FIND
Because diagnosis matters

DIGITAL CHEST RADIOGRAPHY AND COMPUTER-AIDED DETECTION (CAD) SOLUTIONS FOR

TUBERCULOSIS DIAGNOSTICS

TECHNOLOGY LANDSCAPE ANALYSIS

FIND 2021

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>>>>> Patient registration at screening campaign in Viet Nam.

(Image credit: Friends for International TB Relief (FIT), Viet Nam)

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This report has been prepared by Yogesh Jha, Consultant for the Foundation for Innovative New Diagnostics (FIND), with contributions from Dr Morten Ruhwald, Head of Tuberculosis at FIND and Dr Sandra Kik, Consultant and Project manager of CAD-related projects at FIND.

The information covered in this report is based on work done by FIND, the World Health Organization and Stop TB Partnership. It is also based on extensive research and analysis of publicly available information provided by the X-ray equipment and CAD industries; published and unpublished literature; interviews with manufacturers and CAD developers; and the experience of TB programme implementers around the world. None of the members of the FIND team or consultants involved in the preparation of this report have any commercial links or receive incentives from any of the radiology equipment manufacturers or CAD developers mentioned in the report.

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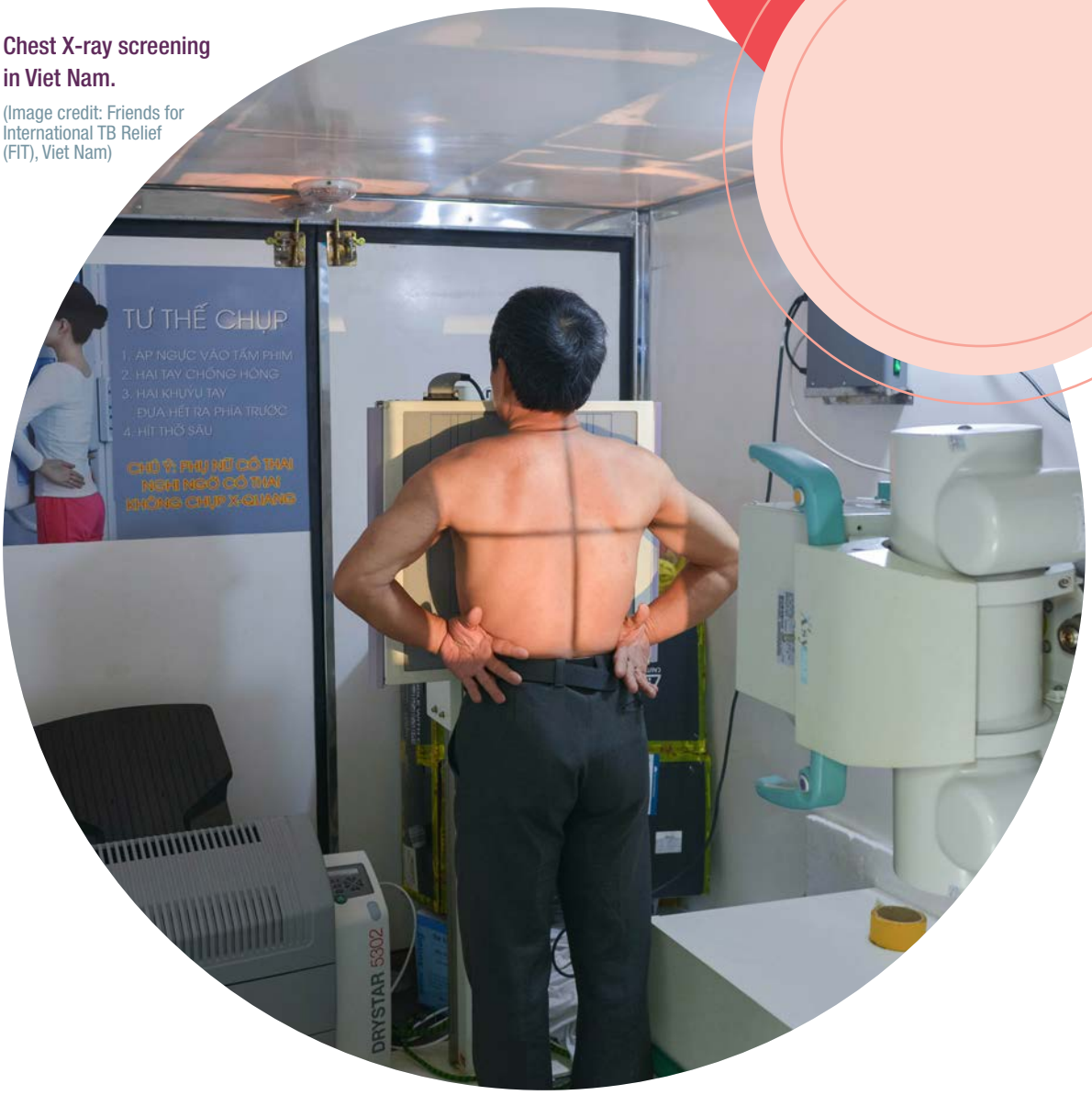
FIND Radiology Landscape Project Team

>>>>> **Chest X-ray screening in Viet Nam.**

(Image credit: Friends for International TB Relief (FIT), Viet Nam)



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ACRONYMS

AC:	Alternating current
AEC:	Automatic exposure control
AI:	Artificial intelligence
AUC:	Area under curve
AP:	Anterior posterior
API:	Application programming interface
APR:	Anatomically programmed radiography
CAD:	Computer-aided design
CE:	Conformité européenne (EU; standard)
CR:	Computed radiography
CXR:	Chest X-ray
DC:	Direct current
DICOM:	Digital Imaging and Communications in Medicine
DR:	Digital radiography
DQE:	Detective quantum efficiency
FDA:	Food and Drug Administration (USA; standard)
FIND:	Foundation for Innovative New Diagnostics
FPD:	Flat panel detector
FS:	Focal spot
GDF:	Global Drug Facility
HF:	High frequency (X-ray generator)
HU:	Heat unit (Anode)
IAEA:	International Atomic Energy Agency
ICU:	Intensive care unit
ICT:	Information and communications technology
Kg:	Kilogram
kV:	Kilo Volt
kW:	Kilo Watt
LMIC:	Low- and middle-income country
mA:	milli Ampere (filament current)
mAs:	milli Ampere seconds
mm AL:	millimetre equivalent Aluminium (filtration of X-ray beam)
PACS:	Picture archiving and communication system
PTB:	Pulmonary tuberculosis
R&D:	Research and development
ROC:	Receiver operating characteristic
TB:	Tuberculosis
WHO:	World Health Organization
VAC:	Volt AC (Input power supply)

EXECUTIVE SUMMARY

Tuberculosis (TB) remains one of the leading causes of mortality worldwide 139 years after the discovery of *Mycobacterium tuberculosis*, the bacteria that causes TB. Although TB is a treatable disease, effective screening and diagnosis remain a challenge due to varied presentations of the disease and its long incubation period. An estimated 2.9 million of the 10 million people who were infected with TB in 2019 were either not diagnosed or not reported to the World Health Organization (WHO) (1). There is an urgent need to effectively deploy evidence-based, innovative, and highly effective screening strategies for TB to reach the ambitious target of diagnosing and treating 40 million people from 2018 to 2022, as per the Political Declaration adopted at the United Nations General Assembly in September 2018 (1).

WHO recommends the use of chest X-ray radiography (CXR) as an effective screening test for pulmonary tuberculosis (PTB), as well as an aid in the diagnostic pathway to complement bacteriological tests (2). However, there are two main barriers to the uptake of CXR technology for TB: limited access to high diagnostic quality digital CXR imaging in low resource settings and a shortage of trained readers (usually physician radiologists) to interpret the images. Recent advances in digital imaging and software technologies have led to the development of highly compact, portable, battery-operated digital radiography equipment and artificial intelligence (AI)-based computer-aided detection (CAD) software solutions to interpret CXRs for signs of TB. Although several studies have reported equivalent performance by CAD compared to human readers, only recently has WHO recommended the use of CAD as an alternative to human readers to interpret CXR for screening and triage of PTB in individuals aged 15 or over (3). Consequently, there is growing interest from TB programmes across the world to use a combination of portable digital X-ray systems together with CAD solutions for effective TB screening.

There are numerous challenges in implementing TB screening using digital CXR and CAD technology in rural and urban communities in high TB burden countries. TB programme implementers in low- and middle-income countries (LMICs) frequently encounter problems with selecting the right type of X-ray equipment and CAD solution, and often face practical hurdles with set-up and workflow. Also, the market of X-ray equipment technology and CAD solution for TB is evolving dynamically, with a significant number of equipment manufacturers and CAD developers now entering the market.

This report

FIND published the first technology landscape report titled *Digital radiology solutions for TB diagnostics in low- and middle-income countries* in 2015 (4) to explore the market status of radiology equipment and CAD solutions for TB screening applicability. The report found very limited choice for facility-based, dedicated CXR imaging equipment and only one commercially available CAD solution.

Coming up to 2021, the market of digital X-ray technology has witnessed radical transformations in design and features, with manufacturers interested in producing highly compact, portable battery-operated digital X-ray products. Similarly, there has been a significant increase in the number of CAD solutions with applicability for TB screening, of which many have been CE certified.

This updated report by FIND aims to provide a comprehensive overview of digital X-ray and CAD technologies for TB diagnosis that are currently available in market. Additionally, the report captures the implementation experiences of some early adopters of these technologies in high TB burden countries.

CHAPTER 1 – INTRODUCTION

BACKGROUND

Chest X-ray radiography (CXR) is one of the most sensitive tests for detecting pulmonary tuberculosis (PTB) (5-7) and is often used as a screening test or diagnostic tool where PTB cannot be ruled out microbiologically. This includes patients for whom bacteriological tests tend to have lower sensitivity, such as people living with HIV or people with other immune-compromising conditions, as well as patients for whom it is difficult to obtain samples for bacteriological confirmation, such as children or patients whose immune systems are severly compromised. Sometimes bacteriological tests are not available, are contaminated, or even negative yet CXR findings are nevertheless suggestive of TB.

The role of CXR in improving TB notification in high prevalence settings has been established (8). While CXR is usually conducted in presumptive or symptomatic TB cases, a subsequent analysis of TB prevalence surveys showed that between 36-80% of bacteriologically-confirmed TB cases have a negative symptom screen. CXR may detect 89% of individuals with bacteriologically-confirmed TB disease and therefore should be considered to be done in parallel to symptoms screening in order to find more of the missing TB patients (7). Recent studies in TB high burden countries have revalidated the role of CXRs in active case finding and present a strong argument why TB programmes need to focus more on community-based TB screening programmes (9, 10). This is even more important due to the significant number of people who aren't screened and therefore missed, not to mention the additional complications arising from the COVID-19 pandemic.

Although CXR is the most commonly performed radiography worldwide (11), it can be challenging to produce a high-quality diagnostic image because of the technical limitations of the equipment and image processing, and the lack of qualified radiographers across LMICs. Maintaining diagnostic quality of CXR images over time (crucial for detecting subtle chest pathologies) is also challenging when having to use traditional X-ray equipment with poor service and maintenance. With increasing access to digital X-ray imaging technologies, it is gradually becoming easier to produce better diagnostic quality CXRs. The introduction of AI-based computer-aided detection (CAD) solutions for interpreting CXRs has addressed not only the intra and inter reader variability among radiologists but also the challenges faced when they are not available.

Most of the global market for digital X-ray equipment is targeted at industrialized countries and privatized health service providers in emerging economies, whereas in LMICs this equipment is used for general radiography purposes, due to the high cost of digital radiography. With innovations in design and technology, several equipment manufacturers have been able to significantly reduce the size of X-ray equipment, some of which even weighs less than 5 kg and fitting easily in a backpack. These highly portable X-ray generators are powered by rechargeable batteries and when used in combination with modern, ultra-sensitive detectors can produce decent diagnostic-quality CXR images at improved radiation-dose efficiency. Resultant digital images can immediately be run through highly sensitive and reasonably specific, dedicated CAD solutions to screen for signs of TB or other radiographic findings and results can be obtained at point of care in under a minute.

With a package combining portable or ultra-portable digital X-ray and an offline CAD solution, it has been possible to bring TB screening into communities in remote locations where healthcare facilities are either nonexistent or often have very limited essential infrastructure, like reliable electricity and internet.

Although CAD technology has been around for more than a decade, the uptake by TB programmes in LMICs remains limited (12). This has been partly due to technical, operational, industry and policy-related factors but also to the lack of independent evidence on the performance of CAD solutions in clinical settings (2, 13, 14). However, in recent years, several independent evaluations of CE-certified commercially available CAD solutions have demonstrated that the accuracy of these products is comparable or sometimes even superior to experienced, certified physician radiologist readings (15, 16). Based on the evidence, WHO released new guidelines which stipulate that CAD may be used as an alternative to human reader interpretation of digital CXR for TB screening and triage, but that its use should be limited to interpreting CXR for pulmonary TB in individuals aged 15 years or more (17, 18). As a result, uptake of CAD is expected to increase, bringing new opportunities for industry to market digital CXR with CAD technology for TB, and for TB programmes across the world to explore the added value of this innovative diagnostic approach in the fight against this highly infectious disease.

OBJECTIVES

This report aims to provide readers with a comprehensive understanding of various technologies used to produce CXRs, commercially available CAD solutions aren't screened and therefore missed, not to mention the additional complications arising from the COVID-19 pandemic for TB screening and practical considerations that may apply during the implementation of CXR and CAD technology in the context of TB programmes.

In Chapter 2, we give an overview of the different X-ray technologies that exist, whereas in Chapter 3 we describe the latest developments in diagnostic X-ray imaging. In Chapter 4, we categorize digital X-ray equipment to support CXR imaging for TB programmes based on the setting and intended use-case. Given the role CXR plays in detecting active TB cases in community-based screening, **this report particularly focuses on portable and ultra-portable digital X-ray equipment from leading manufacturers** and outlines their standard specifications in Annex 2 to support decision makers in making equipment selection.

The report also attempts to summarize existing commercially available, certified CAD solutions for TB screening using CXR and highlights important considerations for choosing a particular product, which are discussed in Chapter 5 and Chapter 6, respectively.

Lastly, **the report briefly discusses regulatory considerations for implementing CXR-CAD technology** (Chapter 7) and aims to provide end-user information for X-ray equipment manufacturers and CAD developers by showcasing several early adopter experiences (Chapter 8).

The intended audience for this report includes governmental as well as non-governmental organizations, and researchers in the TB field with an interest in scaling up TB screening through the use of digital CXR and CAD technology.

METHODOLOGY

This landscape analysis is based on an extensive review of information from industry, interviews with manufacturers and TB programme implementers in LMICs, a review of the scientific literature, and information searches on the internet.

Digital X-ray equipment

An internet-based search was conducted to find manufacturers of portable and ultra-portable digital X-ray equipment with potential applicability for TB programmes in LMICs. Twenty-one X-ray manufacturers were identified and contacted based on information from various sources and contacts from previous work done by FIND after reviewing publicly available information about the products. Manufacturers were asked to share detailed information and specifications about their product(s) using a standard specification template. Seven X-ray equipment manufacturers with experience or interest in CXR application for TB programmes were interviewed regarding their product specifications and market experience.

Given the wide range of X-ray equipment available in the portable and ultra-portable category, **we included field-tested models within TB programmes and/or those that had been certified** (CE/FDA, including those in process of obtaining certification). We focused the internet search on products available for sale mostly in the European Union and in North America for inclusion in the product comparison sheet (Annex 2), as the products available in these markets are more likely to have received CE/FDA certification.

CAD solution for TB

Information on the status of CAD solutions was gathered from review of previous work carried out by FIND in collaboration with the Stop TB Partnership (www.ai4hlth.org), literature reviews and interactions with leading CAD developers with CE-certified commercial products. Eight commercially available CAD developers were contacted and asked to share qualitative information regarding market status and implementation challenges associated with CAD solutions for TB, of which four CE-certified CAD developers complied.

