Screening and Triage for TB using Computer-Aided Detection (CAD) Technology and Ultra-portable X-Ray Systems: A Practical Guide

Annexes

Contents

Annex 1: Deep Neural Networks

A neural network is a complex mathematic model originally inspired by the way nerve cells distribute signals within the brain. Artificial neural networks are composed of three types of layer: input, output and hidden. Each layer consists of multiple artificial "neurons", or "**nodes"**.[9,22] A node is a mathematical function (Figure 13).[23] Each individual node in a layer receives information from the connected neurons in the previous layer, and applies an "activation function", which processes and passes this output to the neuron of the next layer.[9,22] In this way, information from the input is identified and distilled into an output. Neural networks learn a mathematical function that transforms inputs to a target output. AI for X-ray images, for example, comprises a neural network whose input layer takes a monochrome image (224x224x1) consisting of pixel values. The network then transforms this data into an output, such as a number between zero and one signifying the probability of an abnormality.

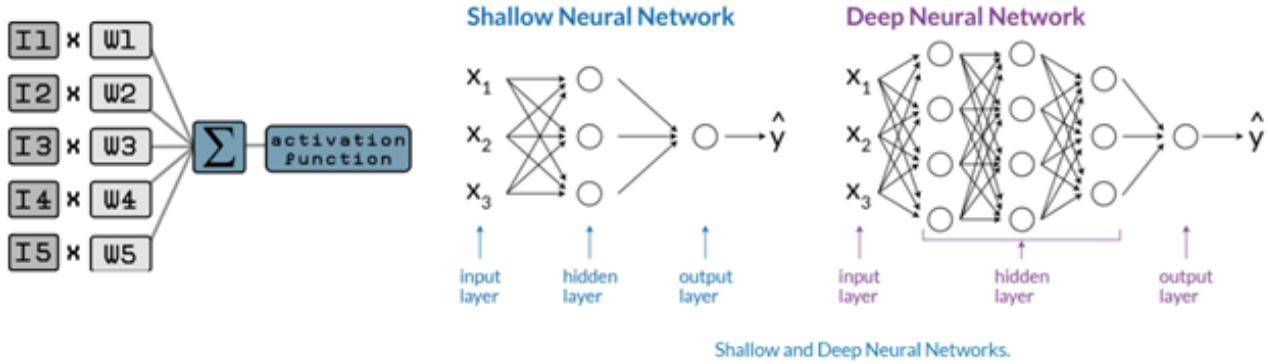


Figure 13 Schematic diagram of a neural network from towardsdatascience.com

Deep learning leverages deep neural networks that contain many hidden layers. Complex inputs such as medical images contain a wealth of information to be processed.[9,22] Consequently, network layers delegate, by operating in a hierarchy whereby earlier layers read at considerable magnification (down to as small as a pixel) and feed information forward to inform later layers, which read at higher levels.[22,24] Increasing the number of layers increases the ability of a neural network to process complex images, such as a chest X-ray.

How does a neural network "learn"?

A deep neural network "learns" to perform a particular task through "training", whereby the relevant algorithm is provided with training data from which to learn. This training data can be labelled (annotated) with the "correct answer" or ground truth (for example, either "truly TB", or "not TB") or left unlabelled.[22,25] Three types of learning (or training) are common:

- **Supervised:** when the AI receives training data that has been labelled with information that can inform the AI decision. Supervised learning is currently the most common type.
- **Unsupervised:** when the AI receives training data that has not been labelled.
- **Partially or semi-supervised**: when the AI receives training data that is a mixture of both those types (labelled and unlabeled).

During supervised training, the neural network compares its performance to ground truth (i.e., whether an image truly shows TB or not) and iteratively improves its accuracy. It does this by fine-tuning the "strengths" of the artificial neurons throughout the network in a way that reduces the difference between its prediction and ground truth, as defined by the supervised training

label.[9] Training is therefore an iterative process, often requiring millions of iterations, using large training datasets, to bring accurate models into convergence.

Understanding neural networks through visualization

A practical approach to understand neural networks is through visualization using TensorFlow Playground. This is an open-source application that is well known for explaining how neural networks work in an interactive way: https://playground.tensorflow.org/

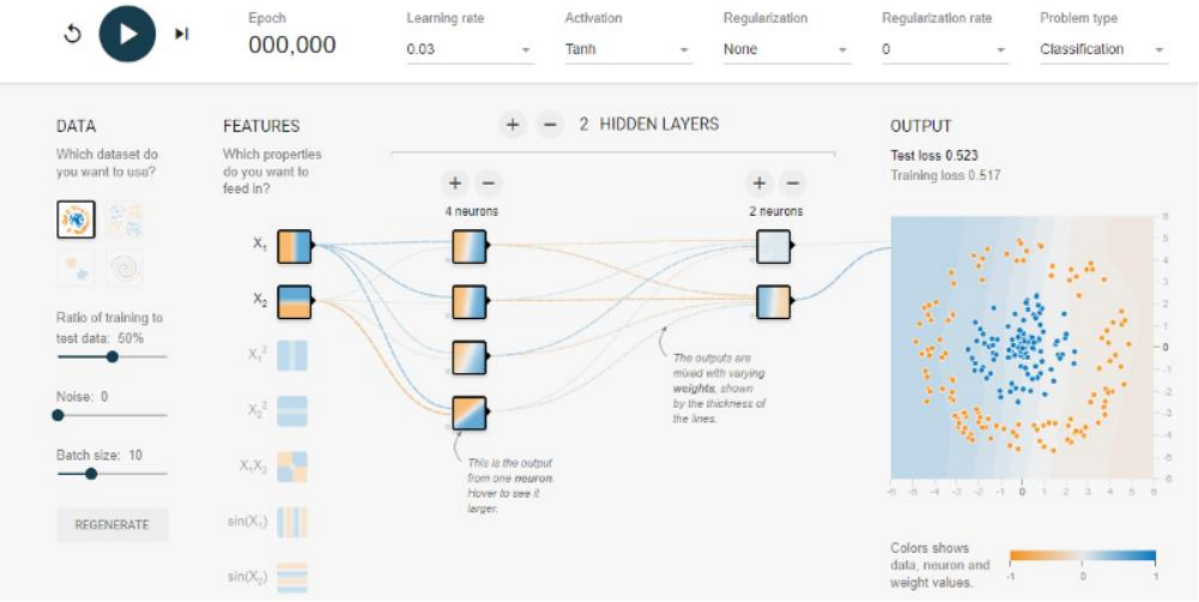


Figure 14 TensorFlow Playground.

