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

MODULE 2
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.
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.
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.

<table>
<thead>
<tr>
<th>Abnormality score</th>
<th>Threshold score = 0.45 (or 45)</th>
<th>45+, all images assigned “Possibility of TB”</th>
</tr>
</thead>
<tbody>
<tr>
<td>0–44, all images assigned “No signs of TB”</td>
<td>0.45 (or 45)</td>
<td>100</td>
</tr>
</tbody>
</table>
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.

<table>
<thead>
<tr>
<th>Type of case/reader</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>WHO target product profile</td>
<td>&gt; 0.90</td>
<td>&gt; 0.70</td>
</tr>
<tr>
<td>Screening use case</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD software</td>
<td>0.90–0.92</td>
<td>0.23–0.66</td>
</tr>
<tr>
<td>CXR with human reader</td>
<td>0.82–0.93</td>
<td>0.14–0.63</td>
</tr>
<tr>
<td>Triage use case</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAD software</td>
<td>0.90–0.91</td>
<td>0.25–0.79</td>
</tr>
<tr>
<td>CXR with human reader</td>
<td>0.89–0.96</td>
<td>0.36–0.63</td>
</tr>
</tbody>
</table>

**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.

*Source: WHO Consolidated Guidelines on Tuberculosis*
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:

<table>
<thead>
<tr>
<th>CAD product</th>
<th>AUC</th>
</tr>
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<tbody>
<tr>
<td>qXR</td>
<td>90.81%</td>
</tr>
<tr>
<td>CAD4TB</td>
<td>90.34%</td>
</tr>
<tr>
<td>Lunit INSIGHT CXR</td>
<td>88.61%</td>
</tr>
<tr>
<td>InferRead DR Chest</td>
<td>84.90%</td>
</tr>
<tr>
<td>JF CXR-1</td>
<td>84.89%</td>
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</table>
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.
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
**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.

**Latest version:** Version 7  
**Certification:** CE marked, class IIb
Screening register in CAD4TB system

<table>
<thead>
<tr>
<th>Patient ID</th>
<th>Name</th>
<th>Sex</th>
<th>Birthdate</th>
<th>Study Date</th>
<th>Study Time</th>
<th>Institution</th>
<th>CAD4TB 7</th>
<th>CAD4TB Report</th>
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</tbody>
</table>
CAD4TB viewer window showing heatmap and score—no TB

Abnormality score and dichotomous classification

Heatmap
CAD4TB viewer window showing heatmap and score—possible TB

Abnormality score and dichotomous classification

Heatmap indicating TB
CAD4TB symptom and GXP report

Patient Information

Patient ID: 010100000001
Name: A. Anonymous
Gender: Male
Date of birth: 1971-10-12

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 Report 90 Possible TB
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**
- **Image receptor:** Solid state detector
- **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**
- **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

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**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
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.

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

**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.
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

**NOT included:**
- Thyroid shield
- Lead shield
Connection with CAD4TB

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

**Online**
- **CAD4TB cloud**
  - Images are stored online.
  - Data are analyzed through a secured data server.

**Offline**
- **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