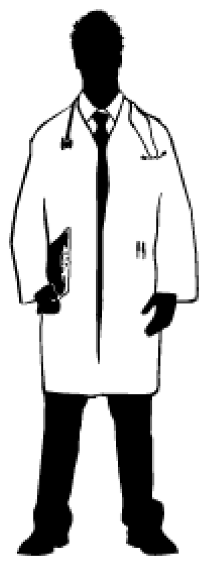
Who needs our solution ?

Scientists from Universities

R&D of scientific companies

Public and private hospitals



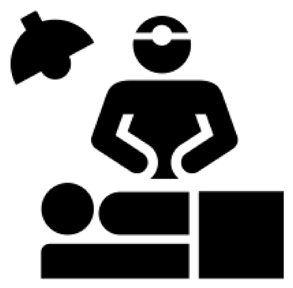
Why most of clinical trials fails ?

There are different reasons:

- Clinical testing of product requires **large financial** and **time expenditures**;
- Require commitment of **extra entities …**

.. and why

we hear more about new medical materials, than we might see in general practice ?



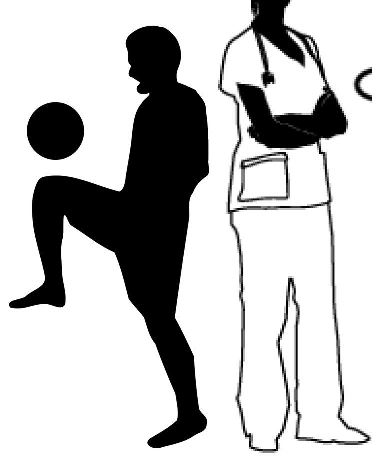
- Presence of various **difficulties** (regarding to long-time and high costs) with **obtaining permissions of ethical commissions** for *in vivo* testing on animal/human models;
- **Limited funds** for ***in vivo* studies** of material – **lack of evidence**, regarding to usage's benefits.

We have evolved since 2015, by using end-customer feedback

The abundant technique is **x-ray (35%)** and **computed tomography (28%)**.
But vey helpful tool is an **interview with patient (25%)**.

We have asked questions to clinicians, researchers and even coaches !

I wish, I have a technology, easy in implementation, which employs methods of general practice.



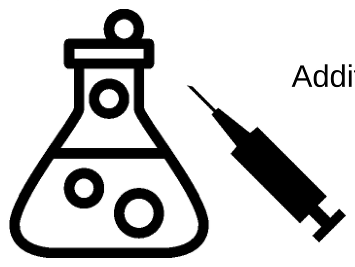
Essentially, I would want to identify fracture patterns and how to treat them.

We have listen their feedback carefully and finally …

We are the **first one**, who:

Set up **diagnosis** of bone fracture, with greater accuracy and precision without risk to the product or patient.

Make this process more efficient and cost effective, it means substantial cost savings for public and private healthcare providers.



Additionally, the software eliminates faults of the medical material – minimalizes negatively effect on the result of clinical trials.

Used multiscale modelling with own algorithms, based on patient specific data set.

73% of Orthopaedists in public hospitals have negative opinion about effectives of current methodologies of bone fracture treatment.

Now, they might change their mind

"Sounds a good idea. Good luck!"
~Lei Ren, *Manchester University, UK*

"It sounds like an impressive idea, good luck Guys !"
~**Patrick Roberts**, NDORMS, University of Oxford

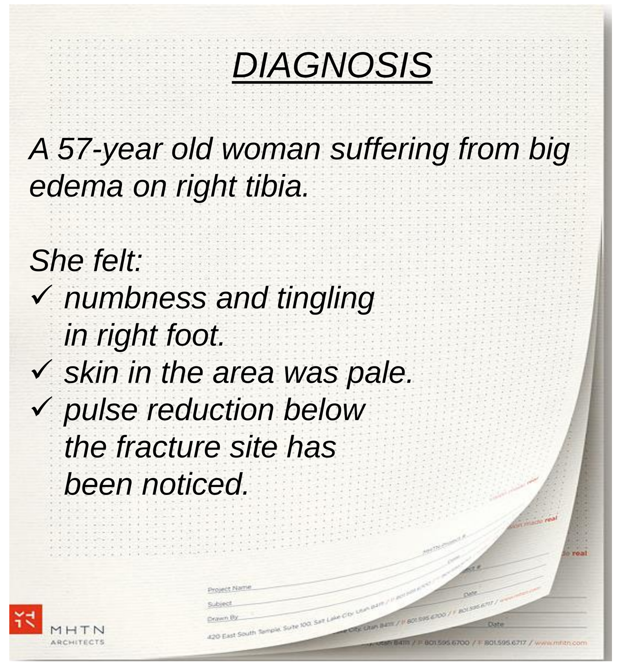
How to improve innovative bone fracture treatments?