TB programme implementer experience

Interviews were conducted with implementers in Malawi, Zambia, and Uganda to explore and document their practical experience with implementing digital portable or ultra-portable X-ray equipment in combination with CAD for TB screening.

CHAPTER 2 – OVERVIEW OF CXR TECHNOLOGY

CXR IMAGING

Applicability of X-ray equipment within the scope of TB programmes is somewhat limited for acquiring CXRs. It is important to appreciate that all types of X-ray equipment can be used to take CXRs and that no X-ray equipment manufacturer makes X-ray equipment exclusively for chest images. This segment of the report attempts to briefly explain various types of X-ray imaging and processing technologies that are currently being used to produce CXRs.

CXR imaging is a two-step process. The first step involves image acquisition, in which X-ray beams (electromagnetic radiation) produced from a source (X-ray generator) penetrate the patient's thorax and sensitize the image receptor. The receptor can be a digital flat panel detector (digital radiography (DR)), a reusable phosphor plate (computed radiography (CR)), or a conventional X-ray film (analog radiography), forming a so-called latent image.

The second step involves processing the latent image into a radiograph with multiple shades of grey. The use of a conventional image receptor (X-ray film) requires wet processing technology and produces an analog image, whereas both the phosphor plate (CR technology-based) and the flat panel detector (DR technology-based) image receptors produce digital images. The only difference between CR and DR is that CR technology requires an additional processing device to scan the exposed phosphor plate (often called digitizer or CR reader), whereas no additional processing device is needed for the DR image receptor, as the processing happens instantly. Final output digital images are in DICOM (Digital Imaging and Communications in Medicine) or JPEG file formats, allowing for electronic viewing, archiving and sharing using standardized PACS (Picture Archiving and Communication System) and teleradiology services (19).

>>>>> People waiting to get screened in the mobile X-ray truck in Viet Nam.

(Image credit: Friends for International TB Relief (FIT), Viet Nam)

DIGITAL RADIOGRAPHY

Digital radiography (DR), also known as complete digital radiography or direct digital radiography, is the latest development in X-ray technology that makes use of different types of solid-state detectors (also called flat-panel detectors or simply detectors). These are made of glittering materials like cesium iodide, or selenium crystals, which act as image receptors, that are then activated by an X-ray generator specifically calibrated to produce a digital image with excellent contrast and resolution. Once the image is formed, it is instantaneously transmitted to the workstation monitor/device and the detector can be used for subsequent exposures without the need for preparation or erasing before a next exam. The current generation of detectors are compact, lightweight, and come in various sizes including portable battery-operated versions able to wirelessly transmit digital images in real time to PACS.

DR is increasingly becoming the preferred modality of radiographic imaging by reducing steps involved in image processing, hence, delivering high throughput with excellent image characteristics (contrast and resolution) and a better radiation-dose efficiency. A modern DR set-up usually comes as an integrated package comprised of a calibrated X-ray generator, a sensitive detector and electronic workstation with the required software, including anatomically programmed radiography (APR), a series of anatomy-specific predetermined settings, which reduces manual steps for the radiographer during the process of image acquisition. All the benefits of digital images such as archiving, sharing via local PACS network for on-site reporting and the option to include CAD screening or teleradiology can be efficiently performed with DR. However, considerable capital investment is needed due to the cost of the detector and calibrated X-ray generator. Furthermore, the detectors are very fragile and need to be handled with care during radiography and/or transportation as even minor mechanical damage can mean total malfunction, large financial implications, and disruption in services.

A less expensive model for a DR set-up can be achieved when an already existing analogue X-ray machine (X-ray generator) is in place. These systems can be retrofitted with a new DR detector and image acquisition software, thereby transforming an analog system into a DR system. This is referred to as analog retrofit digital radiography and is discussed below.

Figure 1

Complete DR X-ray Equipments. **(A)** MinXray Impact portable Digital X-ray system with transportation kit, **(B)** Europa AirTouch battery-operated handheld digital X-ray from Aspen Imaging, **(C)** Stationary U arm digital X-ray system from Swissray.

(Image credit: MinXray, Aspen Imaging and Swissray)

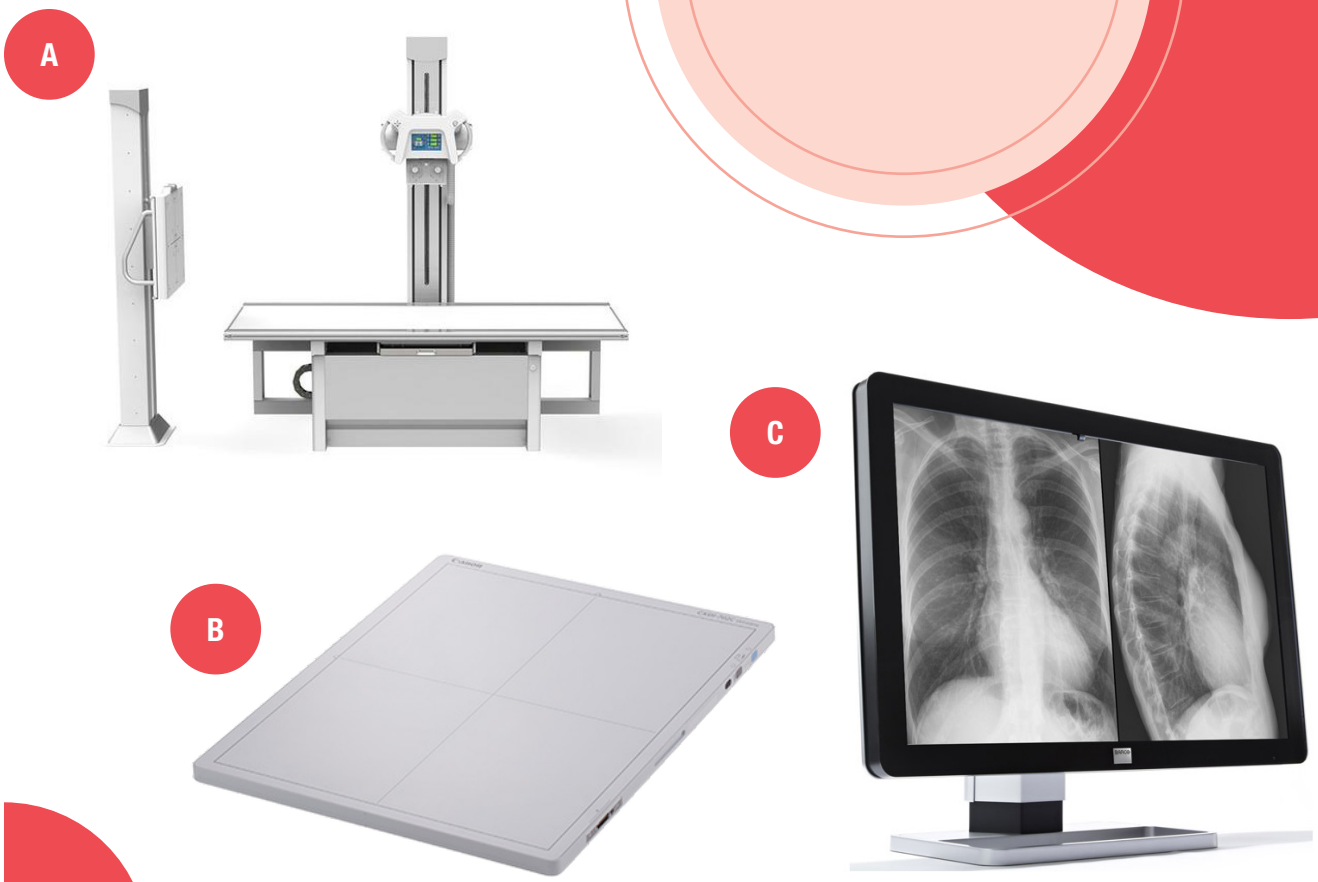


Figure 2

An analog X-ray machine **(A)**, a wireless detector **(B)** and a monitor with image viewing software **(C)**

(Image credit: Maya, Cannon and Barco)

ANALOG RETROFIT DIGITAL RADIOGRAPHY

Analog retrofit DR-based imaging systems make use of existing analog X-ray equipment and are retrofitted with a flat panel detector to produce high-quality digital radiographs. An analog retrofitted digital system delivers a similar image quality as a new DR system but may be less radiation dose efficient since the existing X-ray generator might not be properly calibrated to the new highly sensitive digital detectors. Radiation dose efficiency can be improved by using lower exposure parameters and is often more efficient than computed radiography (CR) and/or analog X-ray equipment, which are discussed later in this chapter. Although image acquisition and post-processing software are usually provided by detector manufacturers while retrofitting the existing equipment, it is often difficult to integrate APR for CXR acquisition, hence manual selection of exposure parameters may have to be done by the radiographer.

Usually, analog retrofit DR set-up is done by imaging service providers with the intention to enhance diagnostic image quality, augment workflow, increase efficiency and throughput at hospitals or busy imaging facilities. There is a significant cost-saving component when making use of existing, traditional X-ray equipment, although these systems are usually heavier, bulkier and require a stable power source to operate. There is also a significant market for portable analog retrofit DR equipment; this means that existing analog portable X-ray equipment can be used with a modern flat panel detector for offsite radiography. The long-term economic considerations linked to the lifespan of the equipment, maintenance cost and type of detectors being considered for retrofitting, cost of image viewing software, type of use (at facility or offsite) etc. need to be considered by TB programmes before deciding to invest in an analog retrofit DR set-up.

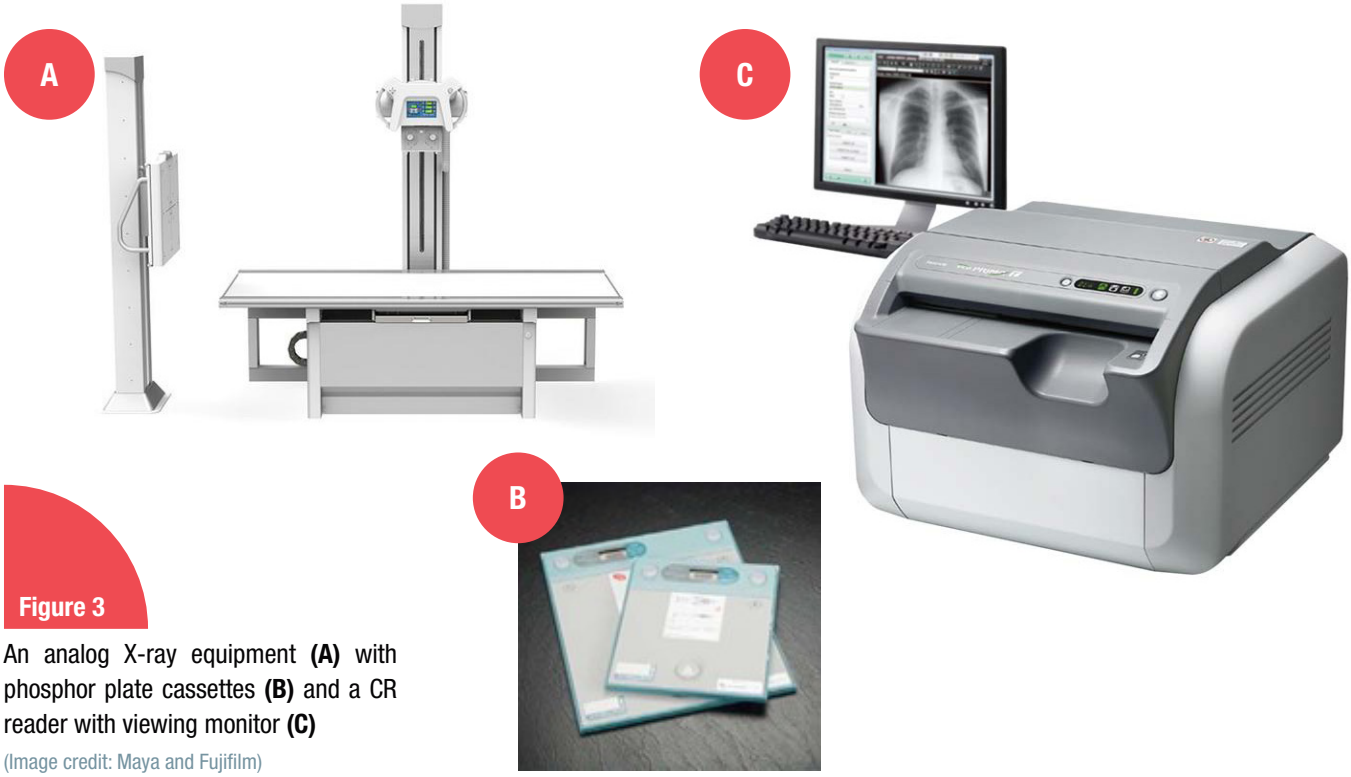


Figure 3

An analog X-ray equipment **(A)** with phosphor plate cassettes **(B)** and a CR reader with viewing monitor **(C)**

(Image credit: Maya and Fujifilm)

COMPUTED RADIOGRAPHY

Computed radiography (CR) systems are a combination of analog X-ray equipment for taking the image combined with reusable photostimulable phosphor (usually referred to as a phosphor plate) technology for image processing. Once the X-ray exposure is made, the exposed cassette containing the phosphor plate is placed inside a special scanner/reader (usually referred to as CR reader or digitizer) that converts the latent image into a digital image (DICOM or JPEG) as output. The image on the phosphor plate is erased during the processing phase and therefore the phosphor plate is immediately available for the next exposure after the processing is completed. The entire cycle of image acquisition up to image processing usually takes about 2 to 3 minutes (depending upon make and model). Since the output image is in DICOM or JPEG format, all the image characteristics and benefits associated with DR-based imaging are also applicable to CR-based imaging, only at the expense of increased radiation dose and reduced throughput compared to DR-based systems (image processing time is usually < 5 sec for DR systems). Radiation dose efficiency can be improved to match DR-based imaging by careful selection of exposure parameters depending upon different body habitus of patients.

The CR reader/digitizer is a separate piece of equipment that needs to be installed in addition to the X-ray generator to scan the cassettes containing the phosphor plate after each exposure. There is a large variation in terms of size of the CR reader and cost based on the capacity to process several cassettes at a time; the average size of a CR reader is like a moderate-sized photocopy machine which has the capacity to process one cassette at a time and there are larger heavy-duty models with capacity to process up to five cassettes (or more) at a time. The number of phosphor plates (cassettes) required at imaging site depends on the volume of examinations, usually two would suffice for a small workload environment, however, multiple CR plates might be needed at a significantly busy radiography site where more people need to be X-rayed in less time. Additionally, specific operational training of the radiographer on the proper use and maintenance of the CR reader, care, and maintenance of phosphor plates (which are susceptible to creating artifacts on images if not cleaned periodically) is needed from quality assurance perspectives. Regarding the life of phosphor plates, there is quite a variation in terms of manufacturers recommendations to replace them every 5 years, after a certain number of exposures (usually in thousands) or visible degradation in image quality. CR remains the most common form of 'digital' imaging system in most LMICs because of the robustness and relatively low initial investment cost compared to a complete DR equipment or analog retrofit DR set-up. While in majority of circumstances CR-based imaging is seen at hospitals and imaging clinics, it can also be implemented for offsite imaging using analog portable X-ray generator, however this usually presents with logistical challenges with transportation, more space requirement, steady power supply and increased susceptibility to mechanical damage.

ANALOG RADIOGRAPHY

Analog radiography is the traditional method of X-ray imaging and is often referred to as film-based radiography. It is still in use in many low resource, high TB burden settings, especially at rural healthcare facilities. Analog X-ray equipment generates X-rays combined with X-ray films (made of silver halide crystals and loaded inside X-ray cassettes) which serve as the image receptor. The exposed X-ray film requires a wet processing mechanism (consisting of developing and fixing the image using chemicals) either done manually in a dark room or using an automatic processor. The dependence on a dark room-based process involving chemicals, complex accessories like X-ray cassettes, and extra human resources, not to mention the difficulty of maintaining quality assurance parameters are all factors that limit the wide-scale use of this method for fast and effective TB screening at the population level.