Understanding how CAD arrives at its prediction

Users need to be able to trust the output of a CAD solution to correctly inform important clinical decisions. Understanding how CAD arrived at an output is one of the best ways to inspire trust in the software; however, it is challenging to understand the underlying neural networks of CAD software. The accurate reading (interpretation) of medical images is a highly complicated task, which accordingly requires an extremely complex tool. It is because modern deep neural networks consist of thousands of layers, and millions of neurons, that it becomes a challenge to understand the overall processing that occurs in them.

There is a whole branch of research aimed at explaining neural network models, and some interpretation techniques have been developed as a result. These techniques can be broadly divided into those that explain how the network works in general, and those that explain how the network arrives at a prediction for a specific example. An example of the former is to visualize outputs at specific layers or neurons, to gain a better understanding of what activates that particular neuron. Examples of the latter – for medical imaging – are saliency techniques that can create a "**heatmap**" indicating which parts of the image most influence the prediction and are thus the most important. Most CAD software provides a heatmap highlighting the areas of abnormalities. Users are thus easily directed – visually – to any areas of tissue that warrant further investigation or intervention.

Annex 2: Procurement Specifications and Evaluation Criteria of CAD Software

The tender template below can be customized and adopted for a Request for Quote (RFQ) designed to elicit bidding proposals for CAD products that exceed minimum requirements.

Technical requirements	Recommended parameters	Requirement	Scoring criteria
Certification			
CE marked / FDA clearance	Yes/No	Mandatory/ Optional	Yes = X; No = X
System performance compared to microbiological culture and/or GeneXpert validated on external dataset unseen by the CAD software and conducted by organizations not associated with the CAD manufacturer			
Area under Receiver Operating Curve (ROC) at least 0.8	Yes/No	Mandatory/ Optional	No information = X Satisfactory (0.80) = X Good (0.81-0.89) = X Excellent (above 0.9) = X
Sensitivity (Se) of at least 90% and a specificity (Sp) of at least 50%	Yes/No	Mandatory/ Optional	No information = X Satisfactory (Se=90%-91%, Sp=50%-55%) = X Good (Se=92%-94%, Sp=56%-60%) = X Excellent (Se>95%, Sp>61%) = X
Input requirement			
Ability to operate	e.g. antero-posterior (AP) or postero-anterior (PA) CXR or lateral	Mandatory/ Optional	No information = X Satisfactory (PA CXR) = X Good (PA and AP CXR) = X Excellent (PA, AP, lateral) = X
Reading X-ray image format	e.g. DICOM	Mandatory/ Optional	No information = X Good (DICOM) = X Excellent (a combination of JPEG, PNG, DICOM) = X
Output requirement			
Ability to provide abnormality score and/or report whether the X-ray is suggestive of TB	Yes/No	Mandatory/ Optional	Yes = X; No = X
Processing time	Less than: 5 secs. or 20 secs. or 1 minute	Mandatory/ Optional	No information = X Satisfactory (less than 1 minute) = X Good (less than 20 seconds) = X Excellent (less than 5 seconds) = X
Results displayed through			
Probability score for TB	Yes/No	Mandatory/ Optional	Yes = X; No = X

Technical requirements	Recommended parameters	Requirement	Scoring criteria
Probability score for other pulmonary findings	Yes/No	Mandatory/ Optional	Yes = X; No = X
Dichotomous outcome for TB	Yes/No	Mandatory/ Optional	Yes = X; No = X
Heat map showing areas of abnormality	Yes/No	Mandatory/ Optional	Yes = X; No = X
Ability to **de-identify / anonymize** patient's DICOM data	Yes/No	Mandatory/ Optional	Yes = X; No = X
Operation			
Score pre-set for TB screening with the option for user to adjust threshold score	Yes/No	Mandatory/ Optional	Yes = X; No = X
Ability to operate offline on image databases	Yes/No	Mandatory/ Optional	Yes = X; No = X
Hardware-diagnostic which works with X-rays of varying quality and exposure from any X-ray machine	Yes/No	Mandatory/ Optional	Yes = X; No = X
Data backup system on a server chosen by user, with flexibility for local server locations – please describe all possible options	Yes/No	Mandatory/ Optional	Yes = X; No = X
Certified for use with adults and adolescents at least 15 years old.	Yes/No	Mandatory/ Optional	Yes = X; No = X
Integration & Compatibility			
Demonstrated compatibility with 3+ portable digital X-ray models using 12-16 bits DICOM 3.0 standard images	Yes/No	Mandatory/ Optional	Yes = X; No = X
Presentation (upon request) of the technical documentation of the software for future integration in the National TB Information System/ National PACS / RIS	Yes/No	Mandatory/ Optional	Yes = X; No = X
Interoperability with Picture Archiving and Communication System (PACS)	Yes/No	Mandatory/ Optional	Yes = X; No = X
Hardware			
Hardware device allowing the analysis of images offline and able to provide server / cloud data synchronization – please describe hardware specifications including storage conditions, operating conditions and weight	Yes/No	Mandatory/ Optional	Yes = X; No = X
Ability to operate without interruption with no external	Yes/No	Mandatory/ Optional	Yes = X; No = X

