Morphometric changes of anatomical structures are a common manifestation of musculoskeletal (MSK) disorders. Osteoporosis and knee osteoarthritis (OA) are two of the most investigated MSK pathologies using magnetic resonance imaging (MRI). Osteoporosis has been defined by the National Institutes of Health as a skeletal disorder characterized by compromised bone strength predisposing to an increased risk of fracture [1]. Knee osteoarthritis is a condition characterized by pain, functional impairment, biochemical and structural changes in articular tissue [2]. In this course, we will discuss the steps needed for the morphometric characterization of relevant tissues involved in osteoporosis and knee OA using MRI.

**Osteoporosis**

Bone tissue is a composite biomaterial made up mainly (~85%) of collagen (type I) and calcium hydroxyapatite, and a very low water content (~15%). In addition, the protons in the matrix and calcified tissue have a very short T2 relaxation time (~250 μs) [3]. As a result of these factors, bone gives no signal in conventional MRI, but the marrow surrounding the trabecular bone network, if imaged at high-spatial resolution, reveals this network due to its higher water and fat content. In high-spatial resolution magnetic resonance images, bone tissue appears as a dark network, and the higher-intensity background represents marrow-equivalent material in the trabecular spaces. Traditionally, due to the high responsiveness to metabolic stimuli and faster turn over than cortical bone (~8 times) [4], trabecular bone has received more attention for the study of osteoporosis using high-spatial resolution MRI. However, cortical bone morphometry (specifically thickness) has also been quantified using conventional MRI, but the advances in ultra short echo-time imaging will soon provide a better alternative for its quantification.

Because the trade-off between high-spatial resolution and signal-to-noise ratio in MRI, high-spatial resolution MRI of trabecular bone has been commonly performed at peripheral sites such as the calcaneus, tibia, and distal radius. However, due to recent advances in hardware, pulse sequence development and coil design, MRI is the only imaging modality with the capability of providing in vivo high-spatial resolution images to quantify trabecular bone microarchitecture of the proximal femur, which is an anatomical site of utmost importance to the study of osteoporosis.

The steps needed to quantify trabecular bone loss and monitor therapeutic interventions based on high-spatial resolution MRI are:

1. Prospective image registration.
2. Surface coil intensity correction (if a surface coil was used).
3. Consistent definition of volumes of interest (intra- and inter-subject).
4. Trabecular bone segmentation.
5. Spatial resolution enhancement.
6. Trabecular bone quantification.
7. Clinical interpretation of trabecular bone parameters.

Many techniques have been developed to quantify trabecular bone morphometry, and they can be subdivided according to those that characterize:

1. Scale.
2. Topology.
3. Orientation.

In this course, we will explain in detail the different pre-processing and trabecular bone quantification approaches, their level of automation, the clinical utility of trabecular bone morphometry in studies of fracture and response to therapy, and future directions in the field of trabecular bone quantification using MRI.

**Knee OA**

Hyaline cartilage, which lines the bearing surface of diarthrodial joints, has a structure composed of chondrocytes and extracellular matrix. Chondrocytes, the cellular component of cartilage, produce and maintain the extracellular matrix, which is primarily made up of hyaluronic acid, proteoglycans, type II collagen, and water. Interactions between the components of the extracellular matrix in articular cartilage form the basis for its unique morphological and biomechanical properties to meet complex mechanical demands without undergoing tear and wear. However, cartilage destruction and loss are common pathophysiological elements of knee OA, which have made cartilage the most investigated tissue in knee OA using MRI.

In contrast to categorical variables of semi-quantitative scoring systems of cartilage morphology (i.e. WORMS [5], KOSS [6] or BLOKS [7]), quantitative imaging-based measures offer continuous variables that are easier to handle from the statistical point of view and that may be less subjective and more sensitive to change. Quantification of cartilage morphometry using MRI requires pulse sequences that are fast, that have short echo times, that yield high-spatial resolution, high signal to noise ratio (SNR), high contrast to noise ratio (CNR), and that minimize artifacts at the bone-cartilage interface. Currently, T₁-weighted spoiled gradient echo sequences with fat saturation or water excitation (spoiled gradient recalled acquisition at steady state (SPGR) or fast low angle shot (FLASH)), and double echo steady-state sequences with water excitation (DESS-WE) are the most widely used for quantification of cartilage morphometry.

The typical approach for the quantification of cartilage morphometry using MRI consists of the following steps:

1. Prospective image registration.
2. Cartilage segmentation.
3. Spatial resolution enhancement.
5. Clinical interpretation of cartilage morphometric parameters.
Many techniques have been developed to quantify knee cartilage morphometry, and they can be subdivided according to those that characterize:

1. Volume.
2. Area.
3. Thickness.

Knee OA is, however, a pathology that involves all of the tissues of the diarthrodial joint including bone, meniscus, and related muscles. Consequently, trabecular bone morphometry of the proximal tibia has been studied in knee OA, and more recently, meniscal and bone shape have also emerged as relevant tissues for morphometric quantification, as well as muscle mass and fat infiltration using MRI.

Trabecular bone quantification in the context of knee OA follows the same processing steps as described for osteoporosis, however, the interpretation of the different parameters has to be performed according to the pathology in question. Current approaches for muscle characterization in knee OA are straightforward after segmentation of the different tissues in the anatomical region of the muscle of interest. In terms of meniscal morphometry, once the menisci have been segmented, a set of positional-, areal-, thickness- and width-based measures have been defined. In order to perform bone shape quantification, bones have to be segmented and spatially normalized.

In this course, we will explain in detail the pre-processing techniques, and the different cartilage, meniscus, muscle, and bone quantification approaches, as well as their level of automation and the clinical utility of morphometric parameters in longitudinal and cross-sectional studies of knee OA. Recent developments in the field of automatic cartilage segmentation and spatial analysis of cartilage thickness measures, as well as future directions in the morphometric field of knee OA using MRI will also be discussed.

In summary, in this course we will cover topics such as image segmentation, image registration, and spatial normalization for the computer-aided diagnosis of osteoporosis and knee OA based on morphometric features such as thickness, topology and shape.

References