The output is an analog image (X-ray film), which in its original form cannot be archived digitally in a PACS or used directly as an input file for CAD solutions, so requires a highly experienced radiologist to interpret the image. However, if the output image can be digitized using a good digital camera or smartphone, it can be transmitted electronically to a remote telemedicine service staffed by consultant radiologists for reporting. Some CAD developers accept non-DICOM images such as JPEG, PNG and even low-resolution smartphone-acquired images of the X-ray film placed on a lightbox. However, there might be concerns with the diagnostic quality of the original image and thus far no scientific studies have reported the performance of CAD solutions using digitized images of manual X-ray films.

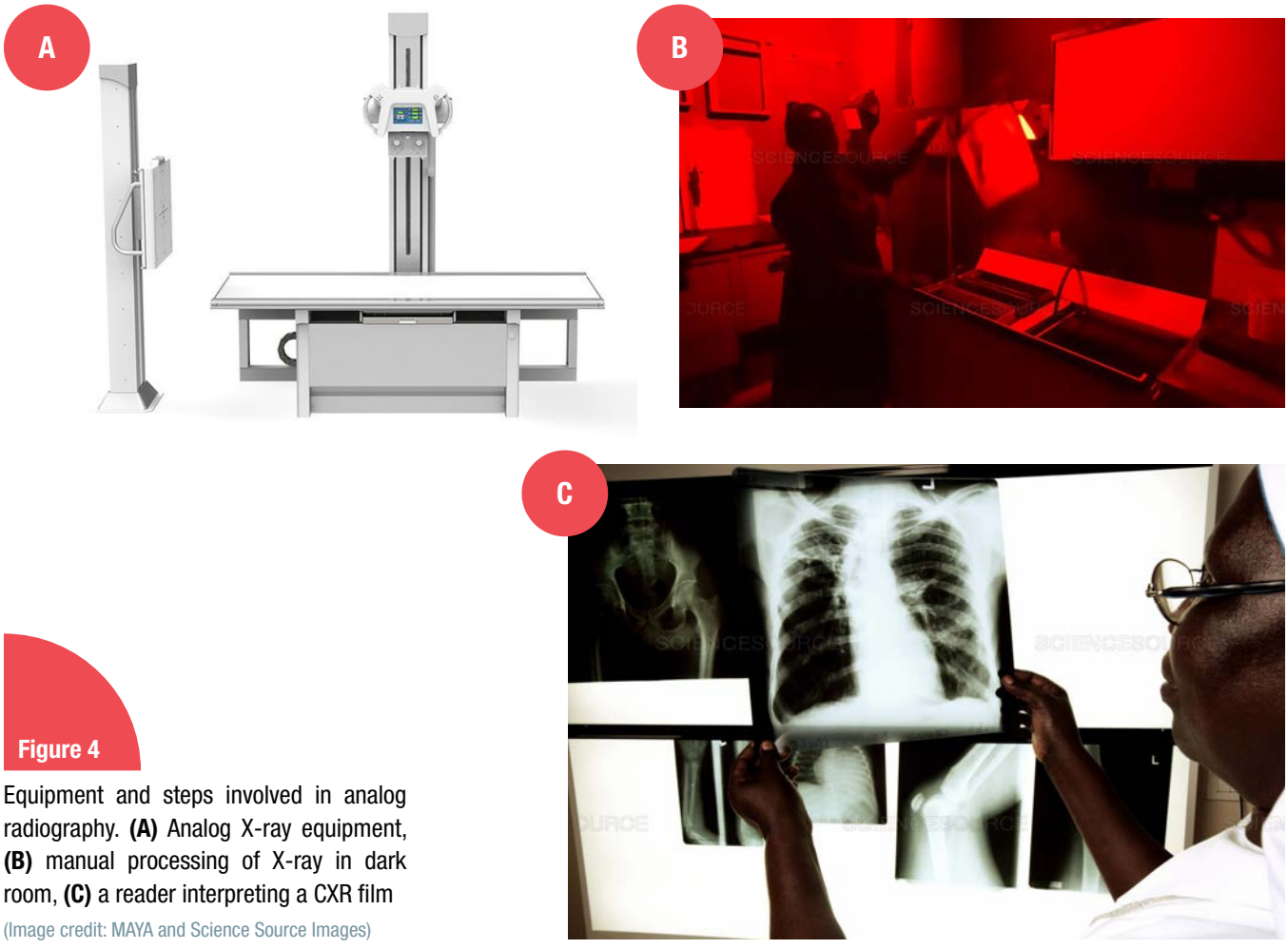


Figure 4

Equipment and steps involved in analog radiography. **(A)** Analog X-ray equipment, **(B)** manual processing of X-ray in dark room, **(C)** a reader interpreting a CXR film

(Image credit: MAYA and Science Source Images)

>>>>> Table 1. Comparative analysis of all CXR imaging technologies

	COMPLETE DR-BASED CXR IMAGING (NEW X-RAY GENERATOR + DETECTOR PACKAGE)	RETROFIT DR-BASED CXR IMAGING (EXISTING ANALOG X-RAY GENERATOR + NEW DETECTOR)
TECHNOLOGY	Combination package of a calibrated X-ray generator and DR panel (no additional processing technology required).	Analog X-ray generator and retrofit DR panel (no additional processing technology required). Existing X-ray generator can be used.
EQUIPMENT MODELS	Available for facility-based or offsite portable application (portable models are highly compact and present with significantly less logistical limitations compared to analog retrofit DR- and CR-based equipment).	Can be used for facility-based or offsite portable application (some logistical limitations may apply in terms of portable applications).
OUTPUT IMAGE, PACS AND CAD IMPLEMENTATION	Digital image (usually DICOM). PACS compatible, can run CAD.	Digital image (usually DICOM). PACS compatible, can run CAD.
IMAGE CHARACTERISTICS	Image parameters (contrast, resolution) are comparable to or sometimes slightly superior to CR-based imaging or retrofit DR-based imaging. Least manual steps in terms of achieving highest possible image parameters. Image is less susceptible to artifacts compared to CR and analog imaging.	Image parameters (contrast, resolution) are comparable to complete DR equipment and CR-based imaging. More manual steps compared to complete DR equipment to achieve highest possible image quality. Image is less susceptible to artifacts compared to CR and analog imaging.
THROUGHPUT	Excellent throughput, modern equipment has less than 5 seconds of image generation time.	Excellent throughput, slightly more image processing time compared to complete DR equipment.
RADIATION-DOSE EFFICIENCY	Highly dose efficient. Modern equipment uses sensitive detectors and X-ray generators calibrated to specific detector.	Better dose efficiency compared to CR-based equipment or analog equipment, slightly less dose efficient compared to complete DR equipment.
SERVICE AND MAINTENANCE	Detectors are highly susceptible to mechanical damage. Usually, replacement needed in case of damage.	Detectors are highly susceptible to mechanical damage. Usually, replacement needed in case of damage.
COST	**Initial investment:** (Additional insurance cost might be needed for detectors.) **Estimated price range of complete package of new equipment set-up** (X-ray generator, detector, viewing software, essential accessories): **Facility-based** US$ 125,000 to US$ 150,000 **Portable** US$ 40,000 to US$ 100,000 **Ultra-portable** US$ 40,000 to US$ 70,000.	**More expensive compared to CR, less expensive compared to complete DR** as there is cost saving in X-ray generator component. Additional insurance cost might be needed for detectors. **Estimated price range of detector, viewing software** (excludes X-ray generator cost): US$ 20,000 to US$ 100,000 (or higher).

	CR-BASED CXR IMAGING (EXISTING ANALOG X-RAY GENERATOR + CR READER)	ANALOG CXR IMAGING (EXISTING ANALOG X-RAY GENERATOR + MANUAL IMAGE PROCESSING)
TECHNOLOGY	Analog X-ray generator and reusable phosphor plates (with CR reader / digitizer for image processing is required). Existing X-ray generator can be used.	Analog X-ray generator and accessories (X-ray films, cassettes with screens) along with darkroom-based wet processing mechanism / automatic chemical processing.
EQUIPMENT MODELS	Can be used for facility-based or portable application (significant logistical limitations for portable application compared to DR-based systems due to requirement of additional processing equipment and multiple phosphor plates depending on workload).	Mostly used at facility-based imaging, very difficult to implement for offsite or portable application due to manual image processing requirements.
OUTPUT IMAGE, PACS AND CAD IMPLEMENTATION	Digital image (usually DICOM). PACS compatible, can run CAD.	Analog image, X-ray film. Not compatible with PACS and CAD unless the original output image is digitized using a digital camera or smartphone (JPEG or PNG file formats only). Narrow choice of CAD solutions as digital image is in non-DICOM format. Reduced diagnostic quality of digital image.
IMAGE CHARACTERISTICS	Image parameters (contrast, resolution) are usually comparable to complete DR and analog retrofit DR equipment. More manual steps compared to complete DR or analog retrofit DR equipment to achieve highest possible Image quality. Image is more susceptible to artifacts as compared to DR-based imaging. Phosphor plates need to be cleaned periodically.	Image parameters (contrast, resolution) are significantly inferior as compared to digital images produced by DR-based and CR-based equipment. Careful selection of exposure parameters and heavy dependency on processing conditions to maintain diagnostic image quality. Image is more susceptible to artifacts as compared to DR and CR-based imaging.
THROUGHPUT	Moderate throughput, usually 2 to 3 minutes of image processing cycle by CR scanner.	Low throughput, huge variation in terms of image processing time depending upon choice of dark room-based processing or automatic processing.
RADIATION-DOSE EFFICIENCY	Less dose efficient compared to DR-based equipment, dose efficiency can be improved by careful selection of exposure parameters because of greater sensitivity range of CR image receptors.	Less dose efficient compared to CR and DR X-ray equipment.
SERVICE AND MAINTENANCE	Greater degree of robustness compared to detectors; however, more susceptible to mechanical issues and needs periodic maintenance.	Manual processing technology usually present with more technical or operational issues. X-ray cassettes, screens need to be maintained, replaced periodically.
COST	**Less expensive option for digital imaging compared to DR** but might be expensive in long run depending upon use-case (throughput, service, and maintenance cost). **Estimated price of a CR digitizer able to process one CR cassette at a time** (excludes X-ray generator cost, additional cost for viewing software may apply): US$ 10,000 (approx. variation in terms of size and capacity) Phosphor plate and cassette US$ 600 (approx.).	**Significant indirect costs** (consumables – X-ray films, cassettes with screens, chemicals, processing tank or automatic processor, plus HR costs) can add up in the long run. **Excluding the cost of existing analog X-ray equipment, significant cost on image processing component:** consumables (X-ray film, cassettes, screens, processing chemicals) and other indirect costs including additional HR which is often required only for processing the images.

CHAPTER 3 – RECENT ADVANCES IN DIGITAL RADIOGRAPHY

Complete DR systems were introduced more than a decade ago by leading radiology manufacturers in the form of multi-purpose stationary equipment and were mostly intended for general radiography applications in hospitals and clinics. The technology also required powerful X-ray generators. Use of such equipment outside typical hospital settings was out of scope due to the size of the apparatus, need for stable power for the X-ray generator and flat panel detector, and difficulties in transporting the equipment to multiple sites. To install DR systems inside vehicles required large trucks, power supply and good road conditions to minimize mechanical damage. Gradually, with the evolution in detector technology (less radiation required to generate an image, battery-powered detectors, wireless image transmission capabilities etc.), mobile DR systems (medium- to large-size X-ray equipment on wheels that could be rolled through hospital corridors for intensive care unit (ICU) or ward radiography) became available in market.

More recently, X-ray detector technology has progressed significantly, allowing the production of sensitive, lightweight, wireless detectors with extended battery power supply, leading to a greater degree of portability. Due to the enhanced sensitivity of these detectors and the simultaneous use of advanced imaging/post-processing software (automated noise correction, anti-scatter suppression, etc.) to enhance image parameters, it is now possible to produce diagnostic quality X-ray images of even thicker body parts, like the abdomen and thorax with substantially less X-ray exposure. This means reducing the power of the X-ray generator while increasing dose efficiency and maintaining diagnostic image quality. As a result, the current market of DR systems consists of a diverse range of compact, lightweight, alternating current (AC)-powered and/or battery-powered efficient X-ray generators combined with highly sensitive detectors capable of producing diagnostic quality X-ray images even in locations lacking electricity (disaster operations, ambulances, makeshift hospitals, refugee camps, community centres, prisons). These hardware and software advancements have completely redefined the standards of "portable radiography", including CXR imaging. However, only a small number of this novel portable and ultra-portable X-ray gear has proven experience in LMICs and in TB programmes.

DETECTOR

The detector is the main component of DR X-ray equipment. Detectors are specialized devices that trap incident X-ray photons and electronically convert them into a digital visual output. Detectors have a wired or wireless connection with the electronic workstation of the X-ray equipment to instantaneously transmit X-ray images to workstation computers. They need either AC or battery power to work. Current generation wireless detectors usually process an image within 1 to 2 seconds of X-ray exposure and can last for 1-200 exposures (depending on the model and specifications) when fully charged. Usually, the charging time ranges between 4 to 8 hours.

Figure 5

Wired detectors. **(A)** A wired CXDI Flat Panel Detector (FPD) from Canon, **(B)** wireless XMARU FPD from Rayence

(Image credit: Cannon and Rayence)

There are **two distinct categories of detectors used in digital radiography** based on the method of conversion of X-ray photons by the detectors:

Indirect conversion detectors	Direct conversion detectors
Indirect conversion detectors are made up of scintillating crystals, which upon activation absorb the X-rays produced by light photons which in turn are detected by a photosensor and converted into a digital image.	Direct conversion detectors are based on semiconductor materials, which absorb X-ray photons and directly convert the absorbed X-ray into a proportionally sized electrical charge that is further processed into a digital image.
Commonly made of Cesium Iodide and gadolinium oxysulphide.	Commonly made of amorphous selenium.
High detective quantum efficiency (DQE), low modulation transfer (MTF), low image contrast, higher quantum noise.	Higher DQE, MTF, and higher contrast-to-noise ratio (CNR).
Suitable for imaging large anatomic structures using more powerful X-ray beams.	Suitable for imaging small or fine anatomic structures (i.e., extremities).
Radiation dose reduction below current clinical levels is difficult.	Low radiation dose compared to indirect detectors but can only function with low energy X-ray beams.
Commonly used for CXR imaging.	Not commonly used for CXR imaging.

There are other technical parameters, such as pixel pitch, pixel matrix, resolution, size of the detector etc., that affect the diagnostic quality of image. The size of the detector is based on the anatomical part to be imaged. For CXR applications, usually 14 x 17 inches (35 x 43 cm) active pixel area detectors are used. Although X-ray detectors are a separate component of the DR system (and manufactured separately), they are usually sold as an integrated package by X-ray generator manufacturers to match with the X-ray energy range (kV) produced by the generator, type application and desired features (small part or large body part radiography, stationary or portable use, wired or wireless transmission). While procuring DR X-ray equipment, all possible detector options recommended by the X-ray equipment manufacturer should be investigated as this can impact the image quality, throughput, and overall cost.

X-ray detectors have high production costs and there is considerable variation in the price among global manufacturers, ranging from US$ 20,000 to US$ 100,000 or higher for a detector, including workstation and software. Usually, the higher price is for FDA or CE approved products with features like wireless capabilities, extended battery life, and inclusion of various image influencing software (for example, automated noise reduction, grid-suppression, specific patented technologies). The current market of X-ray detectors is worth US$ 2.8 billion (as of 2020) and is projected to reach US$ 3.8 billion by 2024, at an annual growth rate of 6.1% (20).

INNOVATION, R&D IN DETECTOR TECHNOLOGY

R&D in detector technology and progress in computational science are driving innovation in a new generation of flat panel detectors. One of the promising substances to be used for production of the next generation of highly efficient flat panel detectors is hybrid methylammonium lead iodide perovskite-based semiconductor material, which shows excellent response to X-ray energies used in diagnostic radiography, including CXR imaging (21).