Technical requirements	Recommended parameters	Requirement	Scoring criteria
power supply, preferably for at least 4 hours			
Can be stored at ambient temperature of +10 to +50°C and relative humidity between 15% and 80%; and can operate continuously at ambient temperature of +15 to +30°C and relative humidity of 15 to 80%.	Yes/No	Mandatory/ Optional	Yes = X; No = X
Weight: must not exceed 3 kg	Yes/No	Mandatory/ Optional	Yes = X; No = X
One-year hardware warranty included	Yes/No	Mandatory/ Optional	Yes = X; No = X
Free software patches, upgrades, and updates	Yes/No	Mandatory/ Optional	Yes = X; No = X
Remote support to resolve a reported problem within one working day of reporting date	Yes/No	Mandatory/ Optional	Yes = X; No = X
Shipment of goods to the NTP within one month of signing the contract	Yes/No	Mandatory/ Optional	Yes = X; No = X
Ability to perform validation of X-ray machines if software requires	Yes/No	Mandatory/ Optional	Yes = X; No = X
Online / off-site installation of software and hardware including calibration	Yes/No	Mandatory/ Optional	Yes = X; No = X
Online / off-site theoretical and practical training delivered for at least six operators / radiographers on software administration and use	Yes/No	Mandatory/ Optional	Yes = X; No = X
Provision of at least one hard copy of training material for each trainee	Yes/No	Mandatory/ Optional	Yes = X; No = X
Provision of at least one digital copy of training material for each trainee	Yes/No	Mandatory/ Optional	Yes = X; No = X
Three-year support & maintenance: Free software patches, upgrades, and any updates	Yes/No	Mandatory/ Optional	Yes = X; No = X
Three-year support & maintenance: Remote support to resolve a reported problem within one working day of reporting date	Yes/No	Mandatory/ Optional	Yes = X; No = X
Corrective maintenance as required: hardware to be replaced, with shipment to site, and disposal of faulty	Yes/No	Mandatory/ Optional	Yes = X; No = X

Technical requirements	Recommended parameters	Requirement	Scoring criteria
hardware, including labour, transport and any associated costs			
Subsequent online / off-site training for at least six additional radiographers per year	Yes/No	Mandatory/ Optional	Yes = X; No = X

Annex 3: Detailed Technical Specification of Delft Light and Fuji FDR Xair X-ray System provided through GDF

		Delft Light	Fujifilm Xair
X-ray generator		**TR90/20 Mikasa Atomed X-Ray**	**XD2000 PORTABLE**
	Voltage range	40-90kV	50-90kV
	Output power	1.35 kW	450 W
	X-ray generated radiation	Depending on image technique (details provided in Delft Light user manual)	0.5-2.5 mA
	Maximum filament current	15mA @ 90kV	5mA at 90kV
	Anode	Stationary anode (Toshiba D-0814) with 0.8 mm focus spot and heat storage capacity of 10 KHU.	Stationary anode with 0.8mm focal spot and heat storage capacity of 10 KHU.
		High anode temperature alarm and automatic blockage	High anode temperature alarm and automatic blockage
	Collimator	Multi-leaf collimator with halogen light source and laser pointer. Total filtration is 2.5 mm @ 75 kV.	Multi-leaf collimator with patient centering light. Total filtration of 2.5 mm @ 70kV.
	Total weight	7kg	3.5 kg
	Exposure Features		
	Time range	0.01 to 1 second (high power mode 0.01-0.03mA)	0.04 – 0.5 seconds with 20 steps
	Automatic exposure control	✕	✕
	Remote control possible?	✓ 3m detachable switch cord.	✓ Stretchable switch unit, maximum 2.5m operating distance
	Exposure capacity when fully charged	200 at 90kV, 1.2mA	100 shots at 90 kV, 0.5mAs *
	Charging		
	Powered by rechargeable batteries?	✓ Lithium-ion battery	✓ Lithium-ion battery
	Rechargeable power source	MB110BC battery charger – 19 V, 2A (charge method CC/CV) Battery charger – 90-240 VAC, 50/60 Hz	110-240V, 50-60Hz Or using appropriate transformer/condenser array
	Voltage stabilizer to allow safe and stable operation at +/- 20% of local rated voltage	✕	✓
	Can charging occur during operation?	Charging cannot occur while taking exposures	Charging can occur while taking exposures

	Sleep mode to prolong battery life?	✓	✓ After 10 minutes
	Charging time	4 hours	4.5 hours
X-ray generator stand		**Delft Light Atomed X-ray stand**	**XD2000 Generator Stand**
	Description	Lightweight stand. Counter-balanced spring arm allows height adjustment, vertical range 40-200cm, with 360-degree rotation.	Lightweight frame. Counterbalanced for safe and easy movement. Vertical adjustment from 38.2 to 164 cm above ground level. Rotation around vertical axis: 90 degrees .
	Weight	10kg	1.7kg
X-ray detector		**CANON CXDI 702c**	**FDR D-EVO II (DR-ID 1211 SE)**
	Active detector area	35 x 43 cm	35 x 43 cm
	Time to display image	< 5 seconds	< 2 seconds
	Weight	3.5kg (including battery)	2.5kg
	Pixel matrix	2800 x 3408	2800 x 2300 pixels
	Pixel pitch	125 µm	150 µm
	Number of pixels	9.5M pixels	6.6M for 35 x 43 cm
	Spatial resolution	4 lp/mm	3.3 lp/mm
	Detection quantum efficiency (DQE) at RQA5	85%	72%
	Dynamic range of A/D converter	16 bit	10 pixels
	Connection type	Wired or wireless	Wired and/or wireless
	Software	Scatter correction software (no need for GRID)	Console Advance software (includes Virtual Grid and Dynamic Visualization II)
	Charging		
	Rechargeable batteries?	✓ Lithium-ion battery	✓ Lithium-ion battery
	Rechargeable power source	Power adapter 90-240 VAC, 50/60 Hz BC-1A battery 9-12 V, 2 Amp	100-240 V, 50-60 Hz
	Voltage stabilizer to allow safe and stable operations at +/- 20% of local rated voltage	✓	✓
	Charging time	2.5 hours Low battery alarm on software and LED on detector	3 hours ‘Low battery’ alarm at 20% of battery

