G A P
Image-*G*uided experimental and computational *A*nalysis of fractured *P*atients

Principal Academic Tutor
Laura Maria Vergani
Mechanical Engineering, PoliMi

Academic Tutor
Federica Buccino
Biomedical Engineering, PoliMi

Irene Aiazzi
Integrated Product Design
PoliMi

Bingqi Liu
Architecture restoration
PoliTo

Alessandro Casto
Mechanical Engineering
PoliTo

Maria Chiara Sbarra
Biomedical Engineering
PoliMi

Giovanni Ziarelli
Mathematical Engineering
PoliMi

Executive Summary

The study of bone damage processes at different scales is essential for understanding fracture mechanisms, which are mostly induced by a trauma or a pathology (such as osteoporosis). Early diagnosis is critical for reducing the burden of bone fractures on the health care system and the economy. This problem is deeply rooted in our society and it will grow more and more because of the increase in average age; in fact, according to data from the Italian Ministry of Health, 40% of the total Italian population, mostly after the age of 65, will have a fracture of the femur, vertebrae or wrist.

However, among the research and experiments on the bone mechanism, the role of bone micro-scale features is yet unclear and the opinions about the presence of small cavities called lacunae are contrasting: lacunae, in the first instance, are stress concentrators that contribute to strength reduction; bone is a damage-tolerant material and lacunae contribute to toughness by deviating crack propagation.

Shedding light on this still fuzzy scenario could be the key to developing early diagnosis methods, avoiding and preventing large numbers of fractures and easing the burden on the health care system. In order to reach our goal, a deeper comprehension of damage initiation and propagation at micro-scale was needed and our approach to achieve it was studying the phenomenon through both experimental tests and computational analysis.

The project has been structured in the following phases:

- Problem definition and Review of the state of the art: A deep study of bone structurehas been the starting point. Later, we have moved to problem definition byinvestigating the economic and psychosocial burden of osteoporosis.
- Preliminary activities for experimental testing: First of all, human femoral heads samples have beencollected prior authorization from the ethics committee of Gruppo San DonatoFoundation and approval of the patients. At the same time, we have designed andrealised a micro-compression device for dynamic image-guided failure assessment ofhuman trabecular bone microstructure and bone microdamage according to ourrequirements.
- Experimental testing: Compression tests under displacement control have been performed on human femur head samples. The tests have been performed at the ELETTRA Synchrotronpremises in Trieste where a technology able to couple μ-CT to synchrotron sources can be found.
- Image post-processing: We designed an AI tool capable of recognizingcracks and lacunaeautomatically through the use of a Convolutional Neural Network. This AI tool hassolved our problem since it is suitable to deal with classification and detection issues.We have realized, trained, and tested two algorithms, one for cracksdetection and the other for lacunae recognition.
- Computational analysis: Owing to the collaboration with ETH, we have succeeded in implementing a sophisticated computational damage model, making more understandable cracks' history, initiation and propagation and clarifying lacunae's role in these processes.
- Bio-inspired structures: The ability of bone to withstand fracture under a wide range of stresses inspires structural uses, while the high surface area to volume ratio and pore connectivity of bone architecture present fascinating aesthetic options. Thus, we have decided to write an article that explores the current state of the art in bone-inspired applications in product design, architecture and fashion, discussing further technological developments ("Down to the Bone: A Novel Bio-Inspired Design Concept" on Journal MDPI).
- Enhancement of convolutional neural network tool: Our AI tool has met the approval of clinicians and seems to have potential for further developments, not only in analysing micro-scale bone images, but could also adapt in many different scenarios. For this reason, we have decided to write a scientific article on it, that is currently in the process of submission.

The main result of our project is a better comprehension of micro-cracks initiation and propagation and of the role played by the lacunae. Indeed, both experimental tests and computational analysis have demonstrated that lacunae act as crack attractors and deviate the crack path. Another strong point of our project is the quality and the quantity of bone sample images at micro-scale that represent a great resource for future studies. Moreover, the convolutional neural networks developed have strongly fastened the image analysis and they are extremely innovative and very promising tools. The multiscale framework of the bone has proved to be very elaborate and resourceful, not only from a biomedical point of view, but also architects, product and fashion designers have appreciated the properties of this structure as the article we have published demonstrates.