Dual energy X-ray detectors

Another recent development in X-ray detector technology are dual energy detectors that automatically separate different energy levels of X-ray beams from a single exposure, resulting in visualization of soft tissues without the superposition of bones. The advantage of this technology is that it does not require extra radiation and is free of motion artifact.

A Canadian manufacturer, KA Imaging has released a portable and retrofittable detector based on this technology (22, 23). KA Imaging's unique patented technology simultaneously captures dual-energy images and very high detective quantum efficiency (DQE) digital radiography images. This technology is particularly promising for detecting subtle pathologies in CXR, which can be obscured by bony thorax or mediastinal structures, and hence has potential applicability for TB diagnosis. However, at the writing of this report, the currently available CAD solutions for TB are not (yet) compatible with bone-subtracted or soft tissue-subtracted images and therefore require human interpreters.

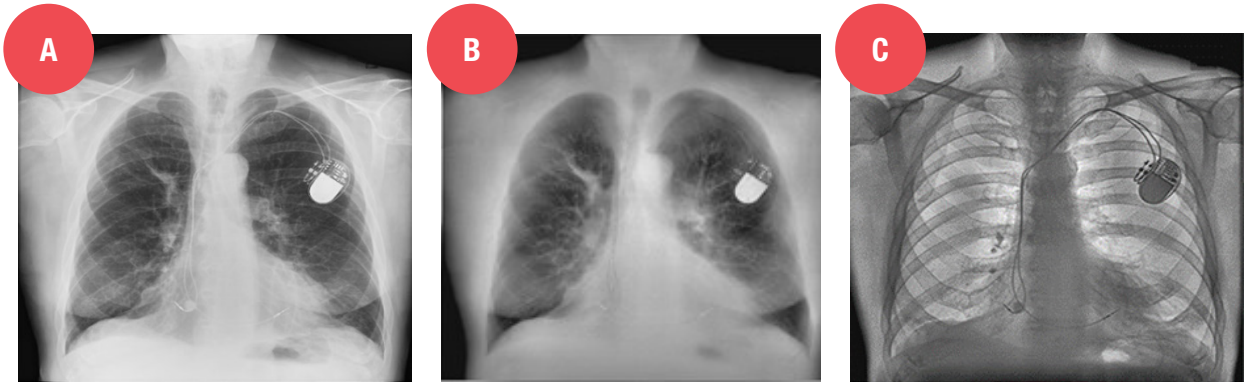


Figure 6

CXR taken in a single exposure using the Reveal™ dual energy detector, **(A)** normal image, **(B)** bone subtracted image and **(C)** soft tissue subtracted image

(Image credit: KA Imaging)

CHAPTER 4 – X-RAY EQUIPMENT CATEGORIZATION FOR TB PROGRAMMES

While it is important to know the technological categorization of X-ray equipment based on image generation and processing mechanism (complete DR, retrofit DR, CR or analog), **it is equally important to understand and assess how and where the equipment will be used,** especially for TB programmes in LMICs that are considering introducing or scaling up CXR screening.

CXR imaging appropriate for TB programmes can be broadly divided into two use-cases: facility-based X-ray screening and non-facility-based screening. Both use-cases might have further applications for CXR imaging depending on specific programme needs. The following schematic representation explains this.

Although a majority of CXRs are taken at hospitals or health-care facilities, some TB programmes have specific needs pertaining to CXR application. To find missing cases, TB programmes are increasingly investing in screening vulnerable populations at elevated risk of acquiring TB infection. It is often difficult to reach out to specific populations in low resource settings who often do not have access to healthcare and do not visit healthcare facilities. Such high-risk populations include but are not limited to the prison population, people living with HIV, coal miners, tribal communities in remote settlements, people living in densely populated urban slums, and crowded refugee camps. However, it is not always the case that only people from vulnerable and marginalized sectors are hard to reach for TB screening; often people from higher socioeconomic sectors in LMICs are also missed by TB screening and diagnostic programmes. While this can be attributed to several reasons, the major one may be a lack of trust on the quality of health services being provided for TB screening and diagnosis.

It may well be that TB programmes have set targets in their national strategic plans to diagnose and treat a certain number of TB patients who can only be found through active case finding/screening. To increase detection of TB, screening needs to be conducted at local communities in the proximity of high-risk populations. Most of these settings lack essential infrastructure such as power supply, internet, functioning roads, etc.

It often requires one or more of the following approaches for TB programmes to run effective screening campaigns or to set up temporary clinics within the reach of these target population:

- Ability to transport the X-ray equipment to multiple locations for temporary use at local healthcare facilities
- Setting up temporary imaging clinics for event-based screening in rural/semi-urban areas
- Transforming a truck or van into a mobile X-ray clinic for TB screening (sometimes also equipped with a a workstation for rapid molecular diagnostic testing)

Depending on the use, size, required infrastructure and portability across a range of scenarios discussed above, **the X-ray equipment needed for TB programmes can be classified into three categories:**

Category 1 - Stationary X-ray equipment

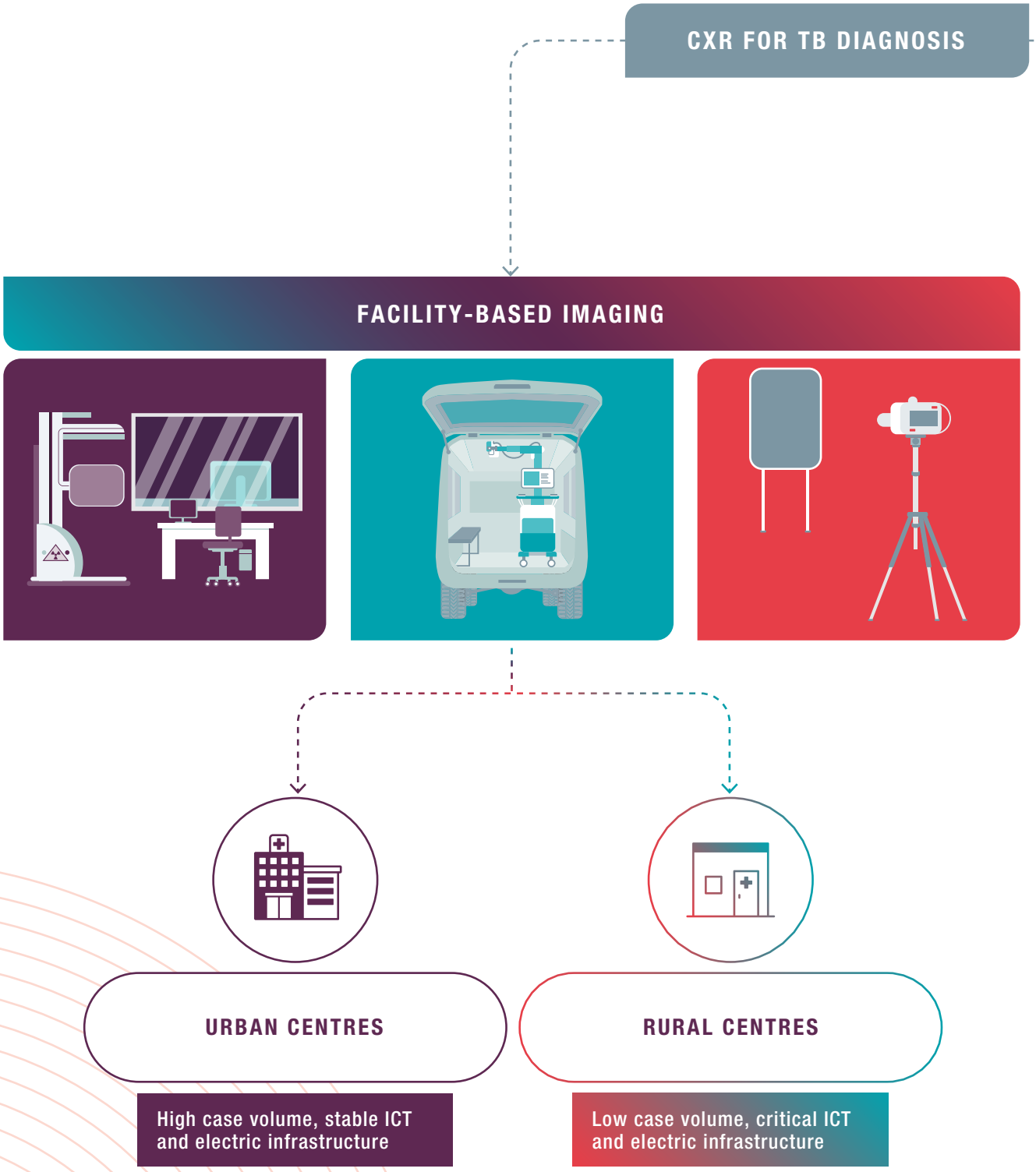
Category 2 - Portable X-ray equipment

Category 3 - Ultra-portable X-ray equipment

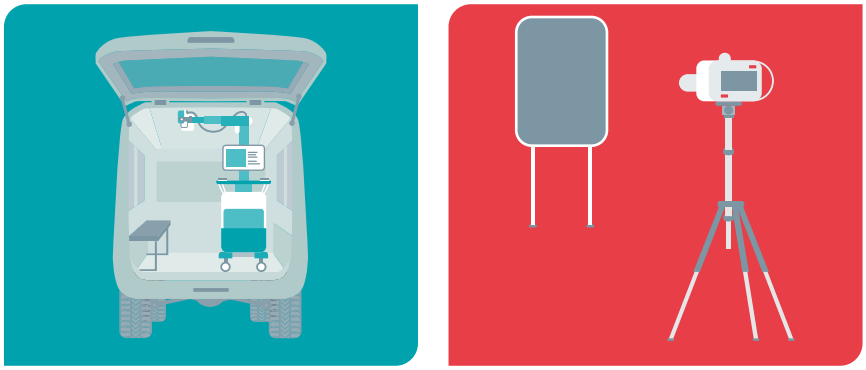
Although the above categorization of X-ray equipment for TB programmes is applicable to all technological classifications of X-ray equipment (complete DR / analog retrofit DR / CR / analog), **in the remainder of the report we present a brief overview of only complete DR X-ray equipment in each category** (stationary, portable, and ultra-portable), with the greatest focus on portable and ultra-portable equipment.

There is considerable overlap between category 2 and 3 equipment. Some industry experts might prefer to collectively put them under one umbrella. However, **in this report, the distinction is made between portable and ultra-portable based on the degree of portability and the input power mode.** For example, ultra-portable X-ray equipment is completely battery-operable, weighs less than 20 kg and can fit into a moderate-to-large size backpack.

>>>>> Illustration 1. Different modes of CXR operation for TB programmes to consider, dependent on the location and use-case where screening will take place



NON-FACILITY-BASED IMAGING



DENSELY POPULATED URBAN SLUMS

Mobile radiography, van/truck or temporary clinic

HIGH-RISK TARGET GROUPS (HIGH THROUGHPUT)

Prisons, refugee camps

REMOTE SETTLEMENTS (MEDIUM TO LOW THROUGHPUT)

Temporary X-ray clinics
Event-based X-ray screening clinics

Footnote: Stable ICT and electric Infrastructure – Reliable power supply and internet bandwidth supporting trouble-free upload and download of DICOM files.

CATEGORY 1 – STATIONARY X-RAY EQUIPMENT

Stationary X-ray equipment is composed of a powerful X-ray generator (mostly AC powered or large rechargeable battery for temporary backup) **and detectors with a chest stand.** It usually weighs over 200 kg and has an output power of 20 kW or higher. Robust, integrated equipment designed with a dedicated chest stand, detector assembly and excellent diagnostic images makes it an ideal choice for facility-based chest imaging in a high workload scenario (>300 X-rays per day).

Several leading X-ray manufacturers produce this category of equipment. There is significant variation in the price of products, ranging from US$ 43,000 to US$ 140,000 depending upon location, brand, and regulatory approvals. Usually, CE or FDA approved products cost over US$ 100,000.

Some of the TB programmes around the world have used this category of equipment also for mobile community TB screening, where the X-ray equipment was installed in a truck. However, there are serious limitations, operational challenges and costs associated with mobile applications, as this equipment is designed for facility-based imaging.

The recommended specifications for this category of X-ray equipment are based on the WHO specifications for stationary digital X-ray equipment (24) (see Annex 1, which includes a comprehensive list of X-ray equipment with CE/FDA certification for this category).

Figure 7

Delft Easy DR stationary X-ray equipment

(Image credit: Delft Imaging)

Product link

(Image credit: Ben Philips, FIND)

CATEGORY 2 – PORTABLE X-RAY EQUIPMENT

It is important to understand the difference between 'mobile' and 'portable' X-ray equipment. Transportability is the principal criterion for a portable system. Traditional, heavy mobile X-ray equipment on wheels used in ICUs or in hospital radiography wards is a mobile, not a portable tool.

Portable X-ray equipment is significantly lighter (usually < 100 kg) with output power in the range of 5–10 kW, can easily be assembled and disassembled and fits in large carry-on cases, allowing for easy transport in a mid-size car or van for temporary use at a local facility and requires only a household power supply or equivalent. It can be installed inside a large van or mini-truck for community-based screening. Portable X-ray equipment can reach medium to moderately high throughput of 100–300 X-rays per day – in some cases even higher depending upon power and X-ray generator components.

New generation X-ray equipment in this category is based on innovative designs with ergonomic features and can produce high quality CXRs, with excellent image characteristics, requiring less X-ray power while still satisfying radiation dose limits.

There is a large variation in terms of cost, depending on the make, regulatory clearance, availability and terms of procurement; FDA or CE approved models cost in the range of US$ 40,000 to US$ 100,000.

Figure 8

MinXray CMDR-2S Portable DR X-ray System with wireless detector

(Image credit: MinXray)

Product link

Figure 9

Fujifilm FDR NANO Portable DR X-ray System

(Image credit: Fujifilm)

Product link

CATEGORY 3 – ULTRA-PORTABLE X-RAY EQUIPMENT

Ultra-portable equipment applicable for TB programmes is the newest to join the market. These machines are fully battery operated, highly compact in design, have an output power < 5 kW, low weight (< 20 kg, fits in a backpack), and can produce digital diagnostic-quality CXR images when used with a recommended highly sensitive detector. The smallest ultra-portable systems are less powerful than their larger counterparts, which impacts image quality. This category of equipment comes with the highest degree of portability and is usually marketed by manufacturers as an integrated package with essential accessories like tripod stand, detector, and workstation (laptop/tablet) in an ergonomic carrying bag or case.

For most equipment in this category there is limited documented experience within TB programmes, but these systems are gaining a significant market for use across a range of applications like disaster settings, veterinary clinics, forensic applications, sports imaging, first responders, and more recently with CXR imaging for COVID-19 screening and severity assessment.

Advanced X-ray generation technology, modern batteries and highly efficient flat detector panels allow this category of equipment to last between 40 to 100 exposures with fully charged batteries (charging time varies between 2–6 hours), hence, making them useful for TB screening in remote communities, temporary clinics, or for event-based screenings with a small number of people to be X-rayed. However, depending on the availability of a recharging power source or replaceable batteries, they can deliver screening volumes comparable to larger systems.

There is large variation in terms of instrument cost, depending on the make, regulatory clearance, availability and terms of procurement; FDA or CE approved models cost in the range of US$ 40,000 to US$ 70,000.

