

1. PHD PROJECT DESCRIPTION (4000 characters max., including the aims and work plan)

Project title: Assessment of the relationship between the morphology of the lower limb and structural and microscopic changes in intra-articular structures

1.1. Project goals

Since morphological variation and morphological changes in lower limb (LL) affect the knee functions and can result in knee pain, the goals of the project are:

-functional testing of LL of patients included in this study in relation to LL morphology assessed by imaging and inflammatory markers of tissues, knee effusion and peripheral blood

-testing the relationship between LL morphology and structural and microscopic changes in intra-articular structures (inflammatory markers of tissues, knee effusion and peripheral blood)

-analysis of vitamin D serum level and knee pain, morphology and biochemical markers.

1.2. Outline

Anatomy of knee: The knee is the largest joint in the body. It is a compound synovial joint that consists of the tibiofemoral joint and the patellofemoral joint. The ends of the three bones that form the knee joint are covered with articular cartilage, that protects and cushions the bones, and two wedge-shaped pieces of cartilage, the menisci, which act as shock absorbers, distribute the weight, improve synovial fluid flow and enhance the proprioception. They are tough and rubbery to help cushion the joint and keep it stable. The anatomical function and stability of the knee depend on muscles, bones, ligaments, cartilage, synovial tissue, synovial fluid, and other connective tissues. The knee joint has a close functional relationship with the remaining joints of the lower limb.

Knee pain: Knee pain can result from osteoarthritis - degeneration of one or more of the

joints that manifests mainly with pain, swelling, and stiffness. The risk factors include overweight, old age, and female gender. Osteoarthritis may be the result of an injury, such as a ruptured ligament or torn cartilage. In addition, some anatomical variations of the knee structures, e.g. patellofemoral dysplasia, synovial plica or discoid meniscus, can also be related to dysfunctions and/or pain, swelling and mechanical symptoms. The location and severity of knee pain may vary, depending on the cause of the problem. Knee pain therapies include drug treatment, physiotherapies and/or surgery (e.g. arthroscopy). Some published data indicated that vitamin D supplementation was effective in improving the pain and function in patients with knee osteoarthritis, but with no effects on the prevention of tibial cartilage loss.

Aims: Thus the aim of this project is to test the relationship between the morphology of the lower limb, intra-articular structure of the knee, pain symptoms and histopathological and biochemical markers and vitamin D status.

1.3. Work plan

Year 1

- completing an application for approval of the bioethical commission for scientific research
- recruitment of the participants to the study (patients and postmortem subjects)-continuing during Year 2
- interview and physical examination of patients
- functional tests of the patients' LL of patients included in this study
- imaging of the knees/legs of subjects included in this study (USG, CT/Arthrography CT of the specimens)
- biological sample collection (tissues, knee effusion, blood)
- assessment of the patients' quality of life (questionnaire)
- applying for research funding: IDUB NCU–Grants4Students

Year 2

- reassessment of functional tests
- histopathological testing of synovial knee tissue samples (morphology, inflammatory markers, e.g. IL17, IL8, IL6)
- testing of inflammatory parameters of knee effusion and blood samples (biochemical markers, e.g. cytokines, CRP, albumin/fibrinogen ratio)
- testing of vitamin D serum level
- applying for funding: NCN-Preludium competition

-data presentation at a scientific conference

Year 3

-reassessment of functional tests

-the analysis of the results related to inflammatory parameters of the knee effusion, vitamin D serum level, synovial tissue histology, knee images

-applying for funding: IDUB NCU–Grants4Students

-data presentation at a scientific conference

-manuscript preparation

Year 4

-manuscript preparation

-PhD thesis writing

1.4. Literature

- Alabajos-Cea A, Herrero-Manley L, Suso-Martí L, Viosca-Herrero E, Cuenca-Martínez F, Varangot-Reille C, Blanco-Díaz M, Calatayud J, Casaña J. The Role of Vitamin D in Early Knee Osteoarthritis and Its Relationship with Their Physical and Psychological Status. *Nutrients*. 2021 Nov 12;13(11):4035. doi: 10.3390/nu13114035.
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 - Helito CP, Demange MK, Bonadio MB, Tírigo LE, Gobbi RG, Pécora JR, Camanho GL. Anatomy and Histology of the Knee Anterolateral Ligament. *Orthop J Sports Med*. 2013 Dec 9;1(7):2325967113513546. doi: 10.1177/2325967113513546
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 - 11-Mathieu S, Soubrier M, Peirs C, Monfoulet LE, Boirie Y, Tournadre A. A Meta-Analysis of the Impact of Nutritional Supplementation on Osteoarthritis Symptoms. *Nutrients*. 2022 Apr 12;14(8):1607. doi: 10.3390/nu14081607.
 - **Paczesny L**, Zabrzynski J, Kentzer R, Gryckiewicz S, Lewandowski B, Szwedowski D, Kruczynski J. A 10-Year Follow-up on Arthroscopic Medial Plica Syndrome Treatments with Special Reference to Related Cartilage Injuries. *Cartilage*. 2021 Dec;13(1_suppl):974S-983S. doi: 10.1177/1947603519892310
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1.5. Required initial knowledge and skills of the PhD candidate

A degree (MSc or equivalent) in medical or natural sciences (physiotherapy, biology, or closely related fields); desirable methodological skills: experience in functional testing of the lower extremity in humans, basic knowledge in knee anatomy and pathology, hands-on basic knowledge of analytical and statistical methods; the ability to work creatively and independently towards developing your own research project; English

communication skills, both written and spoken; a collaborative personality.

1.6. Expected development of the PhD candidate's knowledge and skills

Research skills: Ph.D. candidate:

- exhibits knowledge of advances and developments in their field; exhibits the new methodological skills - flow cytometry, ELISA test, medical imaging analysis; exhibits the new statistical and analytical skills;
- demonstrates knowledge of research in related fields and disciplines;
- critically analyses and synthesizes new and complex information from diverse sources,
- has a broad awareness and knowledge of key relevant funding sources and grant application procedures.

Research project management skills: Ph.D. candidate:

- identifies goals and/or tasks to be accomplished and a realistic timeline for completion,
- identifies sources of information applicable to a given problem,
- prioritizes tasks while anticipating potential problems,
- develops organizing principles to effectively sort and evaluate data,
- maintains flexibility in the face of changing circumstances.

Written and oral communication skills: Ph.D. candidate:

- demonstrates effective preparing posters at academic conferences, writing and publishing skills,
- writes effective grant proposals,
- communicates and explains research to diverse audiences, including both specialists and non-specialists.

Team-working and leadership: Ph.D. candidate:

- develops and maintains effective relationships with colleagues,
- works in a collaborative environment,
- has an awareness of their own working style, that of others, and how they interact,
- understands leadership in team environments, recognizing the strengths of team members and work effectively to achieve mutual goal.