	Exposure capacity when fully charged	200 at 90kV	7.5 hours with sleep mode or 200 shots
X-ray detector stand/ frame		**Delft Light VersariX**	**XD2000 Detector Stand**
	Description	Portable detector mounting system with sturdy hook to suspend the detector at any height from improvised mounts (doors, walls, trees). Vertical range of 40-200cm.	Vertical movement: 38.2 to 164 cm from ground. Can support both vertical and horizontal frame, depending on patient positioning and body thickness.
	Weight	0.4 kg	1.7kg
Workstation / Laptop		**HP EliteBook x360 1030 G3**	**300CL A7 -V14.0 MOB3 SWLE**
	Pre-installed software?	Remote diagnostic software: allow remote assistance, training, or troubleshooting.	✓
	Display Screen	14” colour widescreen with 2Mpixel display size (2736 x 1824 pixels).	14” LED/ LCD widescreen with colour display. 2Mpixel.
	Processor	i5, i7 Dual 1.8 GHz processor	Dual microprocessor, at least 1.7 GHz each
	RAM	8 GB	32 GB
	Hard drive	500 GB SSD	512 GB SSD
	High resolution image retrieval without loss of quality?	✓ (display in Viewport 1440 x 1440)	✓ (for high resolution images of at least 1440 x 1440)
	Ability to store and transfer data to other workstations?	Can transfer images to external storage devices for backup.	Can transfer images to external storage devices for back -up.
	Display languages	English and French (other languages available upon request to the manufacturer)	English and French
	Weight	1kg	1kg
	DICOM 3.0 compatible?	✓	✓
	Software Features		
	• Patient registration	✓	✓
	• Patient data	✓	✓
	• Exposure parameter regulation	✓	✓
	• Image processing, viewing, detail enhancement, noise	✓	✓

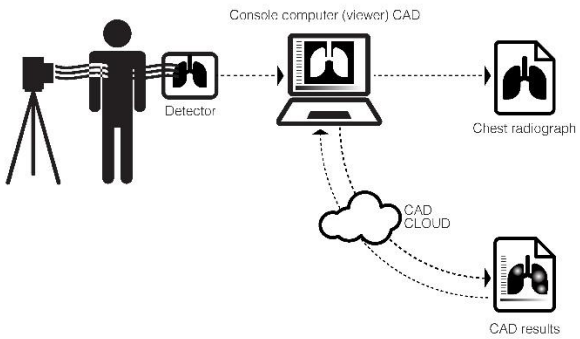
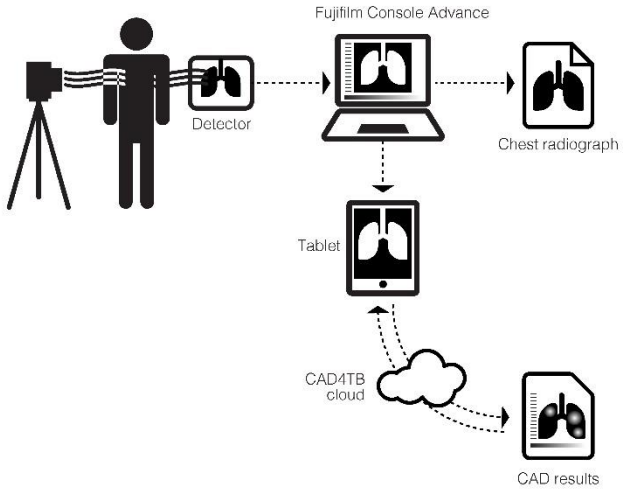
Software	suppression and tissue equalization		
	• Alphanumeric image annotation	✓	✓
	• Default chest X-ray programme	✓ available for different patient thickness (small, medium, or large)	✓ for patient thickness 14-40cm
	Storage capacity	20,000 images additional storage possible using external storage devices (USB/disk)	2,000 images (with additional capacity available through external storage devices).
	Interoperability with local and national PACS	✓	✓
Accessories	**Transport case/ bag**	All Delft Light components (X-ray generator, detector, laptop, and accessories) are packed in a shock resistant backpack. Top of backpack can be used to place the laptop during operations.	Bag divided into 3 parts: 1) generator, 2) detector, batteries, and accessories, 3) detector and generator stands. CAD box and battery fit into generator compartment.
	Safety Equipment		
	• Protective apron	✓ (1x) (apron weighing < 3kg, 0.5 mm lead protection)	✓ (1x) (apron weighing 4.9 kg, 0.5 mm lead protection)
	• Radiation hazard and/or pregnancy warning signs	✓ (5x)	✓
	• Shock detectors	✓ (10x)	✓ (10x)
	Charging Accessories		
	• Power bank	a power bank included in the solar panel	✓ Input/output power is 30Q, AC output at 100 W max.
	• Solar panel	✓ (7kg) 230 VAC @ 500 Watt peak power output Charges all system components	✕

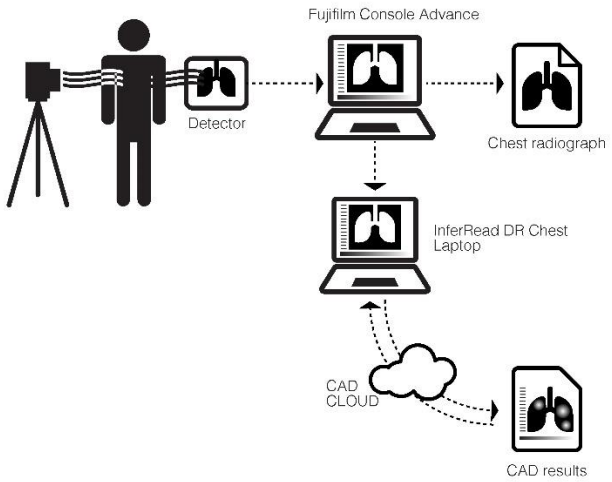
	• AC adapter provided for charging from mains electricity?	Yes. All AC adapters are included (adapter to charge X-ray battery, adapter to charge detector, and adapter to charge X-ray operator laptop).	✓
	• Additional detector battery	✓	✓
	• Additional generator battery	✕	✕
	• All charging cables and connectors included?	✓	✓
Environmental Requirements	**Operating Conditions**	0-60 degrees Celsius, 5-95% RH (no condensation)	5-35 degrees Celsius, 10-80% RH (no condensation).
	Storage Conditions	0-60 degrees Celsius, 10-90% RH. During transport by air, it is recommended to reduce battery charge to 2 bars to preserve lithium-ion cells.	10-50 degrees Celsius, 15-80% RH
Manufacturer and System Standards	**CE marked?**	✓ (for individual components)	✓
	ISO 9001:2015 **ISO 13485: 2016**	✕ ✓	✓ ✓
	IEC compliant?	✓	✓
Operations Manual		Click here to download	Click here to download