A

Product link

B

Product link

C

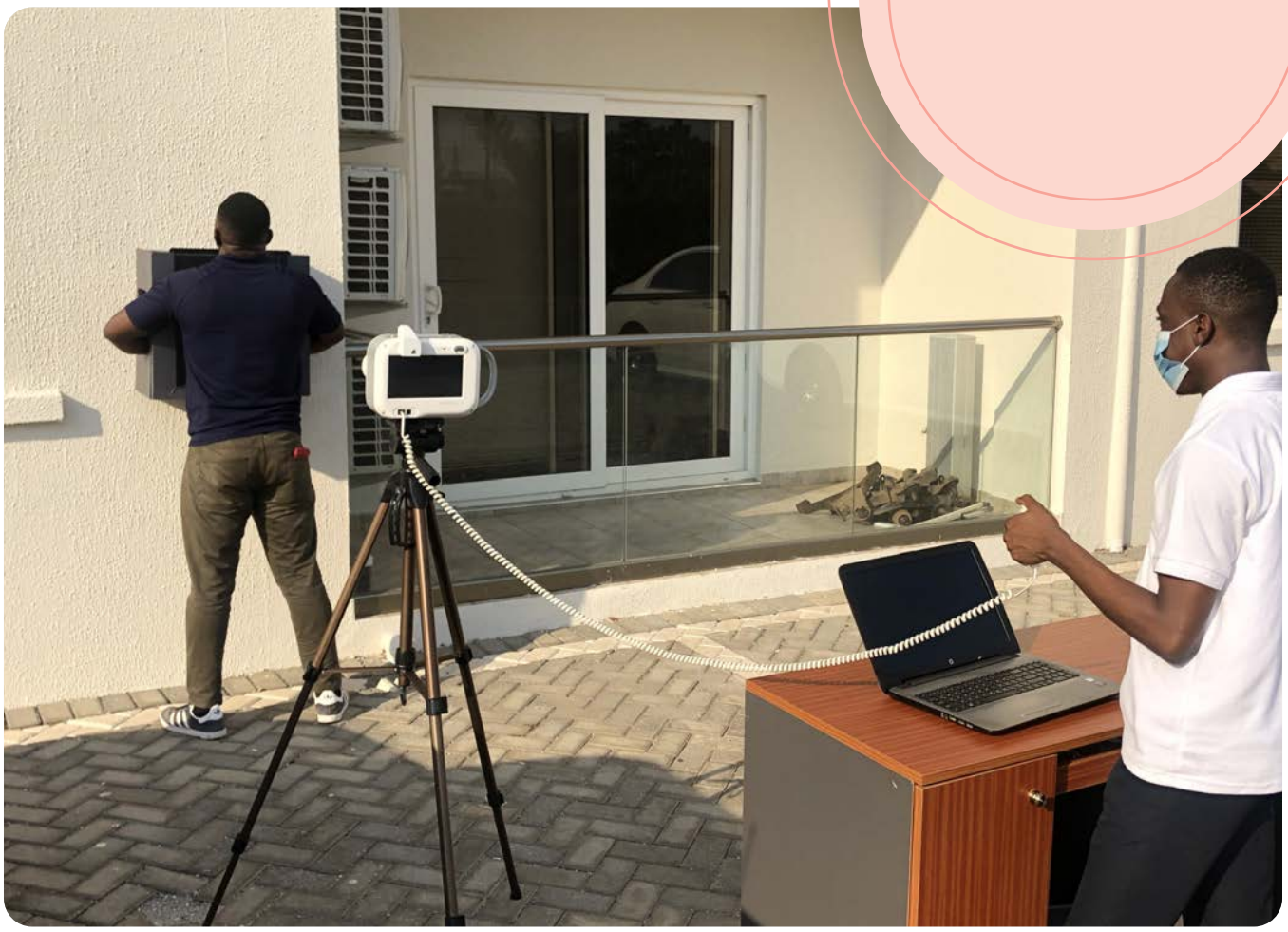
Product link

Figure 10

Battery-operated lightweight ultra-portable DR systems **(A)** Aspen AirTouch Europa from Aspen Imaging, **(B)** Fujifilm FDR Xair from Fujifilm and **(C)** MINE ALNU from HDT

(Image credit: (A) Aspen Imaging; (B) Fujifilm; (C) HDT)

>>>>> CXR screening with the Delft Ultra in Ghana.
(Image credit: Delft Imaging)



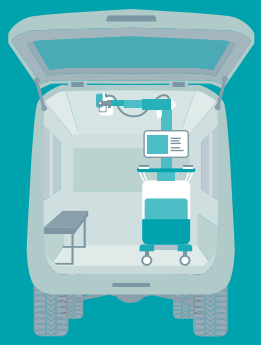
For this report, FIND did extensive internet-based search, contacting X-ray manufacturers and TB programme implementers in various countries who have experience with community-based TB screening using portable or ultra-portable DR X-ray equipment to identify a full range of available products in the market. We outlined a detailed specifications list we collected from equipment manufactures and compared our specifications with existing WHO specifications for stationary digital X-ray equipment (24), WHO-IAEA technical specifications for imaging devices applicable for COVID-19 screening (mobile digital radiography system) (25), and specifications for portable/lightweight X-ray equipment released by Stop TB Partnership – Global Drug Facility (GDF) for the Invitation to Bid (26). We curated our list to include 21 commercially available products from 13 manufacturers with CE/FDA certifications (some products were in the process of obtaining such certification). Only 7 manufacturers provided details regarding their product, including the estimated price and certification status. For the rest of the models, we relied on publicly available information and were unable to verify the CE/FDA certification status. Most of the equipment considered is available in the North American and European Union market, hence more likely to be CE or FDA certified.

Please check Annex 2 - Product Comparison Sheet: Full range of available products in the market for portable and ultra-portable DR X-ray equipment

Table 2. Comparative analysis of stationary, portable, and ultra-portable DR X-ray equipment against various consideration parameters applicable for TB programmes

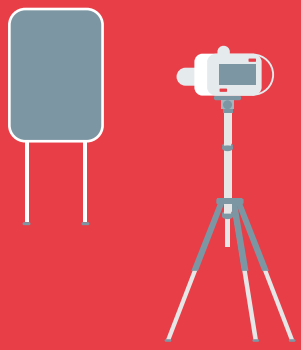
CONSIDERATION POINTS	CATEGORY 1 STATIONARY EQUIPMENT 
THROUGHPUT	High workload >300 X-rays per day
SETTING	Applicable for healthcare facilities with stable electricity and ICT infrastructure.
VEHICLE INSTALLATION	Logistically challenging; presents significant costs (large truck, dedicated driver, etc.).
CAD AI INTEGRATION	May need to check with equipment manufacturer for bundling offer or validation of CAD with images from equipment.
INSTALLATION AND MAINTENANCE	Will require service personnel to visit the installation site; consider having long-term service agreements as part of procurement package.
LIFE OF EQUIPMENT	This class of equipment has longest life span.
POTENTIAL OTHER USES	Can be used for general radiography (at facility).
HUMAN RESOURCES	Equipment must be operated by licensed radiographer. Need additional staff to manage workload if large numbers of people are to be screened on a daily basis.
IMPORTATIONS	Usually approved for use in all countries if meets radiation safety standards; however, registration and licensing of the equipment may be needed at country level.

CATEGORY 2
PORTABLE EQUIPMENT



Moderate workload 100–300 X-rays per day
Applicable for healthcare facilities with intermittent power supply, mobile van installations, temporary clinics.
Relatively easier to install inside a vehicle for mobile application; recommend checking with local equipment supplier if possible to do a bundling offer for complete vehicle installation.
May need to check with equipment manufacturer for bundling offer or validation of CAD with images from equipment.
May require service personnel to visit installation site or provide remote guidance; consider having at least mid- to long-term service agreement as part of procurement package.
Given the lower power of the X-ray generator, check with manufacturer the average lifespan of the X-ray tube and equipment.
Can be used for general radiography (at facility and communities).
Equipment must be operated by licensed radiographer. May need additional staff to manage people presenting and registering at the X-ray clinic; if >100 cases need to be X-rayed, may need dedicated driver if van/truck installation is required.
May need to check with country-specific regulatory authorities for radiation safety standards, registration, and licensing-specific requirements if intended to be used for mobile applications or any other form of non-facility-based imaging (outside X-ray department).

CATEGORY 3
ULTRA-PORTABLE EQUIPMENT



Low workload <100 X-rays per day
Applicable for temporary X-ray clinic, hard-to-reach areas lacking power supply, or event-based screening.
Vehicle installation is not needed but mobile application inside a van can easily be implemented.
May need to check with equipment manufacturer for bundling offer or validation of CAD with images from equipment.
Usually do not require installation visit by service personnel; consider having mid- to long-term service agreement as part of procurement package.
Given the lowest power of the X-ray generator, check with manufacturer the average lifespan of the X-ray tube and equipment.
Limited use for general radiography purposes in medium to long run. Not ideal for imaging thick body parts due to limited power of X-ray generator.
Equipment must be operated by licensed radiographer. May not need additional staff (for X-ray part) if number of people X-rayed per day is < 100 or dedicated driver in case of mobile application.
New generation of equipment. May need to check with country-specific regulatory authorities for radiation safety standards, registration and licensing-specific requirements if intended to be used for mobile or outdoor radiography.

CONSIDERATIONS FOR X-RAY EQUIPMENT SELECTION FOR TB PROGRAMMES

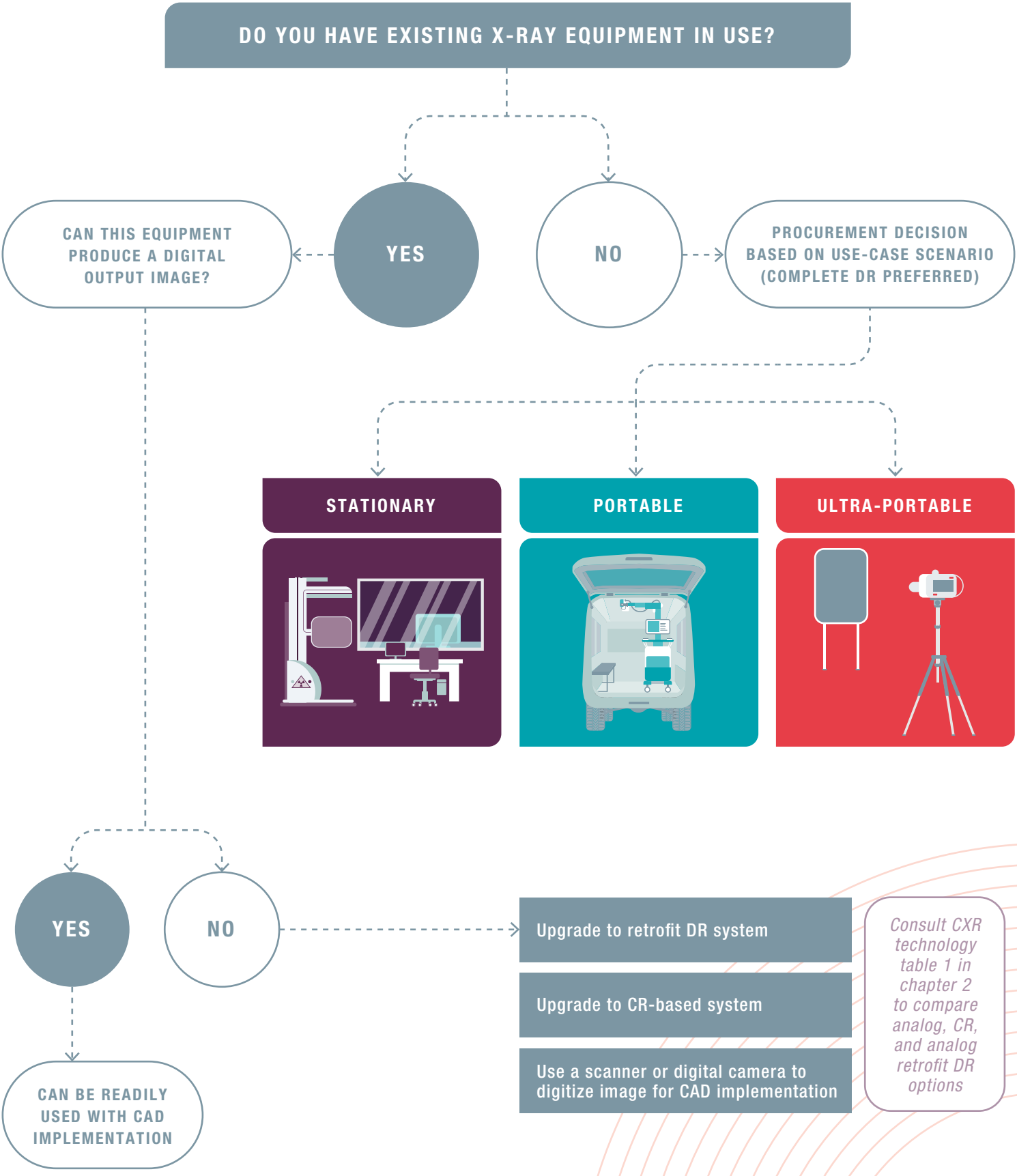
TB programmes should first determine the settings where they are most likely to use the CXR imaging equipment (for example, district hospital, primary healthcare facility, installed inside a van for mobile application or at temporary sites such as community centres), do the sites have adequate space, power supply and what will be the approximate workload. Then comes the question of CXR-only implementation, or both CXR and CAD. If the latter, production of digital image is essential. Hence, before making the decision of whether to procure new X-ray equipment or to retrofit an existing one, TB programme implementers must consider the purpose for which the X-ray equipment was developed (for imaging the whole body at a high-use hospital facility, or for small body part radiography at clinics, or for ICU etc.) and check whether the current requirements of digital CXR generation remain within programme budget. Overheating of the X-ray generator can be a challenge with some of the portable systems when being implemented for high volume use over long periods of time. Smaller and more portable systems are often less powerful than larger ones, which can impact the image quality. Increasing access to CXR through portable systems, can mean slightly lower quality digital images.

TB programme implementers are also encouraged to consult various available resources such as the informative 'Chest X-ray Screening Stop TB Field Guide' (27), to develop a comprehensive understanding of CXR implementation for TB screening, including information on equipment and procurement. Upon request, manufacturers should also be able to provide contact information to customers who are using a similar system to support an informed procurement decision.

Another important consideration when designing your TB screening project is to limit the risk of losing patients during the diagnostic care cascade. One must make sure that X-rays can be read quickly on the spot, and patients with an abnormal X-ray or CAD score above the accepted threshold can be referred for confirmatory diagnosis. For facility or vehicle-based screening, it may be possible to pair X-ray screening with confirmatory testing using rapid molecular tests, but this requires additional human resources and costs that need to be planned for.

The following decision-tree, together with comparing the information found in tables 1 and 2 of this report against TB programme considerations, **may serve as a general guide to help implementers** decide whether to use existing equipment or to procure new gear, as well as to choose the most appropriate technology for their TB screening and management purposes.

>>>>> Illustration 2. Equipment selection decision-tree for CXR-CAD implementation within TB programmes



CHAPTER 5 – OVERVIEW OF AI-POWERED CAD SOLUTIONS FOR TB

One of the barriers for widespread use of CXR screening in TB programmes is **the scarcity of skilled human readers for CXR interpretation** in many high TB burden countries.

AI-powered CAD solutions have been developed as a diagnostic aid because they permit a standardized interpretation of a CXR. After a digital CXR is taken, the CAD software automatically analyses the image according to a preset algorithm generating an abnormality score, which, if above a certain threshold, can be used to triage individuals who need confirmatory testing for TB. Most AI software also generates a second image with a heatmap or bounding boxes, which indicate the location of detected abnormalities.

There are a variety of different CAD solutions on the market, some programmed specifically to recognize PTB findings, while others can also identify additional abnormalities seen on CXR.

In recent years, several studies have demonstrated that CAD solutions can achieve good diagnostic accuracy for detecting bacteriologically confirmed TB on CXR, with the AUC of the ROC curves around 0.80–0.95 suggesting that CAD solutions can achieve an equivalent performance as human readers in identifying bacteriologically confirmed TB (16, 28, 29).

In 2020, WHO convened an expert panel to review the evidence for global policy (3). Several independent evaluations assessed the performance of CAD when used either in a screening use-case (non-facility-based testing) or in a triage use-case (facility-based testing) and showed that three leading CAD products had a similar performance as experienced human readers to detect bacteriologically positive pulmonary TB on a CXR (17, 18).