Keywords: Bone fracture, μCT Imaging, Convolutional Neural Network, Synchrotron, Computational Damage Models, Image Guided Failure Assessment

Project description
written by the Academic Tutor

The contribution of micro-scale features to bone fracture initiation and propagation is essential to provide a more accurate diagnosis of bone pathologies and a better prevention of bone fragility. However, bone micro-architecture could not be identified with clinical imaging techniques, and patient-specific models that investigate its role in fracture are still missing in the research landscape.

GAP will provide a novel approach to the problem by exploring a versatile methodology: human bone samples extracted from femoral heads are considered for this research and tested under micro-compression with an ad hoc designed device. This device is compatible with synchrotron facility and allows to capture realtime micro-damage initiation and progression stages. In addition to this, multi-scale numerical models are implemented and validated with experimental tests. The aim is to localize regions with high fracture probability and to examine microarchitectural features that contribute to damage initiation. More in detail, the project consists of five phases, some of them followed by the whole group and the others by sub-teams, to optimize the achieving of the desired goal:

1) Review on the state of the art (All GAP Team, Months 1-2): analysis of the dualism behind the role of lacunae, small elliptical cavities present in bone micro-structure. In the first instance, lacunae are stress concentrators, contributing to strength weakening. However, bone is a damage-tolerant material and in this sense, lacunae give a beneficial contribution to toughness, deviating crack propagation.

2) Identification of requirements (All GAP Team, Month 3): interaction with different stakeholders and end-users, i.e. primarily orthopaedists (study of limitations of actual clinical techniques to predict bone fracture), but also patients (impact of early diagnosis of bone pathologies in daily life). GAP will define micro-scale fracture indexes to be assessed with the ethics committee.

3) Implementation of patient-specific computational damage models (GAP Subteam A, Months 4-6): study of damage physical principle in bone and formulation of fracture criteria. GAP will translate general fracture mechanics principles to the context of human bone damage. An optimisation of the code is also required for the study of multiscale damage in humans. The goal lies in the identification of the most prominent sites for micro-crack initiation and propagation. The aid of neural networks allows to perform an automatic detection of micro-fractures.

4) Micro-compression device realization and preliminary tests (GAP Subteam B, Months 4-6). GAP team will have to design a micro-compression device, that is compact, transportable, easy to be assembled and disassembled for the mechanical tests of human bone samples. Preliminary tests aim at identify the proper loads that simulate different daily activities for the patients.

5) Final assessments (All GAP Team, Months 7-10): final validation of the micro-scale damage models inside ELETTRA synchrotron, data analysis, demonstration to the end-users, analysis and writing of the final report.

Team skills by member

The team combines different skills that has been the key to address the problem of bone damage from different viewpoints. In particular:

Irene Aiazzi: with her expertise as future Integrated product designer, she provided a valuable contribution in the design of the experimental apparatus and in the analysis of bone-inspired design products. She has also strongly contributed to the post-processing of images for the Neural Network.

Bingqi Liu: with her expertise asfuture Architect specialized in restoration and heritage enhancement, she provided a unique vision in bone-inspired design of architectural structures and the post-processing of images in the Neural Network. She has been the supervisor about all the aesthetic features of our presentations and articles.

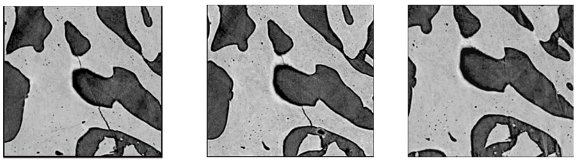
Alessandro Casto: with his expertise as future Mechanical Engineer, he contributed to the development of the experimental set-up and the critical analysis of bone mechanical properties. He has supervised the mechanical definition of the material used in the computational models.

Maria Chiara Sbarra: with her expertise as future Biomedical Engineer, she has coordinated the group in all the activities being the team controller. She has contributed to the development of the mechanical testing set-up, to the finite element computational analysis and to the development of the Neural Network.

Giovanni Ziarelli: with his expertise as Mathematical Engineer, he has been crucial to the development of the computational architecture and to design of the VGG16 Convolutional Neural Network. He has been the supervisor for our second article dealing with the application of the Artificial Intelligence to Synchrotron images.

Goal

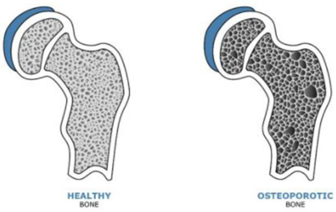
The main aim of the GAP project is to improve the clinical understanding of fracture risk prediction by providing innovative solutions for the early diagnosis of bone fragility to clinicians. In particular,GAP aims to implement a novel framework that combines an experimental and computational approach to study the damage initiation and fracture progression, focusing on the role of micro-scale features of bone structure.
GAP project directly comes from the need of increasing scientific knowledge of bone fracture and micro-cracks propagation, supplying an innovative insight on bone microstructures evinced by both experimental tests and computational simulations.



