

# Genotyping and phenotyping of skeletal deformities in patients with Osteogenesis Imperfecta

No registrations found.

<b>Ethical review</b>	Not applicable
<b>Status</b>	Pending
<b>Health condition type</b>	-
<b>Study type</b>	Observational non invasive

## Summary

### ID

NL-OMON23070

### Source

NTR

### Brief title

skeDOI

### Health condition

Osteogenesis Imperfecta

## Sponsors and support

**Primary sponsor:** Isala, Zwolle

**Source(s) of monetary or material Support:** contract funding

## Intervention

## Outcome measures

### Primary outcome

The main outcome parameters are volumetric BMD and tissue mineral density (TMD), cortical and trabecular microarchitecture, and strength of the distal radius and tibia assessed with HR-pQCT. More specifically, BMD-parameters are determined for the total (Tt.BMD), cortical

(Ct.BMD), and trabecular (Tb.BMD) bone and similar for TMD (Tt.TMD, Ct.TMD, and Tb.TMD, respectively). Microarchitecture parameters include trabecular bone volume fraction, number, thickness and separation (Tb.BV/TV, Tb.N, Tb.Th, and Tb.Sp, respectively) as well as cortical thickness (Ct.Po) and cortical porosity (Ct.Po). Parameters describing bone strength are estimated by means of micro-finite element ( $\mu$ FE-) models of the distal radius and tibia that are based on the HR-pQCT scans and include bone stiffness and failure load (FL). The parameters will be obtained from the scans acquired with fixed and with length-dependent offset distance. For both scan protocols, the parameters will be averaged for each OI-type.

## Secondary outcome

Secondary parameters include clinical characteristics of OI (wheelchair dependency, scoliosis, bone deformity, hear loss, blue sclerae, medical history of fracture) and causative genetic mutation. These parameters have been obtained for OI diagnosis and are available at the OI Expertise Center. Patients have consented use of these data for this study.

# Study description

## Background summary

Osteogenesis imperfecta (OI) is a rare hereditary connective tissue disorder characterized by increased bone fragility and skeletal deformity. Various causative genes are known, resulting in a diversity of phenotypic manifestations and severity of OI. Previous studies on skeletal phenotypes among different types of OI were mainly limited to measurements of areal bone mineral density (BMD), whereas bone quality is also determined by bone microarchitecture. High-resolution peripheral quantitative computed tomography (HR-pQCT) allows detailed assessment of microarchitecture and strength of the distal radius and tibia. Currently, the specific microarchitectural properties of the different OI phenotypes are not well defined and due to the short stature of patients with some OI-types, it is not known whether the standard protocol for HR-pQCT imaging is sufficient to assess microarchitecture in OI.

The primary objective of the study is to identify skeletal phenotypes of adult patients with different OI-types at microarchitectural level with HR-pQCT.

Secondary objectives are:

- to compare the skeletal phenotypes with the genotypes of the OI-types based on clinical symptoms, DXA-based areal bone mineral density and genetic mapping;
- to compare the skeletal phenotypes with sex and site-specific reference data for bone microarchitecture of an adult reference population;
- to explore the preferred site for HR-pQCT scan acquisition (fixed vs. length-dependent offset distance to select scan region).

In this cross-sectional study, approximately 120 patients with known OI, diagnosed and

treated at the Center of Expertise of the Isala Clinic in Zwolle, will visit VieCuri Medical Center once. During this visit, four HR-pQCT scans will be performed; two of the distal radius and two of the distal tibia. The first set of scans (distal radius and distal tibia) will be acquired using the standard HR-pQCT imaging protocol with a fixed offset distance. The second set of scans (distal radius and distal tibia) will be acquired with a HR-pQCT imaging with a relative offset distance depending on the length of the lower arm and leg. Depending on the mobility of a patient, it is possible that a patient is not able to position properly and comfortably before the gantry of the scanner, in which case the scan will not be acquired. All scans will be analysed to quantify volumetric bone mineral density, cortical and trabecular microarchitecture, and bone strength. The bone parameters will be compared with reference data and with type OI (based on clinical symptoms, DXA-based areal bone mineral density, and genetic mapping), which is already available as part of regular care at the Center of Expertise of the Isala Clinic in Zwolle. Finally, the bone parameters will be compared within the OI-types between the fixed measurement site and relative measurement sites.

### **Study objective**

this is an observational study identifying skeletal phenotypes of adult patients with different OI-types at microarchitectural level with HR-pQCT.

### **Study design**

1 visit at VieCuri medical Center

### **Intervention**

not applicable

## **Contacts**

### **Public**

Isala, Zwolle  
Roelina . Munnik

+31384245375

### **Scientific**

Isala, Zwolle  
Roelina . Munnik

+31384245375

## Eligibility criteria

### Inclusion criteria

main inclusion criteria:

- Patients with confirmed Osteogenesis Imperfecta
- Adult (>18 years)
- Recent DEXA-scan ( < 3 years)

### Exclusion criteria

main exclusion criteria:

- Patients who have had a fracture at recent medical history (<2 years) at both distal radii and tibiae.
- Patients who have had a malignancy at recent medical history (<2 years), who have been treated with glucocorticoids less than 3 months ago, who have severe kidney disease (eGFR <30 ml/min) or who suffer from other metabolic diseases affecting bone.
- Female patients who are pregnant.

## Study design

### Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

### Recruitment

NL	
Recruitment status:	Pending
Start date (anticipated):	01-03-2021
Enrollment:	120
Type:	Anticipated

## IPD sharing statement

**Plan to share IPD:** No

**Plan description**

N/A

## Ethics review

Not applicable

Application type: Not applicable

## Study registrations

### Followed up by the following (possibly more current) registration

ID: 51155

Bron: ToetsingOnline

Titel:

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

Register	ID
NTR-new	NL9134
CCMO	NL76107.075.21
OMON	NL-OMON51155

## Study results