One of these evaluation studies was carried out by FIND, using its repository of CXR images from TB screening and triage studies. This CXR repository has been set-up specifically with the aim to assess the performance of current and future CAD products using a manufacturer-independent dataset. While the first evaluation only studied three CAD products, additional products and new versions will be assessed in the near future to support policy development on the use of CAD solutions for TB screening and triaging (30).

Based on the guideline group's review of the available evidence, WHO now recommends the use of CAD as an alternative to human readers to interpret CXR for screening and triage of PTB in individuals aged 15 or over (3, 17, 18). However, the evaluations did show some variation in the diagnostic accuracy of the CAD products between use-cases and geographies, which suggests that local calibration of the threshold may be required before implementation of CAD. Most CAD products do not come with a manufacturer-recommended threshold for triaging individuals who need further confirmatory testing. Also, given the variation seen across different contexs, the same threshold score does not necessarily provide the same sensitivity and specificity. Therefore, WHO recommends carrying out a calibration study of the CAD product in the setting of intended use according to a defined protocol (31).

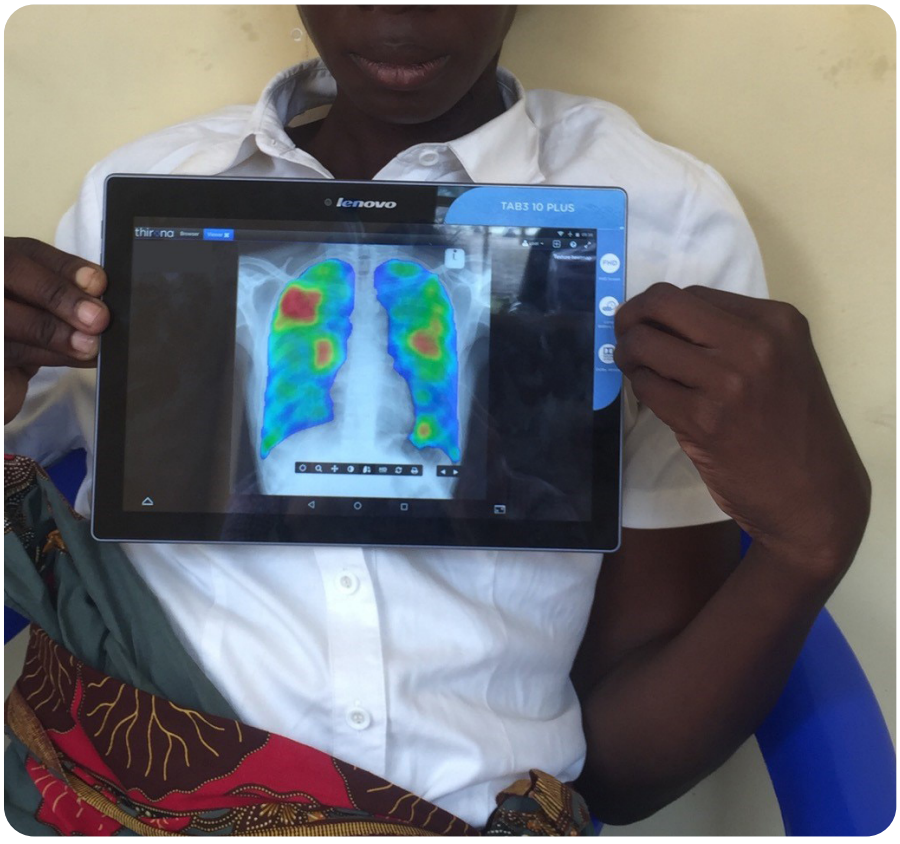
Given the updated screening recommendations, there is **growing interest in using effective combinations of portable and ultra-portable digital X-ray systems** together with CAD solutions for effective and adaptable TB screening programmes.

COMMERCIALLY AVAILABLE CAD SOLUTIONS FOR TB

The market of CAD solutions for radiology and TB is dynamic and evolving rapidly. To guide informed decision-making on selection and procurement of CAD products, FIND and Stop TB Partnership recently launched an open-access online resource (https://www.ai4hlth.org/) with comprehensive information on commercially available CAD solutions for TB (32). The aim of this resource is to provide all necessary information to TB programme implementers on the deployment mechanism (online and offline), machine compatibility, output format, options for integration into a legacy PACS system and existing workflows, costs, data sharing and privacy, and regulatory certifications of the products.

At the time of the writing this report (March 2021), the authors were aware of eight commercially available TB-specific CAD products. Six of these products have received CE certification in the medical device software category and have been validated in clinical studies. For readers with an interest in AI for radiology beyond TB, we suggest consulting the repository of FDA cleared CAD solutions published by the American College of Radiology and Diagnostic Image Analysis Group in Radboud University Medical Center's online database on AI solutions in Radiology (33, 34).

It is important to note that CE or FDA certification of CAD solutions does not necessarily mean that the software will perform well in all settings or can use images produced by any kind of equipment. Careful consideration is required for selection of CAD products based on validation studies specific to the geographical location, use-case and combination with equipment where it will used. There are a considerable number of CAD solutions on the market that can detect TB on CXR (some are also for comprehensive chest pathologies) and which are not (yet) CE or FDA certified.



>>>>> Person showing his X-ray image with CAD4TB result in Malawi PROSPECT study.

(Image credit: Peter MacPherson, Malawi-Liverpool-Wellcome Trust Clinical Research Program)

Table 3. Summary of certified CAD products for TB

(a comprehensive analysis and product comparison based on all essential parameters can be accessed here https://www.ai4hlth.org/)

	CAD4TB DELFT IMAGING, NETHERLANDS	QXR QURE.AI, INDIA	INFERREAD DR CHEST INFERVISION, CHINA
CERTIFICATION	CE Product link	CE Product link	CE Product link
STATUS	On market	On market	On market
DEPLOYMENT METHOD (ONLINE VS OFFLINE)	Online and offline	Online and offline	Online and offline
INPUT FORMAT	DICOM (JPEG, PNG image formats available upon request), standard chest PA	JPEG, PNG, DICOM Standard chest PA, AP	JPEG, PNG, DICOM Standard chest PA, AP
OUTPUT FORMAT	Includes heat map and probability score for TB, fully configurable with existing PACS.	Structured report including: Probability score for TB as well as dichotomous output indicating whether TB is likely present or likely absent. A box indicating the location of the abnormalities. Abnormalities detected by the product for which a separate abnormality score is given include 22 different signs for chest pathologies.	Structured report including probability score of TB, heat map and dichotomous output indicating presence or absence of multiple chest abnormalities.
VALIDATION WITH X-RAY IMAGES FROM NEW EQUIPMENT	Often not required, but option is available.	Can generalize to any X-ray manufacturer (CR/DR) and has been tested with over 20 leading X-ray manufacturers globally.	Validation is required when the product is installed on the X-Ray machine for the first time.
TARGET SETTING	Primary health centres, government/public sector, e.g., national TB programme, private sector.	Primary health centres, general hospital (above primary level), teleradiology companies, government/public sector, e.g., national TB programme, private sector.	Primary health centres, general hospital (above primary level), teleradiology companies, government/public sector e.g., national TB programme, private sector.
HARDWARE AND SOFTWARE REQUIREMENTS	CAD4TB comes as a complete product and is installed on a minicomputer called the CAD4TBbox. CAD4TB 6 runs on Linux. Currently, Ubuntu LTS 18.04 is preferred.	Ubuntu 18.04 is preferred Please contact partner@qure.ai for detail information.	CPU: Intel Core i3 and above and Memory: Above 4 GB Operating system: Windows XP and above Browser: Google Chrome 49.0 and above Requirements for server software: Operating System: Ubuntu 18.04 LTS and above. Browser: Google Chrome 49.0 and above.
CURRENT MARKET	Global, in use over 40 countries.	Global, in use over 20 countries.	Global, 9 countries.

	JLD-02K (JVIEWER-X) JLK, SOUTH KOREA	LUNIT INSIGHT CXR LUNIT, SOUTH KOREA	AXIR RADISEN, SOUTH KOREA
CERTIFICATION	CE Product link	CE Product link	CE Product link
STATUS	On market	On market	On market
DEPLOYMENT METHOD (ONLINE VS OFFLINE)	Online and offline	Online and offline	Online and offline
INPUT FORMAT	JPEG, PNG, DICOM Standard chest PA, AP	DICOM	DICOM
OUTPUT FORMAT	Structured report including probability score of TB, heat map and dichotomous output indicating presence or absence of multiple chest abnormalities.	Structured report including probability score of TB, heat map and dichotomous output indicating presence or absence of multiple chest abnormalities.	Structured report including bounding boxes or heat maps, probability score for TB, ddichotomous output indicating whether TB is likely present or likely absent. Other non-TB abnormalities detected by the product for which a separate abnormality score is given include.
VALIDATION WITH X-RAY IMAGES FROM NEW EQUIPMENT	Validation only required if chest X-ray images are from a low dose machine that affects the image quality.	No info, contact manufacturer.	X-ray machine validation is not needed.
TARGET SETTING	Primary health centres, general hospital (above primary level), teleradiology companies, government/public sector, e.g., national TB programme, private sector.	Primary health centres, general hospital (above primary level), teleradiology companies, government/public sector, e.g., national TB programme, private sector.	Primary health centres, teleradiology companies, government/public sector, e.g., national TB programme.
HARDWARE AND SOFTWARE REQUIREMENTS	Product does not need GPU (offline solution case). Intel 5 or higher generation CPU with Intel Graphics, Full HD monitor, Recommended 20GB HDD or SDD. Compatible with laptop or miniPC. Windows 10, minimum 8 GB RAM.	No info, contact manufacturer.	A Radisen's proprietary box will be provided with the AI software Image viewer provided by Radisen.
CURRENT MARKET	South Korea, USA, India, China, Japan, Indonesia, Laos, Thailand, Russia, Dubai, and Brazil.	Asia-Pacific, Europe, Middle East/North Africa, North America, South/Central America.	No info, contact manufacturer.

CHAPTER 6 – GETTING SET UP FOR CAD AND DIGITAL RADIOLOGY

The selection of a CAD product should not be purely driven by the accuracy claimed by the manufacturer or from reported clinical studies and the cost of the product. First, comparative studies have shown that the accuracy of different CAD products is relatively similar among the latest CE-certified versions (15, 16). Moreover, differences between products become even smaller at accuracy points above a 90% sensitivity on the ROC curve, as was recently shown by Qin et al (15).

Often, practical implementation considerations are overlooked by decision-makers during the selection phase. With a growing number of CAD products entering the market, there are more options to choose from, and therefore an all-round comparison of the different products is useful to help implementers make the best possible choice for their needs. The following points are some considerations for CXR-CAD implementation.

Choice of CAD solution

Some CAD products are developed specifically for TB diagnosis, and therefore analyse the CXR image and generate an abnormality score for TB only. Other CAD products have been developed to aid radiologists identify other forms of lung disease, including TB. Many CAD companies that have TB products also have recently developed a CAD product for COVID-19, which is sometimes even provided for free.

The output images and result reports that CAD products generate are all slightly different. Before choosing a particular product, it is important to consider whether it will be for TB screening only or also for screening other lung diseases, by whom (healthcare workers or radiologists), and where (in a modern facility or in rural communities with limited infrastructure and no connection to the internet).

CAD companies may also offer additional support products or features that may be worth exploring during the decision-making process, such as automated radiology reporting, case prioritization based on severity of findings and modules allowing disease progression monitoring with paired images from different days, etc.

Version and version update

New developments and updates in AI-powered products are relatively frequent. Most CAD providers update their product once or twice a year. If changes made to the CAD product are limited compared to the already marketed, CE/FDA approved version, the updated version does not require a new CE or FDA assessment. In most instances, updated versions are included in the maintenance contract.

Compatibility with X-ray equipment

Most CAD products are X-ray equipment agnostic, meaning that they can be used with any type of DR or CR equipment if the digital output image is compatible with CAD. However, for use in combination with some X-ray equipment, CAD providers may suggest doing a validation of the CAD software before implementing it for the first time.

Some CAD providers collaborate with specific X-ray equipment manufacturers and offer a complete end-to-end package that includes CAD software, which is sometimes even integrated in the X-ray generator using an onboard computer.

Therefore, when considering purchasing new DR equipment and a CAD product, **it is recommended to inquire with several companies about the packages they offer.**

Threshold selection

Some CAD providers offer a recommended threshold that one can use as a binary outcome in a triage algorithm to rule out TB and identify individuals who need further follow-on testing. However, as independent studies thus far have shown great variability in the performance of the same product in different settings, WHO advises countries to do a calibration study before implementation and will release an example protocol for this (31). There is no single 'correct' threshold. A more sensitive threshold will require a higher volume of confirmatory testing, whereas a less sensitive threshold will more often miss TB cases. Careful consideration is needed to determine the most suitable threshold for your setting and intended use.

Validation with X-ray images

If the CAD product is being procured separately from the X-ray equipment, it might need initial validation on images produced by the X-ray equipment. This should be discussed with CAD supplier before procurement and tested during implementation. Sometimes carrying out a validation by the CAD provider comes with additional costs.

Input image format

All CADs accepts DICOM files as input image, but several CAD products also accept other input formats. In case you are working with other image formats like JPEG, PNG, etc., you need to confirm with the developer if such files can be processed by the CAD software and if the accuracy of the CAD is affected by these different input formats. It is not uncommon to see non-DICOM images being used for sharing/archiving over local PACS network across several settings in LMICs.

Compatibility with local PACS

If the TB programmes are already using a patient archiving system such as a PACS system for on-site or teleradiology reporting and there is likelihood that CAD-processed images will be shared over the network for diagnosis and treatment purpose, the interoperability of CAD and local PACS should be checked with the CAD supplier. **Most CAD providers do offer full integration of the CAD results with the PACS system in place, although this may come at an additional cost.**
When no digital archiving system is in place, some CAD providers may offer this as part of their package.

Internet availability (bandwidth, upload and download speeds)

DICOM images are considerably large in file size, approx. 20 MB for a good quality CXR. CAD products may compress the images before they get uploaded and processed. However, **the available internet bandwidth must be taken into account, especially if one wants fast, trouble-free uploading.** This is crucial if online implementation of CAD is being considered and a throughput is anticipated. Some TB programmes might screen large numbers of participants each day, in which case there must be a fast turnaround time from CXR to CAD result. If bandwidth is a constraint, offline implementation may be a better solution.

Implementation mode: online vs offline

Online: Most CAD providers prefer that clients choose online deployment of their CAD product. Reliable internet allows a quick analysis of the CXR images. Also, troubleshooting with the company and upgrading of the CAD software are easier to handle with online deployment. The user usually receives a cloud account for CAD that is unique to their facility. This account allows the user to upload CXR images directly into the cloud where they are processed by the CAD. The dedicated CAD cloud viewer (installed on a laptop or computer) shows the CXR, combined with the CAD score and heatmap or other output format, as applicable. Most CAD developers allow cloud storage at the customer location or within the country to guarantee data protection, data sovereignty and patient privacy. This should be discussed with the CAD supplier and the focal point at the organization responsible for data privacy.

Offline: In situations where internet access is not available or unreliable, offline deployment of the CAD is required. Most CAD providers offer both options (online and offline). For offline use of CAD, one usually receives a box, minicomputer, or laptop with the pre-installed CAD software. This CAD box can be connected to the workstation of the X-ray system that the customer uses. Images from the X-ray system are directly transferred to the CAD box where it is processed by CAD to generate a CAD score, heatmap or other output format, as applicable. The process is fully offline, ensuring that there is no dependence on internet, and that there is full protection of data and patient privacy as all the data is stored locally.

Hybrid online/offline: This method of CAD implementation is applicable when there is occasional internet access for uploading the images to the cloud. The programme can continue optimally without risk of internet availability and speed and cloud backup can be done intermittently for future analysis of the data.