Annex 4: Summary of Potential Configurations and Hardware Required when Combining each of the CAD Products (CAD4TB, InferRead DR Chest) available in the GDF catalog with each of the Ultra-portable X-ray Systems (Delft Light, Fujifilm FDR Xair)

Online (details in section 3.4)

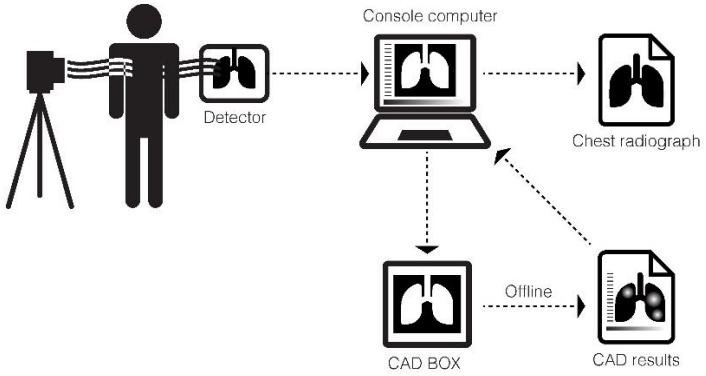
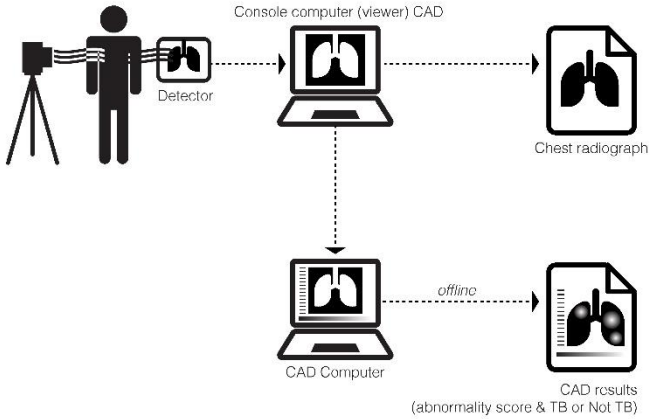
When using the two products online, the configuration with Delft Light is the same regardless of whether integration is with InferRead Dr Chest or CAD4TB as the Delft workstation can be connected to either cloud platform. The configuration of Fuji FDR Xair requires a second device with CAD4TB and InferRead DR Chest, this differs only depending on what the second device is laptop (InferRead DR Chest) or a tablet (Delft Light).

	Delft Light	Fuji FDR Xair
CAD4TB		

InferRead		 Fujifilm Console Advance Detector Chest radiograph InferRead DR Chest Laptop CAD CLOUD CAD results

Offline

When operating offline, a second device is needed on which the CAD is locally installed. Therefore, the hardware required differs depending on which CAD product is used. CAD4TB uses an offline box with both X-ray systems while InferRead DR Chest uses a laptop with both X-ray systems. (Also see section 3.4 above).

	Delft Light | Fuji FDR Xair
CAD4TB	
InferRead DR Chest	

Annex 5: Budgetary Considerations for Implementation

	Budgetary consideration
Planning	• Workshop for stakeholder engagement and planning • Technical workshop for screening policy and algorithm update • Situational analysis cost – human resources (HR), travel and report writing • Printing and distribution costs for revised algorithms • Development of a costed operational plan • Costs of assessing site readiness – travel, HR • Workshop and HR for the development of standard operating procedures (SOPs) • Printing and dissemination of revised procedures • Development, printing and dissemination of revised clinical protocols and guidance for the selection of patients to be tested, ordering tests, interpreting test results, and making patient care decisions • Cost of any external technical assistance needed
Human Resources	• Wages of healthcare workers including nurses, radiologists, community health workers • Wages of field project staff including field coordinators, IT staff, X-ray technicians, biomedical scientists • Fees for any consultants, including CAD threshold score expert, legal expert, education expert
Registration and validation	• Regulatory submission costs (if applicable should be borne by manufacturer) • Costs of local travel to regulatory authority • Importation processes and costs • Validation study, threshold score calibration study – bacteriological confirmation test, HR
IT cost	• Server cost • Internet cost • Cost of IT professional • Cloud storage cost
Procurement and installation	• Equipment cost (X-ray hardware, CAD license) • Delivery and importation costs • Installation by manufacturer or authorized service provider • Basic training • Workshop for stakeholders involved in procurement planning
Additional training	• Workshop and HR to update training packages • On-site training (sensitization) for radiological technicians, clinicians, community healthcare workers, programme staff on the use of CAD technology
Equipment maintenance and servicing	• Extended warranty or service contract • Costs of routine preventive and annual maintenance • Cost of corrective maintenance • Preparation and regular review of CAD and quality assurance documents based on national requirements
Monitoring and Evaluation (M&E)	• Workshop and HR to update recording and reporting forms, registers • Data synchronization and backup • Meetings to update M&E system and regular meetings to review impact of transition and adjust accordingly • M&E refresher training

Annex 6: Checklist to Assess Suitability of a CXR-CAD Screening Site

This checklist should be used to assess the suitability of a site for an ultra-portable digital CXR unit to be used with CAD. The checklist focuses on the key operational and environmental requirements for CAD use. A separate checklist (Annex 7) serves to assess the readiness of a site to begin using CAD for reading CXR to detect TB. Although most questions simply require a 'Yes', 'No' or 'Partial', space is provided for comments as appropriate.