Current treatments are mainly putting broken bone into cement despite of **a ground-breaking solutions** ...

The problem is lacks of tools for testing a new medical solutions, before they will be applied to human body.

We created patient-specific computational model of the injury, on which the user tests materials, considered in treatment process.

Origami BioBandage Software uses a computational modelling to provide **the most effective and safe treatment** of bone injury, **but HOW ?**



DIAGNOSIS

A 57-year old woman suffering from big edema on right tibia.

She felt:
- ✓ *numbness and tingling in right foot.*
- ✓ *skin in the area was pale.*
- ✓ *pulse reduction below the fracture site has been noticed.*

First: **Patient-specific model of medical case.** The input includes:

Information about patient and abnormal situations, which might influence treatment process. The record of medical history is involved too.

PATIENT'S INFORMATION

- Age
- Gender
- Recent fractures
- Immobility
- Non-skeletal diseases (check disease/abnormality)
- Renal problems (Ca2+)

CHECK ABNORMALITY

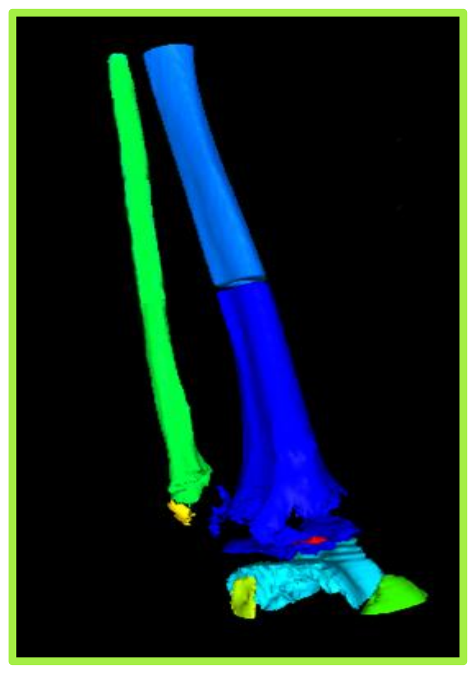
- Local Malignancy
- Radiation of necrosis of bone
- Avascular necrosis
- Intra-articular fracture

MEDICAL CHECKLIST

- Paget's disease
- Fibrous dysplasia
- Osteoporosis
- Hormonal treatment
- Pregnancy
- Bone cancer
- Women: Menopause
- Fibrous dysplasia
- Hormones and corticosteroids + others*
- Exercise and local stress
- Chronical kidney diseases:
- Metastatic carcinoma
- Gaucher's disease
- Chusing's syndrome

Second: **Apperance of bony tissue injury.**
The data comes from 3D medical imagining methods (Computed Tomography, CT):

The set of DICOM files is loaded to the software.



Then, system transformed its into structural 3D model.

Third: **Biochemistry of cellular model in the injury.**
The data comes from biomarkers assays, informs about their level and action in tissue regeneration.

Markers, responsible for:

Bone formation

ALP	Alkaline phosphatase
OC	Osteocalcin
PINP	Procollagen type I N-terminal propeptide