Data protection, data sovereignty, patient privacy, and local regulation

It is important that the TB programme always knows how their data is processed, stored, and protected. TB programmes need to be aware that implementation of a CAD software through the cloud means that CAD providers will use a server to process the data, which can potentially be hosted within the country of the customer or at a central server in a different location. TB programmes need to ensure that the server is hosted locally if they wish to protect their sovereignty over patient data, otherwise their patient data is sent outside of the country for processing and sent back once processed. A local cloud server is possible depending on where the customer is located; otherwise offline implementation should be considered for processing and storing data.

Need of middleware software solution

Some CAD products require middleware solutions to run on local devices. This can be the case for online, offline or hybrid implementation or for interoperability with local PACS. Such solutions are often provided by the CAD manufacturer as part of the installation.

Customer service and support

Customer service, support, training with implementation and troubleshooting support should be part of the purchase contract or procurement license.
Verify how and where customer support is given and whether there are any local distributors and service providers in your region.

(Image credit: Ben Philips, FIND)

CHAPTER 7 – REGULATORY CONSIDERATIONS FOR IMPLEMENTING CAD AND PORTABLE CXR

There are certain **regulatory considerations** that TB programmes need to be aware of before implementing portable CXR and CAD technology.

REGULATORY CONSIDERATIONS FOR IONIZING RADIATION EQUIPMENT IN NON-HOSPITAL ENVIRONMENTS

Since X-ray equipment produces ionizing radiation, most countries have strict guidelines regarding X-ray use for diagnostic and therapeutic applications on humans. Usually, atomic energy regulatory councils, radiation protection councils or equivalent organizations at country level have the authority for equipment certification, making national guidelines, setting reference dose limits for diagnostic radiography, validating X-ray equipment for medical applications, and ensuring that overall radiation safety standards are met. Most of the time, reference dose limits and radiation safety requirements are in accordance with guidelines and recommendations set by the International Commission on Radiation Protection and the International Atomic Energy Agency (35, 36); however, there may exist some variations.

An often-encountered barrier is that radiation protection guidelines and protocols as set by national authorities generally apply to departmental radiography and might not reflect requirements for community-level TB screening programmes (for example, installation of lead shields at temporary clinics and for van/truck installations) and some regulatory authorities may not permit temporary installations of X-ray facilities in schools, or religious/community areas. Regulatory issues can be further complicated when modern ultra-portable X-ray equipment is to be implemented at community level. Some of these instruments only emit negligible background radiation, so operators do not have to wear lead aprons if exposures are made more than 2 meters from the X-ray generator. Radiation protection authorities can perform inspection visits and dosimetry testing to assess leakage/background radiation from the equipment before validating its use; it is recommended to consult regulators as part of the implementation planning.

Generally, most countries require properly trained and/or accredited radiographers (or radiation technologists) to operate X-ray equipment. TB programmes must consider HR needs and alternatives such as task-shifting by training health workers in consultation with applicable authorities, in case it is difficult to hire dedicated radiographers in a timely manner.

(Image credit: Ben Philips, FIND)

REGULATORY CONSIDERATIONS FOR USE OF CAD

Although WHO has recently endorsed the use of CAD as a screening tool for TB in high prevalence settings, national TB programmes (NTPs) in several countries might not have clear guidelines in TB diagnostic algorithms for the use of CAD as an alternative to physician radiologists. Close collaboration with NTPs regarding the choice of CAD, and the setting of threshold scores – preferably based on clinical studies done in the same or similar contexts – should be considered before making any decision to procure or implement CAD.

If implementers are considering CAD application as part of research studies, **the questions around data confidentiality/sharing policy and patient privacy need to be discussed with concerned stakeholders** and must be in full compliance with local regulations. This becomes even more important if cloud-based implementation of CAD is planned.

>>>>> CXR examination with the MinXray system.
(Image credit: Michael Cairnie, MinXray)

CHAPTER 8 – EARLY ADOPTER EXPERIENCE WITH CXR CAD IMPLEMENTATION FOR TB DIAGNOSIS

Some TB programmes have pioneered the use of CAD and portable CXR technology, successfully demonstrating the use and challenges across a range of scenarios. In the following narratives, **we describe experiences based on semi-structured interviews with programme implementers.**

IMPLEMENTATION EXPERIENCE OF PORTABLE X-RAY SYSTEM AND CAD TECHNOLOGY FOR TB DIAGNOSTICS IN MALAWI

CONTRIBUTORS:

- Peter MacPherson, Malawi-Liverpool-Wellcome Trust Clinical Research Program (Principal Investigator for the PROSPECT study)
- Rachael Burke, London School of Hygiene and Tropical Medicine, UK (Principal investigator of the CASTLE Study, and RCT of CAD among hospitalised adults)

Project scope

Digital CXR acquisition followed by CAD interpretation for TB screening was one of the integral steps involved in a randomized study to optimize screening, prevention and care for tuberculosis and HIV in Malawi (PROSPECT Study). **The study was conducted by the Malawi-Liverpool-Wellcome Trust Clinical Research Programme, Blantyre, Malawi in 2018.**

CONTEXT OF IMPLEMENTATION

The PROSPECT study was carried out in urban primary healthcare centres in Blantyre, Malawi. The population being screened had a high prevalence of HIV (approx. 20%) at the time of study. Adults with symptoms of TB were screened by CXR and images were interpreted by CAD4TB version 5. If their CXRs had a CAD score above the threshold of 45, they were subjected to GeneXpert testing for confirmation of TB. For enrollment in the study, about 10 participants who met the inclusion criteria for the study were screened each day even though the centre can facilitate the screening of approximately 100 patients per day in a normal TB screening scenario.

X-RAY EQUIPMENT USED

Commander CMDR.T.120.60. S from MinXray USA, X-ray output 60–14 mA @ 40–120 kVDC, 0.6–212 mA

Complete set of equipment (X-ray source, detector, PACS and radiation protection accessories were procured as a package from MinXray).

CAD SOLUTION USED

For the PROSPECT study: **CAD4TB version 5** from Delft Imaging, Netherlands, was used as it was the only commercially available and validated (CE-certified) CAD product on the market at that time.

The implementers also shared the experience of using another CAD solution **qXR version 2** from Qure.ai later in 2019 in a similar context as with the MinXray equipment (at community level) for a different study on TB screening.

TECHNICAL CONSIDERATIONS AND DEPLOYMENT EXPERIENCE

A range of technical expertise (radiology/radiography/ICT) was required for the initial phase.

X-ray equipment: Experts from Liverpool School of Tropical Medicine, UK were involved with procurement of X-ray equipment. The entire set-up for CXR screening was done in a container clinic on the grounds of the public health centre facility. Battery backup and an inverter were used when electric power was not available. Internet, connectivity related works, data backup arrangements required significant IT expertise on the ground, which was not easy to organize. MinXray provided a technical expert for installation of the equipment and PACS set-up as part of the procurement package. The X-ray equipment was equipped with a detector which worked well but could be susceptible to damage from physical/mechanical issues. Once the set-up was completed, the X-ray and detector assembly performed very satisfactorily.

CAD: Significant time was spent by implementers communicating with Delft Imaging regarding the integration of CAD4TB and X-ray unit on the laptop. The Delft team provided excellent training and implementation support. The initial recommendation from Delft Imaging was for cloud-based implementation since the available internet bandwidth (approximation < 1 MBPS) would have made the data processing extremely slow. As an alternative, offline deployment of CAD (installed on the CAD4TB box) was chosen. The study also required CXRs to be reported by a radiologist; a 4G cellular network was used to upload images to the PACS. The bandwidth performance was adequate, but not optimal.

The implementation experience with another CAD software, qXR v2 (Qure.ai, Mumbai, India), was similar. Cloud-based implementation of qXR was undertaken but was not successful despite numerous attempts. This was most likely due to limited internet bandwidth in the region. Ultimately, the decision was made to switch to offline box implementation. Initially, there were technical issues with the qXR hardware configuration and connectivity with PACS, but once established, the offline performance was satisfactory. Qure.ai also provided a competitive financial package, technical support throughout the implementation phase and additional reporting options, dashboard, a cardiac abnormalities detection algorithm, all of which were found to be helpful by implementers.

COST

Overall operational cost for CXR and CAD implementation was very high and would not have been possible without funding from the Wellcome Trust. The cost of the X-ray equipment was approximately US$ 50,000 (excluding the CAD component).

The cost for CAD implementation, screening, equipment maintenance and running the system were not disclosed by implementers.

POLICY AND REGULATORY CONSIDERATIONS

The implementers did not face any significant challenges from policy and regulation perspectives. The regulatory framework for CXR and CAD implementation for TB screening in Malawi was in the process of being strengthened during the time of implementation. This provided an opportunity for the implementers to support and contribute to national efforts during research activities.

OVERALL POSITIVE EXPERIENCES AND OPPORTUNITIES WITH CXR-CAD IMPLEMENTATION

- CXR and CAD technology used by professionals and patients presented numerous opportunities for finding active TB cases
- Archiving of medical images was possible locally and presented research opportunities
- Patients could see color-coded CXR images at the point of clinic assessment (on dedicated CAD4TB tablet), which encouraged sputum submission for confirmatory diagnosis

CHALLENGES WITH CXR-CAD IMPLEMENTATION

- Automated patient identification and validation system (barcode scanning) prior to X-ray procedure could have optimized/augmented the workflow. For the PROSPECT study implementation, radiographers were performing manual identity verification and entry
- It would have been better to incorporate some API/other interoperable mechanism within the CAD solution to connect with other research databases (interoperability of solutions for research purposes)
- The implementers also shared the experience of CXR-CAD use in a different hospital in Malawi; there were concerns/ issues with confidentiality and data privacy, especially managing CXRs with PACS system when X-ray equipment was not exclusively used for CXR application. In most such settings, chances were high the equipment would be used for other examinations. This should be taken into consideration during early implementation.

Figure 11

Images from Malawi PROSPECT study CXR-CAD Implementation

(Image credit: Peter MacPherson)

IMPLEMENTATION EXPERIENCE OF ULTRA-PORTABLE X-RAY SYSTEM AND CAD TECHNOLOGY FOR TB DIAGNOSTICS IN UGANDA

CONTRIBUTORS:

- Dr Aldo Burua, TB Case Finding Advisor (NTLP, Defeat TB Uganda)
- Moses Eyaru, Medical Radiographer
- Dr Turyahabwe Stavia (NTLP, MoH)

Project scope

The Uganda Ministry of Health National TB and Leprosy Program (NTLP), in collaboration with the Global Fund Against AIDS, Tuberculosis and Malaria (the Global Fund) and partners, has been **implementing digital chest X-ray and CAD technology for increased case detection, notification, and better treatment outcomes** in the fight against the TB epidemic in the country.

CONTEXT OF IMPLEMENTATION

Uganda is one of the countries in sub-Saharan Africa with a high HIV coinfection rate among people with TB (40%) and also has high HIV prevalence in the general population (7.0%) (37). In June 2020, MoH initiated digital CXR and CAD implementation for TB screening in 5 districts with high TB prevalence. Healthcare facilities (district hospitals) within densely populated sub-urban areas with poor access to radiology services have been equipped with compact, portable digital X-ray equipment and CAD for TB for instant interpretation of CXRs to increase active case finding. Symptomatic patients visiting the healthcare facilities and high-risk populations irrespective of symptoms are subjected to CXR followed by CAD interpretation. The cases with CAD scores above a certain threshold (>60) are referred for microbiological testing using GeneXpert.

X-RAY EQUIPMENT USED

Delft Light, the battery-operable, portable Backpack X-ray machine, 40–90 kV, 20 mA, 1.35 kW from Delft Imaging, Netherlands.

The complete set of equipment (X-ray source, detector, PACS and radiation protection accessories) was procured as a package.

Experts from NTLP and USAID Defeat TB viewed the integrated assembly of the Delft Light equipment and CAD4TB during one of the technical exhibits at the 50th Union World Conference on Lung Health in 2019. Easy portability, minimum operational requirements, and availability of CAD4TB as an alternative to radiologist reporting of CXR have been the main reasons for the choice of this equipment.

CAD SOLUTION USED

CAD4TB version 6 from Delft Imaging, Netherlands.
CAD and X-ray equipment were procured together as a bundle offer from Delft.

COST

The project was funded by the Global Fund.

- Overall cost of CXR and CAD implementation (incl. several X-ray sources, detectors, accessories, generators, etc.): approx. US$ 200,000
- CAD: the cost of CAD screening was < 1 US$ per X-ray; CAD installation cost not available
- Maintenance, tech support and operational costs not available

TECHNICAL CONSIDERATIONS AND DEPLOYMENT EXPERIENCE

X-ray equipment: A temporary chest radiography room was set up at designated hospitals/healthcare facilities without any logistical challenges. X-ray source, digital detector, stands (for generator and detector), workstation laptop (with PACS), batteries for detector and generator (with charger) and CAD4TB box were the 'integrated assembly' components of the Delft Light DR X-ray system, which are easily assembled/disassembled. The radiographers received initial technical training on set-up and installation (including CAD use) from the Delft team. Approximately 30–40 patients were screened daily at each facility.

As per the information provided by the radiographer, Delft Light's battery lasts up to 100 exposures (more than 2 days in this case) and the detector lasts for approximately 30 consecutive exposures after full charge (5–7 hours standby time). The battery charging time for Delft Light is 3–4 hours and for the detector 2 hours; the pack comes with two detector batteries, allowing for periods of uninterrupted work.

Some of the facilities with high workload and unreliable main power supply sometimes have problems with charging the batteries and must arrange for an alternative power source. This has been highlighted as one of the constraints for this equipment, especially if there are high workloads.

The equipment has an approximately 30 second image acquisition time (the time taken for the image to be displayed after exposure is made), using a wired connection to the detector. Apart from occasional connection errors during the process of image acquisition, radiographers were very satisfied with equipment performance and the diagnostic quality of the chest radiographs produced.

CAD: CAD4TB version 6 was implemented in offline mode (CAD4TB Box) in this context. Once the CXR image is generated in DICOM format, it takes approximately 1 minute to run it through CAD4TB software and to get a CAD score with a heat map.

Cloud-based implementation of CAD4TB was initially proposed and tried during the set-up, however, it was not successful due to limited internet bandwidth. Hence, offline box implementation remains the preferred mode for the programme.

POLICY AND REGULATORY CONSIDERATIONS

- The Atomic Energy Council of Uganda oversees radiation protection guidelines, including safety standards for medical X-ray equipment. On-site inspection by authorities, plus testing of the equipment on radiation safety standards, are usually required.
- Properly trained and accredited radiographers are generally required to operate X-ray equipment in Uganda; in this case, however, clinicians are also trained to operate the equipment since operator involvement is minimal. This has been done with the intention to help with implementation work in regions where radiographers might not be available.
- Occupational radiation dosimetry is required but not mandatory at rural, peripheral healthcare facilities.
- There is no additional regulatory or policy requirement for using CAD software as a read-out solution for TB in Uganda.

CHALLENGES WITH CXR-CAD IMPLEMENTATION

- Currently, there is no provision to print out the images or reports with a CAD score to give to patients, which they often demand
- There are some concerns with the technology being expensive, but the project endorses it, and the operational costs are lower, so the capital investment is considered cost-effective in the long run. TB programmes in similar contexts are encouraged to use this technology for active case detection.