Crack initiation and propagation in the neighbourhood of a lacuna at increasing compression steps

GAP project provides new tools for fastening recognition of both cracks propagation and lacunae through the implemented Convolutional Neural Network, based on processed µCT images from ELETTRA Synchrotron tests under compression. GAP project highlights the great value of exploiting bone structure features, not only in the biomedical field but also in other industrial applications, like architecture, fashion and design.

Understanding the problem

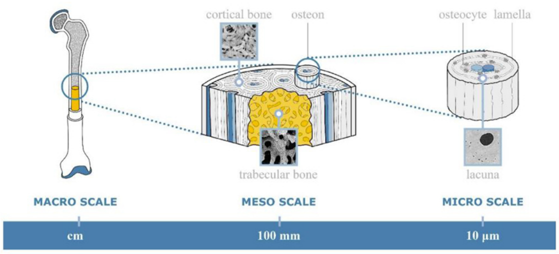


Illustrative comparison between healthy (left) and osteoporotic bone (right), with trabecular tissue enlarged details

The investigation of bone damage process is a crucial issue to understand the mechanisms of age-related fractures, which constitute a major health concern, resulting in high economic burden, morbidity and increasing mortality. This problem is deeply rooted in our society and it will grow more and more because of the increase in average age; in fact, according to data from the Italian Ministry of Health, 40% of the total Italian population, mostly after the age of 65, will have a fracture of the femur, vertebrae or wrist [1]. Besides, the economic treatment costs due to fracture diseases are also more than the treatment costs of many other diseases [2]. Indeed, in the United States, annual fractures and costs are expected to increase by 50% from 2005 to 2025, reaching 3 million and $25 billion, respectively [3].

Therefore, the impact of fractures on the expenditure of the health care system cannot be ignored. Bone fractures are mostly induced by a trauma or a pathology and the age-related ones are strongly linked to osteoporosis, a widespread pathology that induces a significant lowering in bone mass and a consequent increase in bone fragility and susceptibility to fracture. Osteoporotic fractures occur at older ages and more frequently in women rather than in men, with a risk of such a fracture from the 50th year to the remaining lifetime of respectively 50% and 20% [3]. Osteoporosis affects about 5,000,000 people in Italy, of which 80% are postmenopausal women and mortality from fracture of the femur is 5% in the period immediately following the event and 15-25% after one year [1].

Early diagnosis could be the key to reducing the burden of bone fractures on the health care system and the economy. The existing studies showed that one of the fundamental aspects of the research on fracture injury is to study bone injuries on different scales, their external or internal causes and targeted solutions. Due to lack of technology, many symptoms of osteoporosis were not paid attention to and resolved in the early stage which further increased the risk of fractures. Nowadays, although it was demonstrated that it is notable to predict all the fractures alone, the only clinical parameter used to diagnose osteoporosis is Bone Mineral Density (BMD).
However, due to the complex hierarchical structure of bone (up to nine levels can be highlighted), it is particularly difficult to predict bone fracture and to define different levels for bone fragility. Moreover, among the researches and experiments on the bone mechanism, the role of bone micro-scale features is yet unclear and the opinions about the presence of small cavities called lacunae are contrasting: lacunae, in the first instance, are stress concentrators that contribute to strength reduction; bone, on the other hand, is a damage-tolerant material, and lacunae contribute to toughness by deviating crack propagation.

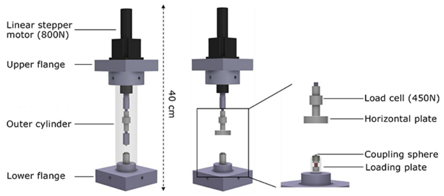


Schematic representation of bone multiscale hierarchical architecture. (a) Macro scale represents the whole bone features, while at the mesoscale (b), it is possible to distinguish cortical and trabecular structures. At the microscale (c), lacunae, small cavities where ostecytes recides

Shedding light on this still fuzzy scenario could be the key to developing early diagnosis methods, avoiding and preventing large numbers of fractures and easing the burden on the health care system.