Bone resorption

NTX	N-terminal telopeptide
BCTX	Human beta-crosslaps

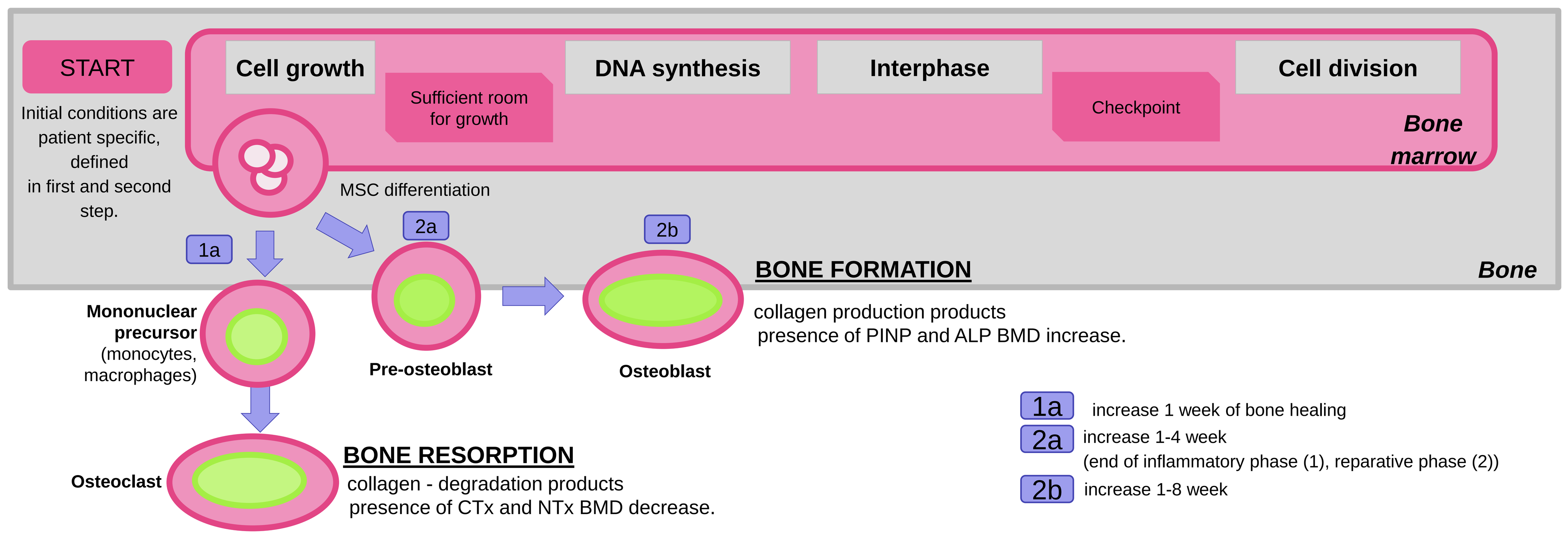
Blood composition

- Ca2+ serum level
- Count of white blood cells
- Value of Blood pH

Records from biomarker's serum level are introduced by user. The ranges are validated regarding to standards of Mayo Clinic.

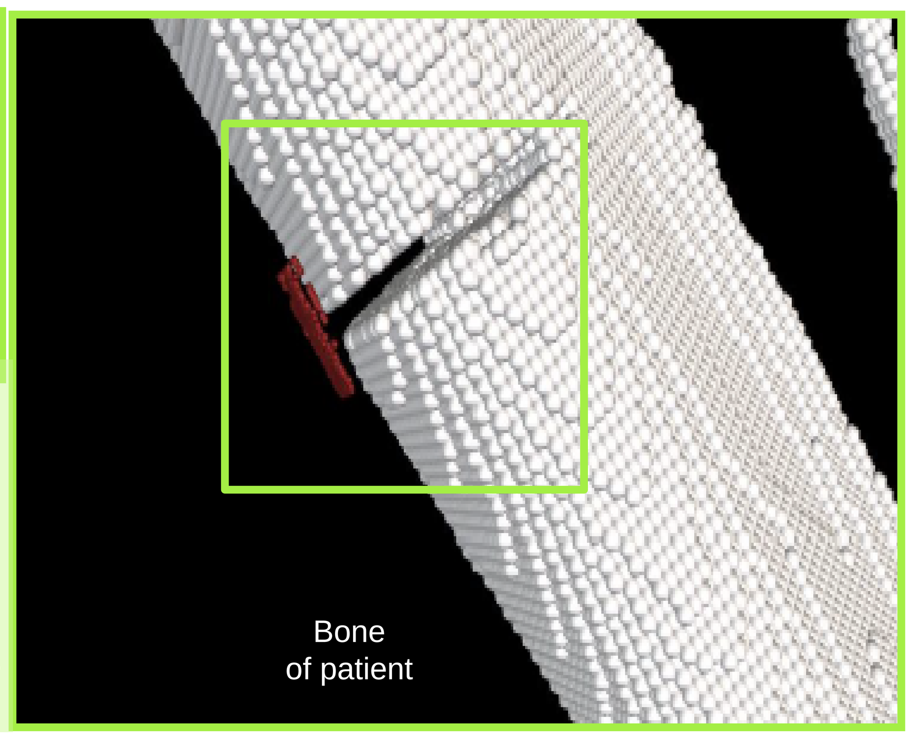
Final: **Integration of apperance and cellular model. Simulation of medical material influence on injury**
The outcomes are simulated parallel on either cellular mechanical interaction.

