



The Study Protocol Lung Nodule Detection X-ray has been updated as of September 2, 2021 based on feedback provided by vendors and clinical institutes on v1.0. Changes have been made in articles 3.1, 3.2, 5.1.3 and 5.2.3. Earlier versions remain available in the archive on [www.AIforRadiology.com/project-air](http://www.AIforRadiology.com/project-air).

# Study Protocol

## Lung Nodule Detection X-ray

as part of Project AIR

### 1. Objective

Validate and compare the stand-alone diagnostic performance of commercial artificial intelligence (AI) based software for the detection of CT confirmed lung nodules on chest radiographs in a clinical population.

### 2. Study design

An ongoing retrospective study in which commercial AI software is being validated on a dataset from multiple centers. Vendors make their algorithm temporarily available to the researchers to generate the results. The data will not be shared with the vendors. Reader studies on the same dataset are performed by radiologists to provide context to the stand-alone software performance.

### 3. Study population

#### 3.1. Inclusion criteria

- Centers: Academic, non-academic
- Patient age: >18 years old
- Posteroanterior chest radiograph with CT within 3 months before or after radiograph
- Maximum one study per subject
- Radiograph acquired from 2012 and onwards
- Nodules:
  - Nodule types: (part) solid nodules according to Fleischner
  - Nodule size (solid component) based on CT: 5 to 30 mm
- Controls:
  - Normal appearance or other pathologies that cannot be confused with nodules.

#### 3.2. Exclusion criteria

- Bedside radiographs
- Low quality imaging
- Diffuse (nodular) pathology on CT and/or radiograph (e.g. metastases, interstitial lung disease, large masses)



### 3.3. Sample size

- Data will be collected from at least six centers in Europe, with a minimum of 50 samples per center.
- Initial target 600 samples
- Positive/negative ratio: 1/1

## 4. Possible investigational products

Preliminary selection of products that are potentially eligible for this study. We welcome feedback about additional products.

- Arterys - Chest | MSK AI
- Infervision - InferRead DR Chest
- JLK - JLD-02K
- Lunit - INSIGHT CXR
- Milvue - Milvue Suite
- Oxipit - ChestEye CAD
- Quibim - Chest X-Ray Classifier
- Qure.ai - qXR
- Riverain Technologies - ClearRead Xray - Detect
- Samsung Electronics - Auto Lung Nodule Detection
- Siemens Healthineers - AI-Rad Companion Chest X-ray
- VUNO - VUNO Med-Chest X-ray

## 5. Methods

### 5.1. Study parameters

#### 5.1.1. Metrics

- AUC ROC
- Sensitivity at average reader false positive rate.

#### 5.1.2. Subgroup analysis

Subanalysis is performed for e.g. nodule size, visibility of the nodule and X-ray manufacturer.

#### 5.1.3. Not-processed-rate

If there is no prediction for an image by the algorithm (rejected, error, or other reason), the empty field will be filled with "Probability nodule present: 0" to enable the metric calculation.

### 5.2. Data collection

#### 5.2.1. Imaging

- DICOM file of posteroanterior chest radiograph
- DICOM file of lateral chest radiograph (if present)
- DICOM file of confirmatory CT within 3 months of radiograph

#### 5.2.2. Clinical data

- Center: coded
- Patient age: years



- Gender: M/F
- Acquisition machine brand: coded
- Acquisition date: years
- Nodule/healthy/other chest pathology

5.2.3. The following data are determined by a radiologist research team member

- Nodule size: in mm (on CT)
- Nodule conspicuity: well visible / moderately visible / subtle / very subtle / invisible (on XR)

**5.3. Reference standard**

CT within three months of radiograph acquisition date.

**5.4. Software prediction outcome**

5.4.1. Probability nodule present (0-100)

**5.5. Reader study questions**

5.5.1. Nodule presence: 0-100

**6. Statistical analysis**

**6.1. Comparing with average readers**

- AUC ROC: Multi-reader multi-case ROC analysis based on U-statistics and t-statistics for significance.
- Sensitivity at average reader false positive rate: confidence intervals with the Adjusted Wald Method, Bonferroni-corrected.