

# VPHOP

## the Osteoporotic Virtual Physiological Human

The fight against Osteoporosis now has a new ally. The VPHOP research project will develop, validate and deploy to pilot clinical studies the next generation of technology for predicting the risk of fracture in patients with low bone mass and assisting clinicians in prognosis and treatment planning (both pharmacological and interventional). The most advanced multiscale modelling technologies will be used to predict the patient-specific risk of fracture, and how it would change as a result of the various potential treatment options.

### Objectives of the Project

**Context:** Nearly four million osteoporotic bone fractures cost the European health system more than € 30 billion per year. This figure could double by 2050. After the first fracture, the chances of having another one increase by 86%. We need to prevent osteoporotic fractures. The first step is an accurate assessment of the patient-specific risk of fracture that considers not only the skeletal determinants but also the neuromuscular condition.

**Osteoporotic fractures cost the European health system more than €30 billion per year**

**Project:** The aim of VPHOP is to develop multiscale modelling technology based on conventional diagnostic imaging methods that makes it possible, in a clinical setting, to assess *for each patient individually*, the strength of his/her bones, how this strength is likely to change over time, and the probability that the he/she will overload his/her bones during daily life. With these three assessments, the evaluation of the risk of bone fracture will be much more accurate than any estimation based on external and indirect determinants, as happens in current clinical practice. These assessments will be used to improve the diagnostic accuracy of current clinical standards, and to provide the foundation for an evidence-based prognosis with respect to the natural evolution of the disease, to pharmacological treatments, and/or to preventive interventional treatments aimed at selective skeletal strengthening. The various modelling technologies developed during the project will be validated not only *in vitro*, on animal models, or against retrospective clinical outcomes, but will also be assessed in term of clinical impact and safety on small cohorts of patients enrolled at four different clinical sites, providing the factual basis for effective clinical and industrial exploitation.

### Project Description

**Project Description:** Currently, the risk of fracture is estimated empirically, i.e. based on observations of past cases. However, in theory we could imagine developing a patient-specific computer model that is capable of assessing the risk of fracture in a deterministic way, with much higher accuracy. The problem is that the occurrence of an osteoporotic fracture is a multiscale event:

- the daily loading spectrum, which includes para-physiological overloading events is defined at the Body level;
- the fracture event occurs at Organ level;
- the bone elasticity is due to the tissue, which is defined at the Tissue level;
- the composition and the morphology of the bone tissue changes over time due to the metabolic activity, which is defined at the Cell activity level;
- the strength of the tissue is due to the molecular composition of the bone matrix, which is defined at the Constituents level.

By creating a patient-specific hypermodel – a model composed by many sub-models, each describing the relevant phenomena taking place at one of the many dimensional scales involved – we will be able to solve this incredibly complex problem.

This modelling technology will be specialised to solve four clinically relevant problems:

- a. Screening (level 1): to supplement the conventional Dual X-ray Absorptiometry (DXA) screening of subjects at risk, in order to include in the diagnosis also the propensity to fall, and possibly 3D densitometric information.

#### SCENARIO

The best-case scenario is a complete multiscale model parameterised on all clinically available information on the patient, but also on a full population-based probabilistic representation of such inputs. Independently from the level of specificity of the input parameters, the model will always predict the risk of fracture of all critical bones, with an associated confidence interval, larger or smaller depending on how detailed are the available information on the patient. The practical effect of this would be the possibility to design clinical protocols progressively demanding in terms of costs, time, and invasiveness. The VPHOP technology would not only drastically improve the clinical practice, but also help in modulating the level of detail of the clinical assessment to the severity of the disease.

- b. Diagnosis (level 2): In osteoporotic subjects, use 3D densitometry information to develop a personalised assessment of the risk of fracture at the hip and the lower spine that clinicians can use to better modulate the life-style recommendations and the treatment options.
- c. Prognosis (level 3): for patients at high risk of fracture, develop a predictive model based on tissue-level imaging that estimates the variation of such risk over time due to bone remodelling with and without pharmacological treatment.
- d. Interventional treatment planning: simulation-based pre-operative planning to decide which vertebral body is at higher risk, and in which region of that vertebrae the augmentation would be more effective.

## Expected Results & Impact

### *Clinical innovations:*

- prognosis
  - predicting the risk of femoral or vertebral fracture under low energy loading
  - predicting, at the tissue level, the probability of developing micro-fractures
- pharmacological treatment planning
  - predicting changes over time due to the evolution of the disease and to the pharmacological treatment
- interventional treatment planning
  - Predicting the location within each bone that is most susceptible to fracture
  - Predicting the changes in risk due to interventional augmentation

### *Industrial innovations:*

- Imaging technology to generate whole bone patient-specific models with very low radiation dose
- Wearable activity monitor capable of capturing the patient's life style for one week including para-physiological events
- Hypermodelling technology for the creation of massive multiscale models using heterogeneous codes
- Tissue level imaging in vivo at the spine and hip with clinically acceptable radiation doses
- Cellular activity models, capable of predicting the functional outcome of different pharmacological modulations of bone metabolism
- Software technology for patient-specific deterministic prediction of fracture risk

### KEYWORDS

Virtual Physiological Human, Physiome, Multiscale Modelling, Osteoporosis, Bone Fracture



### VPHOP

The Osteoporotic Virtual Physiological Human

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