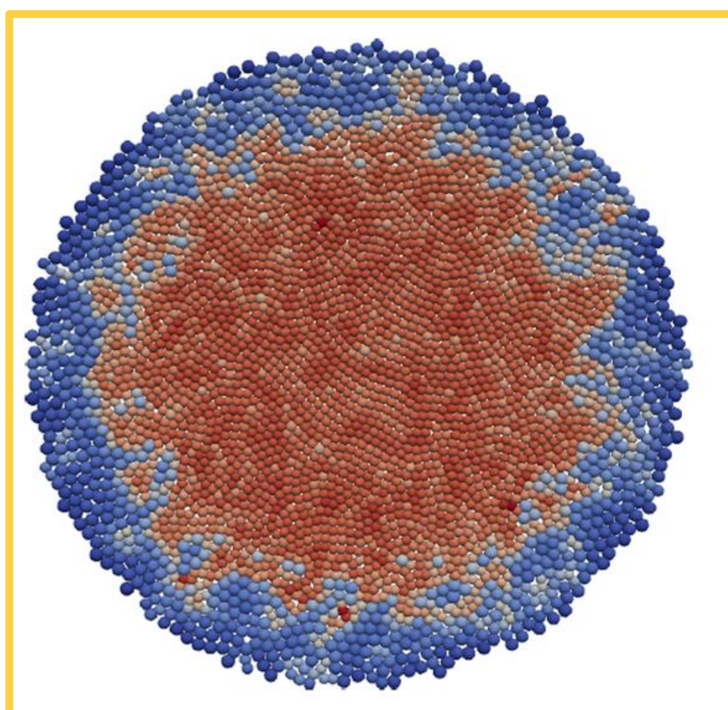
Mesenchymal stem cell (MSC) life cycle in bone marrow (computational description)



Visualisation of the process: integration of models – patient sepicfic and considered medical material.

A visual representation of tissue structure with cellular framework (every sphere represents cell). The colour represents different type of cell, defined by three types of bony tissue regeneration stages.



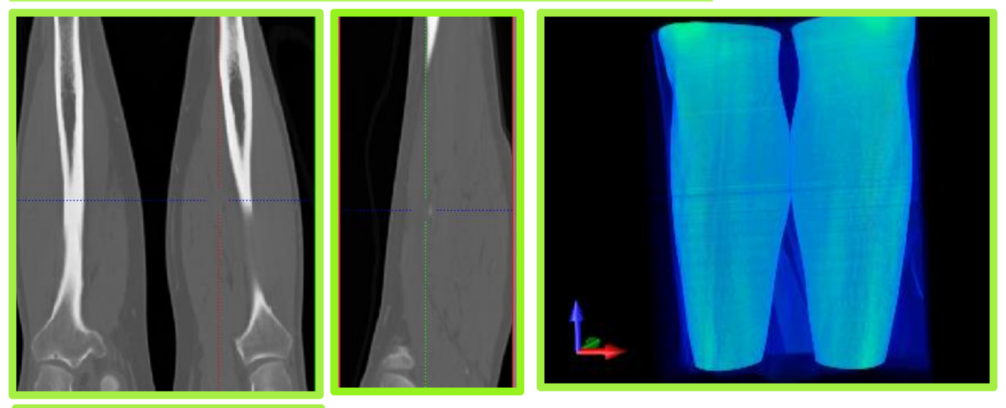


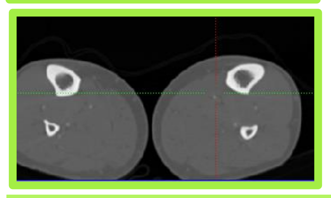
Computed tomography (CT) images of real patient's bone

The segmentation of bony tissue from CT image

Separation bony structure from other tissue, based on differences between the shades of grey of CT images.

Loading set of 250 images from CT





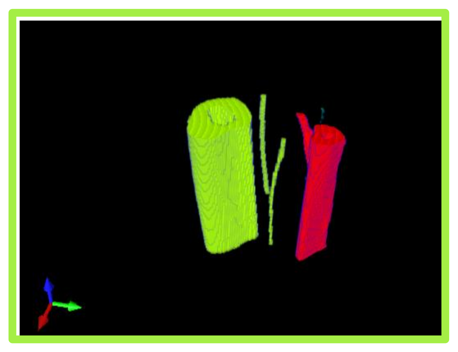
The view on images in three dimensions. We received data, permision and license from ***National Center for Biotechnology Information in the USA.***