Exploring the opportunities

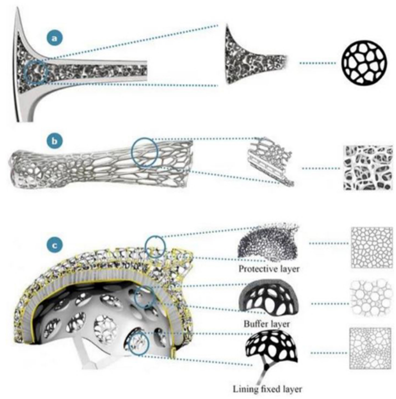
A deep study of the mechanisms undergoing bone fractures has been the starting point that has moved the focus of our analysis on the microscale features. Currently, the opinions about small cavities called lacunae are contrasting. Lacunae - in the first instance - can be interpreted as stress concentrators reducing bone strength. On the other hand, bone is a damage-tolerant material and lacunae contribute to its toughness by deviating crack propagation. As a consequence, the need of clarifying the impact of lacunae distribution on damage initiation and fracture progression is undoubtedly impellent.



Our concept for the design of the Micro-Compression Device.

Micro compression devices are suitable to examine not only bulk properties of the material but also their internal morphology if the experimental set-up is coupled with synchrotron radiation computed tomography (SRμCT).
Once the experimental campaign has been carried out, the huge amount of high-resolution images can be furtherly exploited to validate computational damage models that constitute non-invasive promising tools for prevention and Computer-Aided diagnosis of osteoporosis and bone fractures.

Parallelly, the pandemic situation, that has slowed the experimental campaign, has fostered the study of bone aesthetic and structural properties. In complete ASP-spirit, our group decided to devote part of the project to analyse different applications of bone-inspired structures in various fields, especially architecture, fashion, and design.



(a) “Bone Hammer” by H. Balzer; (b) “Cortex Cast” by D. Karasahin; and (c) “Voronoi bicycle helmet” by Y. Zhou, Z. Xu and H. Wang. In (a,b), the source of inspiration is represented by the mesoscale features of bone’s hierarchical structure, while in (c), the idea of three protective helmet layers is derived from bone’s microscale.

Generating a solution

Based on the state of the art and taking advantage of the peculiar knowledge of the team, we tackled the problem from many different perspectives:

Understanding the bone structure itself and the important value of studying it.

This stage focuses on studying research related to bone structure and bone diseases (such as osteoporosis) and the economic impact of these diseases. The precious value of this structure can be demonstrated, not only in biomedical, but also by the presence of several architectural, fashion and design products inspired by bone framework;

Design of a micro-compression device for dynamic image-guided failure assessment for experimental testing on bone samples.

In order to bring down the research from macro scale to micro scale, one important part of the project consists in an experimental campaign that needs a specific micro-compression device. This device has been designed according to several specifications. The tests have been carried out at SYRMEP beamline of the ELETTRA Synchrotron Trieste that requires specific limits in the height, the weight and the materials of the device. Moreover, the device has to be able to reproduce loads and environment conditions similar to the ones found in vivo in the human body.

Investigation of the apparent mechanical properties at the sample level.

Compression tests under displacement control have the aim of understanding mechanical properties of the samples to better characterise mechanical bone features both in healthy and pathological samples.

Implementation of a computational damage model.

Starting from the images acquired in the experimental section, we would achieve the design of a new computational damage model based on finite element model approach. This model would be used to study from a computational point of view the phenomenon.

Introduction of innovative tools for image analysis and processing to speed up the procedure.

Computer-assisted and artificial intelligence instruments represent promising tools in the analysis of medical pictures to assist clinicians, since they are very suitable to deal with classification and detection issues.

Main bibliographic references

[1] Ministero della Salute. (2021, April 19). Osteoporosi, Salute della donna. Retrieved fromwww.salute.gov.it/portale/donna/dettaglioContenutiDonna.jsp?lingua=italiano&id=4491&area=Salutedonna&menu=patologie

[2] Prisco, P. et al, (2011) Epidemiology of fragility fractures in Italy. Clin Cases Miner Bone Metab.

[3] Burge, R.; Dawson-Hughes, B.; Solomon, D.H.; Wong, J.B.; King, A.; Tosteson, A. Incidence and Economic Burden of Osteoporosis-Related Fractures in the United States, 2005-2025. J. Bone Miner. Res. 2007, 22, 465–475, doi:10.1359/jbmr.061113

[4] Buccino F, Aiazzi I, Casto A, Liu B, Sbarra MC, Ziarelli G, Vergani LM, Bagherifard S. Down to the Bone: A Novel Bio-Inspired Design Concept. Materials. 2021; 14(15):4226. https://doi.org/10.3390/ma14154226