OVERALL POSITIVE EXPERIENCE AND OPPORTUNITIES WITH CXR-CAD IMPLEMENTATION

- This has been the first experience for NTLP and the USAID Defeat TB project using digital CXR and CAD technology for TB diagnosis in Uganda. The overall experience of the programme implementers was described as very positive.
- Easier acquisition of high-quality CXR and automated instant reporting has received greater acceptability from health professionals and patients in Uganda, where access to quality medical imaging and expert radiologists is limited.
- The project has helped to bring TB diagnosis closer to affected communities

Figure 12

Radiographer positions a patient to demonstrate TB screening using ultra-portable DR equipment during the official launch of the project at Katakwi Hospital, Uganda

(Image credit: Dr Aldo Burua)

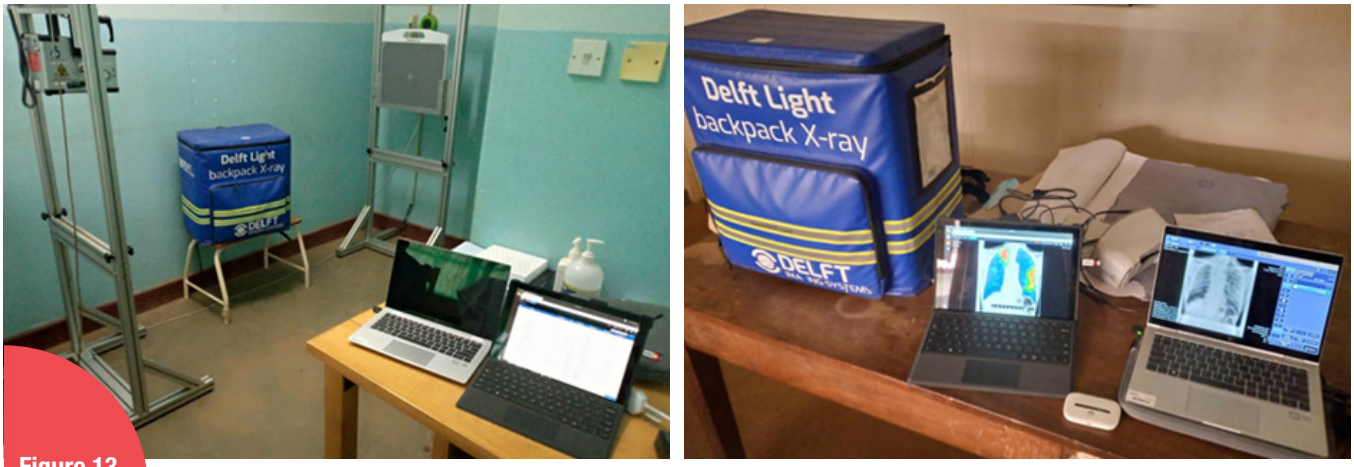


Figure 13

Delft Light ultra-portable X-ray machine and CAD4TB offline implementation set up for TB screening in Uganda.

(Image credit: Dr Aldo Burua)

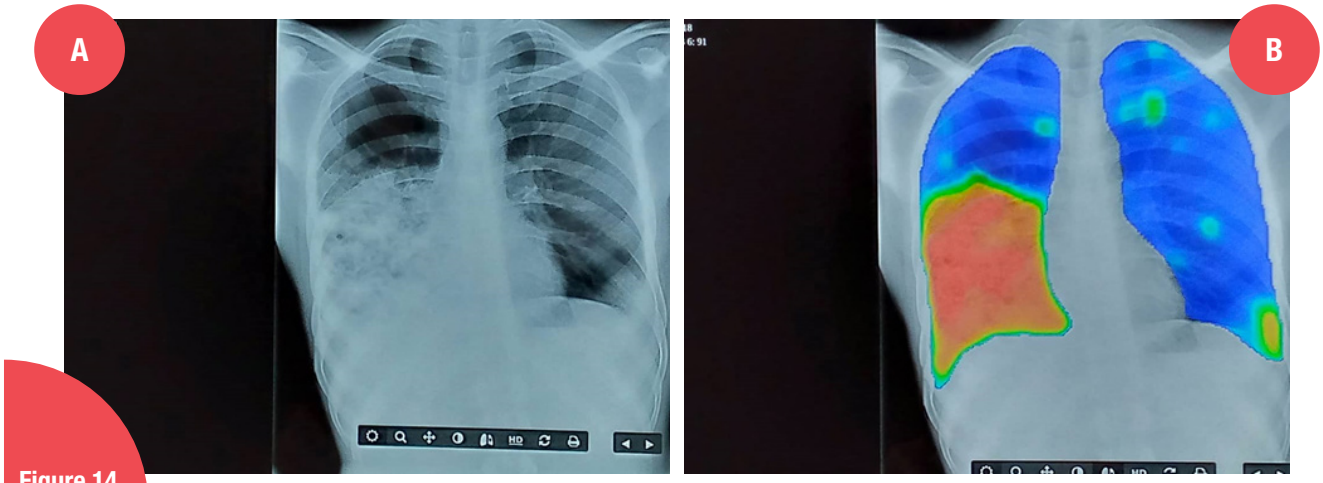


Figure 14

Case study 1 from Uganda - A 30-year-old patient presented to the radiology department with history of productive cough and fever lasting for 4 weeks. CXR shows right middle and lower lobe lung consolidation **(A)**. Image **(B)** shows heatmap image with CAD4TB score of 91%. The GeneXpert test performed was positive.

(Image credit: Dr Aldo Burua)

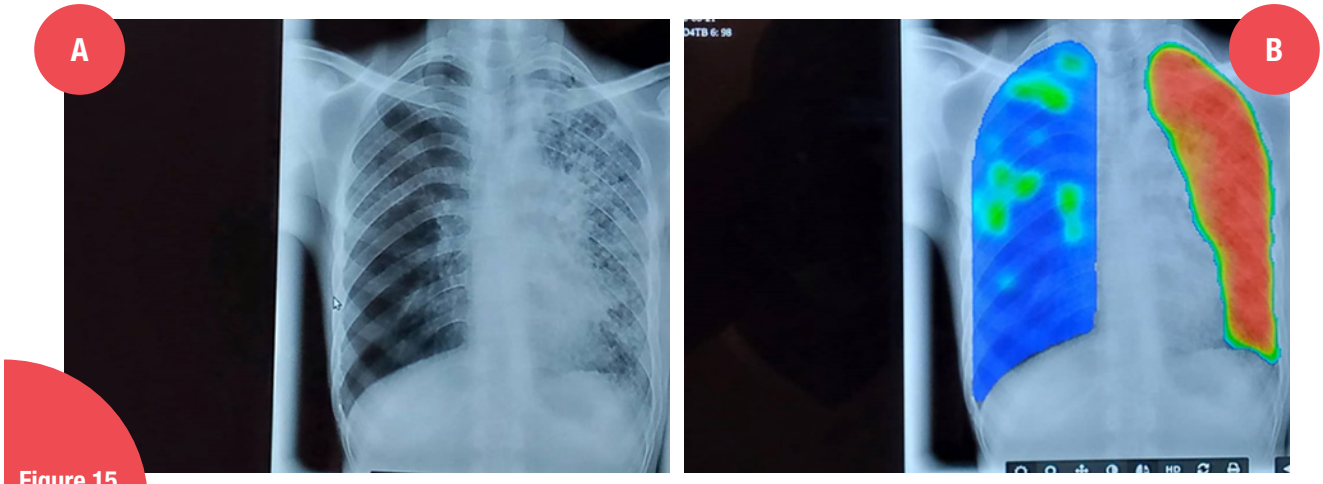


Figure 15

Case study 2 from Uganda - A 30-year-old outpatient with negative serostatus presented to the radiology department with history of cough and persistent fevers for 3 weeks, CXR **(A)** shows extensive left lung consolidation. Image **(A)** shows heatmap with CAD4TB score of 98%. The GeneXpert test performed was positive.

(Image credit: Dr Aldo Burua)

IMPLEMENTATION EXPERIENCE OF ULTRA-PORTABLE X-RAY SYSTEM AND CAD TECHNOLOGY FOR TB AND COVID-19 SCREENING IN ZAMBIA

CONTRIBUTORS:

- Tila T.M. Mainga, Study Manager, TREATS Project, Zambia
- Christabel Nkonde, Radiographer TREATS Project, Zambia

CONTEXT OF IMPLEMENTATION

Digital CXR and CAD implementation are part of multiple studies/surveys being rolled out under the TREATS project and the TREATS-COVID study in Zambia. One of the objectives of the TREATS project is to establish the prevalence of TB in the adult population through the TREATS TB prevalence survey (TBPS), which started in 2019 and is being conducted in 12 urban/semi-urban densely populated communities. A follow-on study – the Intensive Diagnostic Phase (IDP) follow-up study – was conducted in the first 3 communities of the prevalence survey and aimed to gain more insight in the patient pathways of participants who had bacteriologically confirmed TB or a CAD score of 70 and above in the TBPS. As part of IDP, all participants being followed up had an X-ray done. Temporary X-ray clinics were set up in the community at central locations such as church, community clinic, or school where participants were X-rayed and given CAD-generated results at point of time to facilitate further investigations, as per the study protocol.

The more recently launched TREATS-COVID study measuring the prevalence and spread of SARS-CoV-2 in one urban community in Zambia is also making use of the portable DR X-ray system and CAD solution for COVID-19 screening.

Project scope

The Tuberculosis Reduction through Expanded Antiretroviral Treatment and Screening for Active TB (TREATS) project in Zambia has been actively using portable digital chest radiography in combination with CAD technology in accordance with the 'universal test and treat' approach – whereby **people in high burden areas are actively offered TB and HIV testing and linkage to care, if needed (38).**

X-RAY EQUIPMENT USED

Delft Light, the Backpack X-ray, 1.35 kW @90 Kdvc, 15 Ma, with tube voltage from 40–90 Kdvc and tube current 0.20–20.0 mA, from Delft Imaging, Netherlands.

The complete set of equipment included an aluminum detector stand, a CXDI-701 wireless flat panel detector, a battery-operated X-ray tube, operator laptop and a light-weight lead apron. The X-ray source, detector, PACS and radiation protection accessories were procured as a package.

CAD SOLUTION USED

CAD4TB version 6 for the TBPS study and **CAD4COVID** for the TREATS-COVID study.
A CAD threshold score of 70 was used for the TBPS study.
Due to the novelty of the COVID-19 pandemic, the CAD4COVID has no clinical threshold, as the data being collected aims to inform the ideal threshold; for the purpose of the clinical algorithm, the study has adopted a threshold of 50.
Delft Imaging offered both the CAD software and X-ray equipment as a package.

TECHNICAL CONSIDERATIONS AND DEPLOYMENT EXPERIENCE

X-ray equipment: As per the information provided by the radiographer, the backpack X-ray is light and compact and relatively easy to assemble (taking less than 10 minutes). This includes setting up the X-ray source, stand and detector. The image quality is good and comparable to one produced by standard equipment. The battery life is very good, lasting for 7 hours and capable of producing approx. 100 radiographs. Detector batteries last for 5–7 hours and have a short charging time; the equipment comes with an extra battery. A highly portable solar panel is included, allowing easy charging in the absence of a power supply. One of the community settings where the X-ray clinic was set up lacked a power supply; there were no issues for the smooth operation of the X-ray.

Occasionally, there were delays and errors with data transfer. Overall, the performance of X-ray in terms of image acquisition and quality has been satisfactory.

CAD: Cloud-based implementation of CAD was considered; however, this was not done at the point of X-ray because of limitations with the internet bandwidth. Images were transferred onto an encrypted external hard drive, taken to the Head Office, and then uploaded into Thirona cloud where a CAD score could be generated.

POLICY AND REGULATORY CONSIDERATIONS

- All -X-ray equipment which enters the country for medical use needs to be inspected by the Zambia Radiation Protection Authority (RPA). This is done to ensure that the machinery is meeting all standards, as well as to safeguard the welfare and health of patients and operators. If approved, a one-year license is provided. The RPA also performs inspections during implementation.
- For community-based radiography, the most decisive factor for operation is how much radiation the machine produces. A machine that produces more than 50 mSv (or 5 rem) of scatter radiation per year is not accepted. Additionally, the sites where the X-rays are performed need to be relatively remote from a densely populated area.
- Only certified radiographers can operate the X-ray machine.
- Occupation radiation dosimetry is required, and every radiographer must wear a radiation badge during work hours.
- No specific policy or regulatory barrier exists for CAD use to screen TB and COVID-19.

COST

The project received external funding.

- X-ray equipment (X-ray source, detector, accessories, generator, etc.) – approx. US$ 85,000.
- CAD: the cost of CAD and installation was not shared by the implementer; however, different pricing options, including pay-per-screen options, were offered.
- Maintenance, tech support and operational costs – approx. 5–10% of the listed price.

OVERALL POSITIVE EXPERIENCE AND OPPORTUNITIES WITH CXR-CAD IMPLEMENTATION

- Mobile X-ray was very helpful to reach out to more participants in the community
- Appreciable acceptability of 'backpack X-ray' by community and professionals
- General set-up and workflow worked very well; image quality was acceptable
- Easy deployment

CHALLENGES WITH CXR-CAD IMPLEMENTATION

Nothing specific indicated except internet connectivity.

Figure 16

CXR and CAD implementation by TREATS project in Zambia using ultra-portable digital X-ray in a tent

(Image credit: Tila T.M. Mainga)

ANNEX 1 – COMPLETE RANGE OF STATIONARY (FACILITY-BASED) X-RAY EQUIPMENT FOR CXR IMAGING FOR TB PROGRAMMES (SPECIFICATIONS AS PER WHO CRITERIA FOR STATIONARY DIGITAL X-RAY EQUIPMENT)

EQUIPMENT	MANUFACTURER
EASY DR	Delft Imaging, the Netherlands Product link
1600PLUS X-SERIES	Imaging Dynamics Company Ltd, Canada Product link
UNIVERSAL CHIROPRACTIC STRAIGHT ARM	UMG/DEL MEDICAL, USA Product link
ECOVIEW9 PLUS- CHEST EXAM	ECORAY, South Korea Product link
PERFORM-X DR CHEST SYSTEM	Control-X Medical, Hungary Product link
DDR AURA U SWISSRAY	Swissray, Switzerland Product link
AMADEO S SYSTEMS	Oehm and Rehbein GmbH, Germany Product link
DIGIX U	Allengers, India Product link

COMMENTS	EQUIPMENT
U-arm design, complete digital X-ray equipment as per specifications applicable to TB programmes.	EASY DR
U-arm design, complete digital X-ray equipment as per specifications applicable to TB programmes	1600PLUS X-SERIES
U-arm and straight arm designs, complete digital X-ray equipment as per specifications applicable to TB programmes	UNIVERSAL CHIROPRACTIC STRAIGHT ARM
Straight arm and chest stand-based designs, complete digital X-ray equipment as per specifications applicable to TB programmes	ECOVIEW9 PLUS- CHEST EXAM
U-arm design, complete digital X-ray equipment as per specifications applicable to TB programmes	PERFORM-X DR CHEST SYSTEM
U-arm design, complete digital X-ray equipment as per specifications applicable to TB programmes	DDR AURA U SWISSRAY
U-arm and straight arm designs, complete digital X-ray equipment as per specifications applicable to TB programmes	AMADEO S SYSTEMS
Universal U-arm design, complete digital X-ray equipment as per specifications applicable to TB programmes	DIGIX U

ANNEX 2 – PRODUCT COMPARISON SHEET: FULL RANGE OF AVAILABLE PRODUCTS IN THE MARKET FOR PORTABLE AND ULTRA-PORTABLE X-RAY EQUIPMENT

Delft Light

Delft Ultra

MinXray Impact TR90BH

MINE ALNU

Aspen AiR Touch Europa

Amadeo P-100/35HB, Leonardo DR nano

ATXtreme, ATOMED X-Ray GmbH

Amadeo M-DR mini

Rayence GO DPX

Epsilon EP Corsa 2.4P

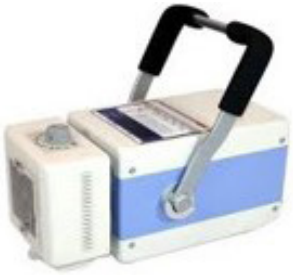
Fujifilm FDR Xair

Fujifilm FDR nano

MINE 2

Aspen Air
Touch Europa+

Medical ECONECT meX+20



RadmediX Acuity PDR

MinXray CMDR HF100H+
Wireless

ATX QUANTpower400
AiO

PRODUCT COMPARISON SHEET:
FULL RANGE OF AVAILABLE PRODUCTS IN THE MARKET FOR PORTABLE AND ULTRA-PORTABLE X-RAY EQUIPMENT

PDF link

Medical ECONECT meX+100

Dragon LW

ECO RAY ULTRA200/200A

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