Denoising

Isosurface for dividing bone + cartilage

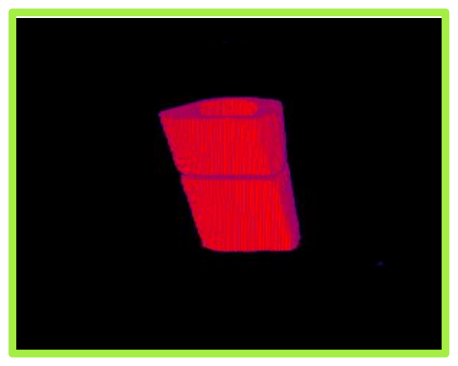
Localizing the fracture

A doctor will pick an area including the fracture, and the software will automticilly delete the rest



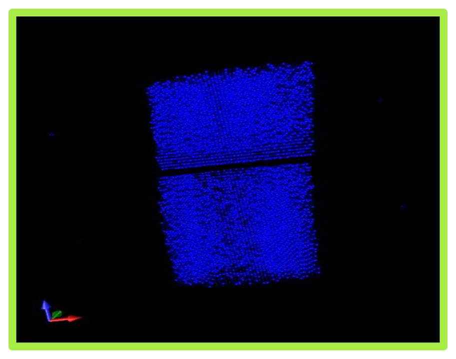
Cut part of bone with fracture

Sotware will then delete everything except the correct bone.



LAST STEP: export to VNF file

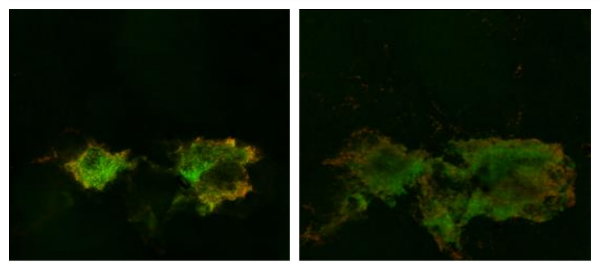
This type of data is accepted as input in the simulation software.



Preparation of comitutional model of medical material for treatment: *bioimplant*

We have developed our bioimplant, based on polymeric material, which was covered by human stem cells. We used it to create algorithm, which describes the its influence on the fracture.

Set of 20 images of bioimplant structure from confocal fluorescence microscopy (3D)



Direction of deepness of bioimplant structure.

Green colour – alive cells, orange colour – dead cells.

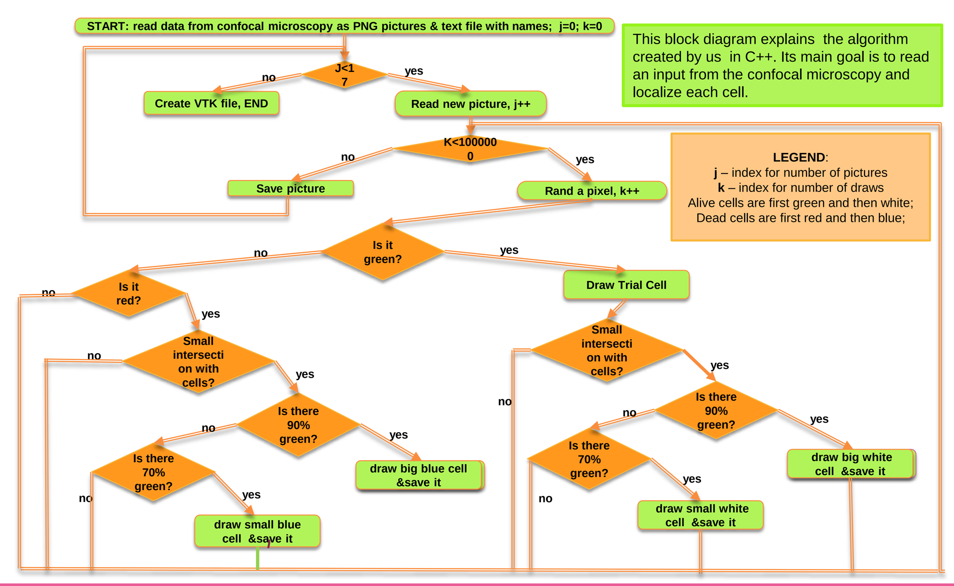
Processing of confocal microscopy images, based on algorthim in C++

Parameters for separating cells from confocal microscopy images:

cell overlaping	average cell size	draw of the pixel	when pixel is a centre of new cell
max 25% allowed	diamater 20 μm = 17 pixels	happened 100 000 times	min 70% green pixels in surrounding

All algorithms have been written in C++

Bock diagram presenting our algorithm:



Processing result: reading and localization of each cell focal microscopy images

Scale: 1pixel =1.24um. White - alive, blue – dead cells.

LAST STEP: VTK file