Name of health facility

Location of health facility (City/town, District, State)	
Type of digital CXR technology	__Stationary digital radiography __Mobile digital radiography __Ultra-portable digital radiography __Other_____
CXR image format	__DICOM 3.0 standard images __ JPEG __PNG __Other_____
Input	__Postero-anterior CXR __ Antero-posterior CXR __Lateral CXR
CXRs performed at this site	Average number of tests conducted daily
How are people referred for CXR in this unit?	__Pulmonologist/TB specialist __NGO/Community worker __Self-referral __Active case finding campaign __Other_____
Estimated monthly number of CXRs to be read using CAD based on planned algorithm for TB screening	

Persons interviewed

Name	Position and contact details

Assessor name **Contact details:**

Date of assessment	

	Yes	No	Partial	Comments
Human resources				
1. Are sufficient numbers of qualified staff available to oversee CAD CXR implementation?	Y	N	P	
2. Is an IT specialist (part-time or full-time) available to provide support as requested?	Y	N	P	
A safe and functional X-ray unit				
3. Is there adequate space to perform CXR investigations in compliance with national regulatory requirements?	Y	N	P	
4. Are there sufficient sockets available for battery charging of essential devices: CXR detector, generator, PACS laptop, CAD laptop/box?	Y	N	P	
5. Would a solar panel system or storage battery need to be procured to provide the required electricity? (optional)	Y	N	P	
6. Was the ambient temperature recorded in the X-ray unit below +10°C or above +50°C?	Y	N	P	
7. Was the relative humidity recorded in the X-ray unit below 15% or above 80%?	Y	N	P	
8. Does the testing site use appropriate disinfectants and are they prepared correctly?	Y	N	P	
9. Is suitable personal protective equipment (PPE) provided at the CXR unit and are staff trained in its correct use?	Y	N	P	
Equipment service and maintenance				
10. Are routine maintenance procedures performed (monthly, quarterly, or every six months) and recorded for existing instruments?	Y	N	P	
11. Is there an SOP in place to obtain repairs or service for existing instruments?	Y	N	P	
Digital data and diagnostics connectivity				
12. Does the CXR unit or referral facility have Wi-Fi or data plan coverage, to allow for data transfer?	Y	N	P	
13. Are procedures in place that ensure the confidentiality of patient information?	Y	N	P	
14. Is an electronic CXR management system in use? If yes, which?				
15. Is unique patient identifier (and unique test identifier) available to link patient's X-ray results with laboratory confirmation test results?	Y	N	P	
16. Is suitable secure storage available for X-ray test and subsequent laboratory confirmation test data?	Y	N	P	
Recording and reporting				

17. How are the CXR results currently returned to clinicians?				
18. If a TB electronic information system is in use, are the CXR results entered into it for all CXR investigations performed or only for those suggestive for TB?	Y	N	P	
19. If an electronic recording and reporting system is in place, is the result of any patient with non-TB abnormal CXR entered into it with subsequent referral and follow-up tracked?	Y	N	P	
20. If an electronic recording and reporting system is in place, can CXR results that have been read using CAD software be directly sent for recording and reporting in the system?	Y	N	P	

Annex 7: Checklist to Assess Readiness of a CXR-CAD Screening Site

This checklist should be used to assess the readiness of a digital CXR unit to be used with CAD, such that clinicians can immediately use the results for patient care. The checklist may also be used at the beginning of the implementation process to identify areas in need of improvement. Although most questions simply require a 'Yes', 'No' or 'Partial', space is provided for comments as appropriate.

Name of health facility where CXR is placed

Location of health facility (City/town, District, State)	
Type of digital CXR technology	__Stationary digital radiography __Mobile digital radiography __Ultra-portable digital radiography __Other_____
CXR image format	__DICOM 3.0 standard images __ JPEG __PNG __Other_____
Input	__Postero-anterior CXR __ Antero-posterior CXR __Lateral CXR
Validation of the X-ray machine for CAD software use	__Yes __No __Not applicable
CXR performed at this site	Average number of tests conducted daily
How are people referred for CXR in this unit?	__Pulmonologist/TB specialist __NGO/Community worker __Self-referral __Active case finding campaign __Other_____
Estimated monthly number of CXR to be read using CAD based on planned algorithm for TB screening	

Persons interviewed

Name	Position and contact details

Assessor name **Contact details:**

Date of assessment	

	Yes	No	Partial	Comments
Planning and HR				
1. Has a staff member (part-time or full-time) been appointed in the unit to oversee the roll-out of TB-CAD?	Y	N	P	
2. Are partners available who are supporting readiness for TB-CAD roll-out, and how are they contributing?	Y	N	P	
3. Are adequate resources available (e.g., funding, staff, screening infrastructure) to support ongoing TB-CAD:	Y	N	P	
• Equipment maintenance and service contracts?	Y	N	P	
• Ongoing costs associated with IT (server, internet, IT professional, cloud storage, etc.)	Y	N	P	
• Ongoing training and competency assessments?	Y	N	P	
• Quality assurance (radiologists to ensure quality control, bacteriological confirmation, monitoring indicators etc.)?	Y	N	P	
• Projected ongoing costs related to CAD for TB CXR screening (staff, costs for X-ray reading, etc.)?	Y	N	P	
4. Are sufficient numbers of qualified clinicians available to provide TB care for the increased numbers of TB patients likely to be identified?	Y	N	P	

	Yes	No	Partial	Comments
Equipment, service and maintenance				
5. Are copies of the user manuals on CAD software work readily available and accessible at the X-ray unit?	Y	N	P	
6. Was the CAD software verified on site prior to routine use for patient CXR reading (optional)	Y	N	P	
7. Is a routine maintenance log available indicating daily, weekly, and monthly tasks?	Y	N	P	
8. Is there an SOP in place to obtain repairs or service for X-ray device and CAD software?	Y	N	P	
9. Is a service contract in place to provide comprehensive service and maintenance?	Y	N	P	

	Yes	No	Partial	Comments
Screening facility readiness				
10. Is there secured storage for the X-ray machine?	Y	N	P	

11. Is there adequate space to perform CXR investigations in compliance with relevant national regulatory requirements?	Y	N	P	
12. Are there sufficient sockets available for battery charging of essential devices: CXR detector, generator, PACS laptop, CAD laptop/box?	Y	N	P	
13. Does the X-ray unit ensure an optimal working temperature (+10°C to +50°C) and environment (humidity 15-80%) for the CAD software?	Y	N	P	
14. Is available electricity adequate to run CAD software and charge batteries?	Y	N	P	
15. If needed, is a solar-powered generator or storage battery available for charging digital X-ray and CAD tools?	Y	N	P	
16. Does the testing site use appropriate disinfectants and are they prepared correctly?	Y	N	P	
17. Is suitable personal protective equipment (PPE) provided at the CXR unit and are staff trained in its correct use?	Y	N	P	

