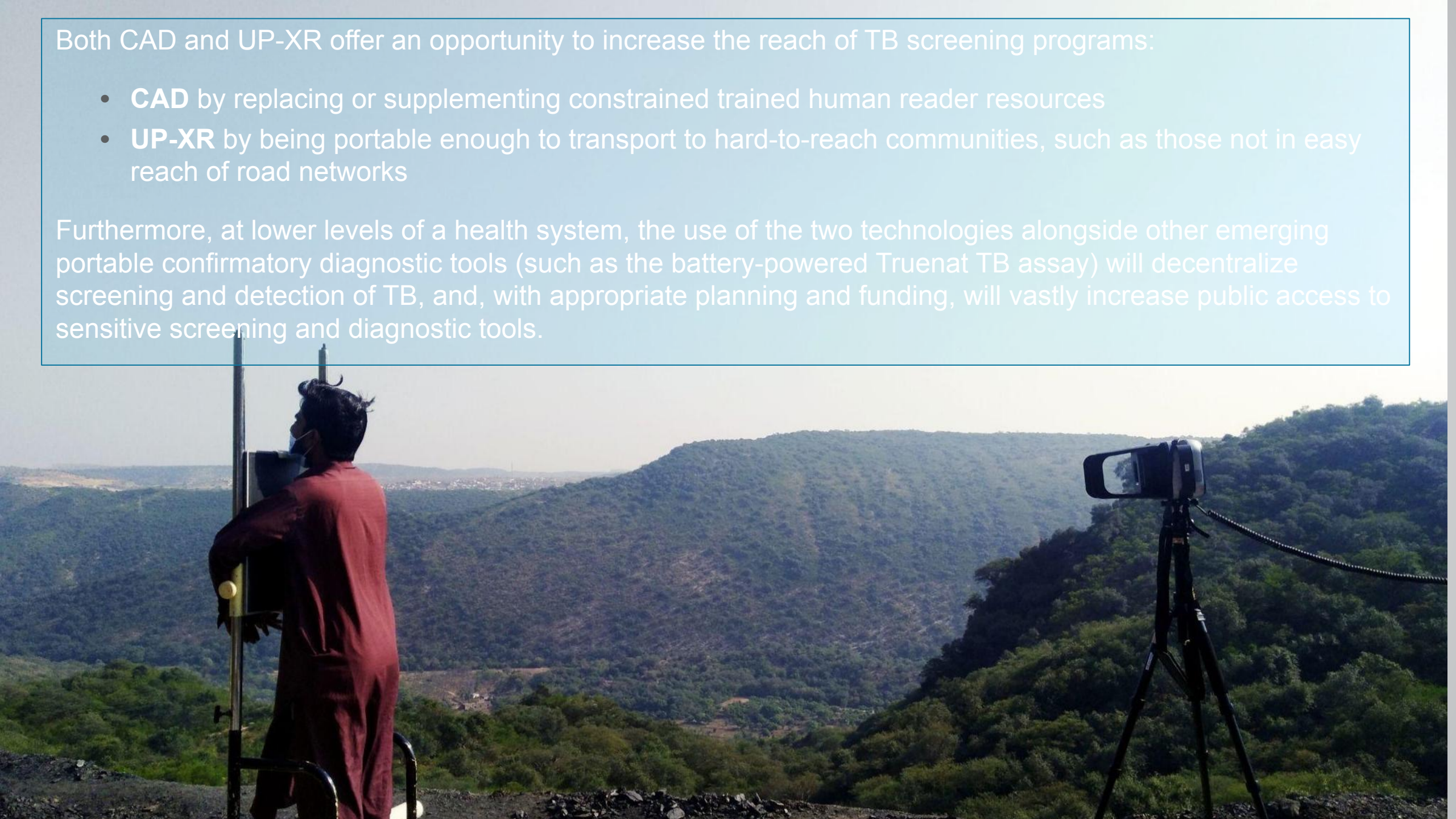
Hybrid

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.