



The Study Protocol Bone Age Prediction Hand 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, 5.1-5.4, and 6.1. Earlier versions remain available in the archive on [www.AIforRadiology.com/project-air](http://www.AIforRadiology.com/project-air).

# Study Protocol

## Bone Age Prediction Hand 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 bone age prediction from radiographs of the left hand in a clinical pediatric 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: 0-18 years old
- Posterior anterior (PA) left hand radiograph
- Maximum one study per subject
- Radiograph acquired from 2012 and onwards

#### 3.2. Exclusion criteria

- Low quality imaging
- Right hand radiographs

#### 3.3. Sample size

- Data will be collected from at least four centers in Europe, with a minimum of 50 samples per center.
- Initial target: 300 samples
- Consecutive patients

### 4. Possible investigational products



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

- ImageBiopsy Lab - IB Lab PANDA
- Visiana - BoneXpert
- VUNO Med® - BoneAge™

## **5. Methods**

### **5.1. Study parameters**

#### **5.1.1. Metrics**

- Root mean squared error
- Mean error

#### **5.1.2. Subgroup analysis**

Subanalysis is performed for e.g. age groups, gender, 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 chronological age will be used to enable the metric calculation.

### **5.2. Data collection**

#### **5.2.1. Imaging data**

- DICOM file of pediatric hand radiograph

#### **5.2.2. Clinical data**

- Center: coded
- Patient age (chronological): years and months
- Gender: M/F
- Acquisition machine brand: coded
- Acquisition date: years

### **5.3. Reference standard**

Average of Greulich-Pyle atlas-based bone age provided by three pediatric or musculoskeletal radiologists individually. Cases with a strong disagreement ( $\pm$  2 year difference) are read again by the same readers, individually.

### **5.4. Software prediction outcome**

- #### **5.4.1. Bone age in decimal years, Greulich-Pyle method (subject's sex is provided)**

### **5.5. Reader study questions**

- #### **5.5.1. Bone age in years and months, Greulich-Pyle method (subject's sex is provided)**

## **6. Statistical analysis**

### **6.1. Comparing with average readers**



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- Confidence intervals, Bonferroni-corrected non-inferiority analysis.
- Bootstrap analysis