	Yes	No	Partial	Comments
Procedures				
18. Are all the standard documents, records and forms related to X-ray reading using CAD readily accessible to all staff?	Y	N	P	
• CAD software maintenance log	Y	N	P	
• Register of CXR investigations performed	Y	N	P	
• Reporting form for X-ray result	Y	N	P	
19. Are the following TB-CAD standard operating procedures (SOPs) approved and accessible at the X-ray unit?	Y	N	P	
• Recording and reporting	Y	N	P	
• Quality indicator monitoring and data analysis	Y	N	P	
20. Is there evidence that all SOPs, documents and forms have been read by relevant staff?	Y	N	P	

	Yes	No	Partial	Comments
Digital data and diagnostics connectivity				
21. Are X-ray unit staff familiar with use of CAD for CXR reading for TB?	Y	N	P	

22. Is an electronic CXR management system in use? If so, specify which one (as a comment).	Y	N	P	
23. Is a mechanism in place for data transfer (via data plan or Wi-Fi)?	Y	N	P	
24. Are procedures in place to define data sharing protocols and ensure the confidentiality of patient information?	Y	N	P	
25. Is suitable secure storage available for the archived or backup CXR investigations using CAD for TB detection?	Y	N	P	
26. Are adequate resources available for projected ongoing costs of data transfer, storage, and analysis?	Y	N	P	

	Yes	No	Partial	Comments
Establish and monitor quality controls				
27. Are protocols in place to ensure required use of X-ray results?	Y	N	P	
External quality assessment				
28. Is an external quality assessment programme in place?	Y	N	P	
• Radiologists reading?	Y	N	P	
• Bacteriological confirmation?	Y	N	P	
• On-site supervisory visits?	Y	N	P	
29. Does the X-ray unit receive on-site supervisory visits? If yes:	Y	N	P	
• who conducts the supervisory visits?				
• is feedback provided to the X-ray unit site following a supervisory visit?	Y	N	P	
• when was the last supervisory visit, and what was the feedback?				
Monitor and analyze quality indicators				
30. Which radiology statistics and performance indicators are currently reported to the TB programme and how?	Y	N	P	
31. Will the following quality indicators be routinely monitored and analyzed by the X-ray unit and reported:	Y	N	P	
• Number of people screened for TB using X-ray and CAD (for diagnosis)				
• CAD threshold score used to determine positivity	Y	N	P	
• Positivity rate of chest X-ray with CAD for TB diagnosis at implementation sites	Y	N	P	
• Percentage of people screened positive for TB with X-ray and CAD that were referred for confirmatory testing	Y	N	P	

• Positivity rate of confirmatory test (e.g., Truenat or Xpert) for people screened positive for TB with X-ray and CAD	Y	N	P	
• Percentage of people screened positive for TB with X-ray and CAD who were diagnosed without bacteriologically confirmed TB (clinical diagnosis)	Y	N	P	

	Yes	No	Partial	Comments
Recording and reporting				
32. How will results be returned to clinicians? Via email or using the TB electronic system?	Y	N	P	
33. Is an approved 'request for examination' form available to request CXR reading using CAD?	Y	N	P	
34. Is an approved reporting form available to report results of CXR reading using CAD?	Y	N	P	
35. Are the radiology and clinical registers suitable for recording the results of TB diagnosis based on CAD reading of CXR?	Y	N	P	
36. If a TB electronic information system is in use, are CXR results entered into it for all CXR investigations performed, or only for those suggestive of TB?	Y	N	P	
37. If an electronic recording and reporting system is in place, is the result of any patient with non-TB abnormal CXR entered into it with subsequent referral and follow-up tracked?	Y	N	P	
38. If an electronic recording and reporting system is in place, can the CXR results that have been read using CAD software be directly sent for recording and reporting in the system?	Y	N	P	

	Yes	No	Partial	Comments
Training and competency assessment				
39. Are terms of reference available for key staff involved in overseeing CAD for TB screening?	Y	N	P	
40. Are records in place documenting that all staff have been trained on assigned work processes, procedures, and tasks?	Y	N	P	
41. Are standard procedures used to assess and document the competence of all staff involved in CAD for TB screening?	Y	N	P	
42. Have all relevant clinicians and healthcare workers been trained on TB screening	Y	N	P	

algorithm before working at sites that will be referring people whose X-rays are flagged up by CAD?				
43. Are there any additional training needs for clinical staff?				

Annex 8: Proposed Indicators for Monitoring the Performance of CAD Technology for TB Screening and Triage

Indicator name	Calculation	Frequency of Collection	Data collection by	Data Source	Baseline	Target
CAD error and invalid results	Number of error and invalid CAD results					
X-ray system malfunction	Number of X-ray system malfunction					
Number of people screened for TB using X-ray and CAD (for diagnosis)	Number of people screened for TB using X-ray and CAD		Register	Registers (possibly software dashboards)		
CAD threshold score used to determine positivity	CAD threshold score used to determine positivity		NTP/Implementing Partner	NTP/Implementing Partner		
Positivity rate of chest X-ray and CAD for TB diagnosis at implementation sites	Numerator: Number of people screened positive for TB diagnosis with X-ray and CAD Denominator: Number of people screened for TB diagnosis using X-ray and CAD		Register	Registers (possibly software dashboards)		
Percentage of people screened positive for TB with X-ray and CAD that were referred for confirmatory testing	Numerator: Number of people screened positive for TB with X-ray and CAD and referred for confirmatory testing Denominator: Number of people screened positive for TB with X-ray and CAD		Register	Registers		
Positivity rate of confirmatory test (e.g., Truenat or Xpert) for people screened positive for TB with X-ray and CAD	Numerator: Number of people testing positive for TB using confirmatory test Denominator: Number of people screened positive for TB using X-ray and CAD who received confirmatory test		Register	Registers		
Percentage of people screened positive for TB	Numerator: Number of people screened positive for TB with X-ray		Register	Registers		

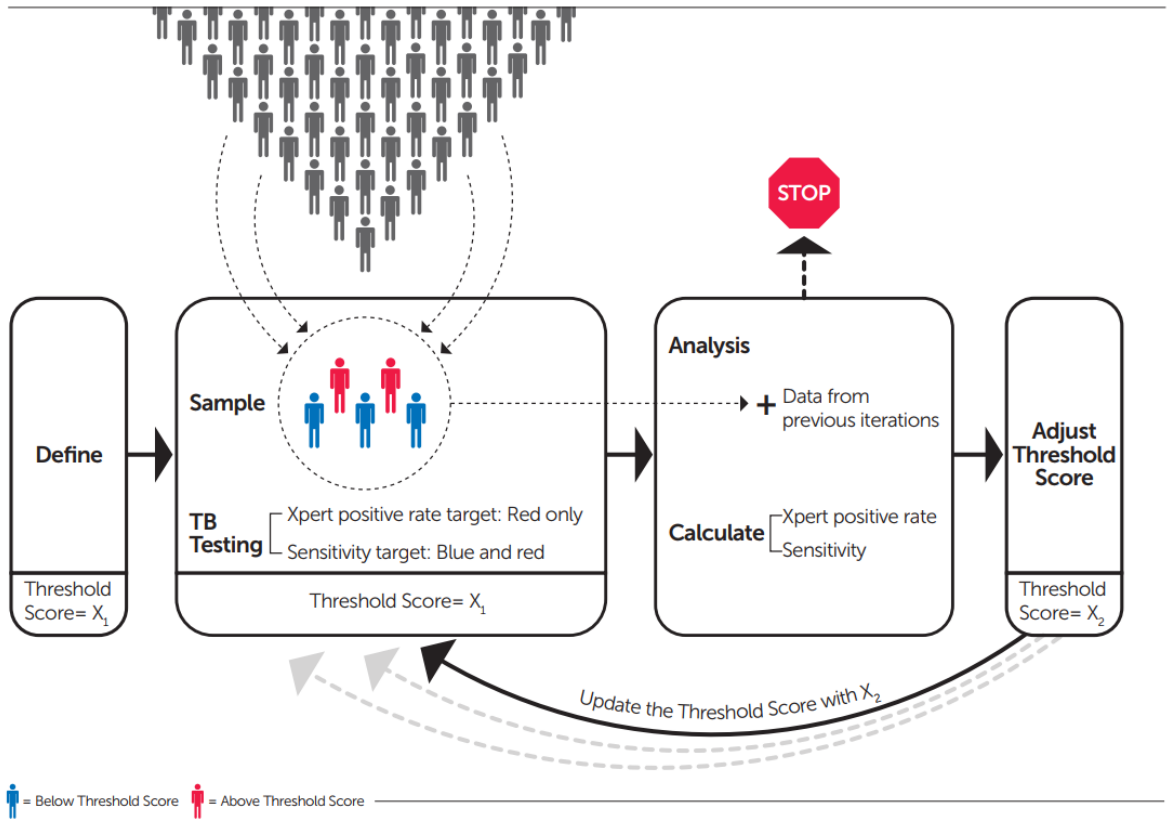
with X-ray and CAD and were diagnosed without bacteriologically confirmed TB (clinical diagnosis)	and CAD who were diagnosed not to have bacteriologically confirmed TB (clinical diagnosis) Denominator: Number of people screened positive for TB with X-ray and CAD	

Annex 9 Detailed Description of the Iterative Threshold Score Calibration (ITSC) Model

The ITSC model can help implementers tune their threshold score to reach one of three possible targets, which should be defined initially:

- Target sensitivity value
- Confirmation test positive rate
- Percentage of patients recalled for confirmation testing.

Work on the mathematical model is ongoing, and the results are intended to be published in a peer-reviewed journal. The following diagram is a schematic overview of the four steps involved.



Step 1 – Define

During this step, implementers should decide which programmatic targets they are aiming for:

- Initial threshold score (e.g., this could be chosen based on manufacturer recommendation or current literature),
- Sample size of new data in each iteration,
- Maximum number of iterations.
- Programmatic targets. The ITSC model is explained below using three programmatic targets:
  - Positive confirmation test rate
  - Sensitivity
  - Percentage of patients recalled for confirmation testing

To set a sample size for each iteration, take the sample size required by the comprehensive operational research method, and divide it by the maximum number of iterations.

Step 2 – Sampling and TB testing

During ITSC, sampling under the current operating point will vary slightly according to the programmatic target envisaged:

- If the target is to reach a certain positive confirmation test rate or percentage of patients recalled for confirmation testing, only individuals with CAD scores above the current operating point need be sampled and tested by Xpert. This is because that target does not depend on capturing all the true positives and false negatives. These three targets are thus a relatively straightforward programmatic target, more easily used to calibrate threshold scores.
- If the programmatic target is to reach a certain sensitivity, then we need to test everyone in each iterative sample with Xpert regardless of the CAD scores. This is because we need to obtain information on the TB status of all patients receiving CXRs — even those with low CAD scores. If only individuals above the current operation point are tested with Xpert, the sensitivity of CAD will always be 100%. There may be some advantages to more thoughtful sampling approaches to the sensitivity target, such as sampling only those with scores close to the current threshold score, as well as pooling specimens. Future research is needed. Future work is being pursued to formalize and simulate these strategies.

Step 3 – Analysis and calculate

Add the newly sampled data in the current iteration to the previously collected data in the previous iterations. The previous iteration data is reused to account for the correlation between iterations. Calculate the new Xpert test positive rate or sensitivity. Hypothesis testing can be employed to determine if the target is reached, and early termination is possible. The model due to be published will demonstrate a method of hypothesis testing.

Step 4 – Adjust threshold score

The operating point (threshold score) can be updated on the basis of all the samples collected so far. In terms of the positive confirmation test rate, the new operating point should be the one that achieves the desired testing rate taking into account all previously observed data during calibration. In terms of sensitivity, the next operating point can be obtained by finding the model score which obtains the desired performance based on the sampled data.

In the early stages of ITSC, when very little data has been sampled, the variance can be high, and this may also be used to determine whether additional iterations are needed. It has been noted that there can be ‘noise’ (high variation) in the early iterations, thus future work is needed to improve damping through operating point adjustment between iterations.