PhD Thesis subject 2017

Laboratory: Laboratoire d'imagerie biomédicale CNRS UMR 7371 – INSERM UMR-S 1146
University: UPMC
Title of the thesis: Development and validation of intraosseous functional ultrasonography
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Collaborations within the thesis: Hôpital Pitié Salpêtrière (Paris), Erasmus MC and TU Delft (The Netherlands)
Program affiliation: No
Cotutelle: No
University:
This subject can be published on the doctoral school’s web site: Yes

**Thesis’s summary (abstract):**

Although intraosseous blood circulation is thought to have a key role in bone growth and remodeling, in fracture healing and in the development of bone disorders, it is rarely considered because of the absence of a suitable technique for its in vivo evaluation in humans. We hypothesize that the development of intraosseous functional ultrasonography will enable the characterization of intraosseous blood circulation, i.e. the blood flow in the cortical bone tissue and in the bone marrow. The work of the PhD student will try to achieve this by 1) an adaptation of time-tested seismic imaging methods, 2) an adaptation of automatic sound speed selection developed for conventional ultrasonography in soft tissues or seismic imaging, 3) an adaptation of recent advances in ultrafast ultrasonic assessment of blood flow in soft tissues and 4) taking advantage of the advent of fully programmable ultrasound scanners. The success of this work will help gaining new in vivo knowledge on vascularization-related bone physio-pathological processes. It may provide in the long term a clinical tool that misses today, and help in the early diagnosis of bone diseases or the monitoring of bone healing. Besides it will broaden the range of clinical uses of ultrasonography, which fails to image bone so far.
Subject

Context

The Laboratoire d’Imagerie Biomédicale (LIB), under the umbrella of the CNRS, INSERM and UPMC, focuses its research on the development of preclinical and clinical morphological, functional and molecular imaging methods, targeting pathologies related to aging, including skeletal, cardiovascular, neurological disorders and cancer. New diagnostic and therapeutic approaches are developed around ultrasound imaging, MRI, CT and SPECT-PET and diffuse optical imaging, and new biomarkers are proposed in the context of early diagnosis, prognosis and assessment of new theranostic modalities.

The PhD student will work in the team "Determinants of Bone Mechanical Status" (DBMS). It is a world-class team who has been involved for more than 20 years in sustained research in the field of bone quantitative ultrasound. The group has done much of the groundbreaking work and technological breakthrough in bone quantitative ultrasound. Intraosseous functional ultrasonography is a new emerging topic at the laboratory.

The mechanisms of regulation of intraosseous blood circulation and its role in bone physiology and diseases are relatively poorly understood because they are difficult to study in vivo, especially in humans. This PhD project aims to develop a non-invasive and relatively inexpensive way of assessing intraosseous blood circulation in vivo in humans, which is currently unavailable. Intraosseous functional ultrasonography will help gaining new in vivo knowledge on vascularization-related bone physio-pathological processes. The success of this work will enrich the diagnostic armamentarium for bone assessment. It may help in the early diagnosis of bone diseases, in the monitoring of the effect of drugs or therapeutic treatments that have an action on intraosseous blood circulation, or in the monitoring of bone healing (after fracture or grafting). Besides it will broaden the range of clinical uses of ultrasonography, which fails to image bone so far.

Objectives

The PhD student will work on two challenges:
1) Enable anatomical ultrasonography of bone by adapting time-tested seismic imaging methods
2) Enable detection and characterization of intraosseous blood flow by adapting to bone the recent advances in ultrafast ultrasonic assessment of blood flow in soft tissues

A first requirement to achieve intraosseous functional ultrasonography is to relax two major assumptions made in conventional ultrasonography, namely the speed of sound in the human body is assumed to be uniform and the multiple reflections experienced by ultrasound waves in the human body are neglected. The reconstruction of an anatomical image of bone will be performed by an adaptation of time-tested seismic imaging methods and an adaptation of automatic sound speed selection methods developed for ultrasonography in soft tissues or seismic imaging. The selected seismic imaging method must take into account refraction and elastic anisotropy of cortical bone tissue. Anatomical ultrasonography of bone will be implemented in a fully programmable ultrasound scanner and first validated with in vitro experiments. Next, ultrasound images of the forearm of healthy volunteers will be validated with gold standard x-ray imaging.

The second challenge will be to develop transmission pulsing schemes and signal processing for intraosseous functional ultrasonography by adapting recent advances in ultrafast ultrasonic assessment of blood flow in soft tissues. Blood vessels in bone are small (Figure 1) and blood flow is slow. Therefore the detection of blood flow in bone is challenging, especially in cortical bone tissue where blood vessels have a diameter close to 20µm. Therefore we will adapt to bone the most recent advances in ultrasonic assessment of blood flow in soft tissues. In particular, blood flow detection relying on ultrafast ultrasound imaging provides today the highest sensitivity (work by the Institut Langevin, Paris). Blood vessels in the marrow have a larger diameter (hundreds of micrometers) and hence blood flow is expected to be higher than in cortical bone tissue. Consequently the characterization of blood flow in the marrow is expected to be less challenging than in cortical bone tissue. The developed methods will be implemented in a fully programmable
ultrasound scanner and first validated with in vitro experiments. Next, the sensitivity of those methods to characterize intraosseous blood flow will be tested in healthy volunteers.

Figure 1: Schematic representation of vascular organization in the diaphysis of a long bone [Cowin & Cardoso, J Biomech, 2015]. Cortical bone thickness varies typically from 1 to 8 mm in humans. These illustrations depict a cortical bone shell with a small thickness (about 1 mm).

Expected results

- Literature study on seismic imaging methods
- Identification of the most suitable seismic imaging technique(s) for anatomical ultrasonography of bone
- Implementation of the methods on a fully programmable ultrasound scanner
- In vitro validation of anatomical ultrasonography of bone with bone-mimicking material
- In vivo validation of anatomical ultrasonography of bone with healthy volunteers, gold standard anatomy obtained by high-resolution x-ray imaging
- Literature study on ultrasonic characterization of blood flow
- Identification of the most suitable methods for the characterization of intraosseous blood flow
- Implementation of the methods on a fully programmable ultrasound scanner
- In vitro validation of intraosseous functional ultrasonography with blood-mimicking fluid and bone-mimicking material
- In vivo evaluation of intraosseous functional ultrasonography with healthy volunteers

Candidate

The ideal candidate has excellent academic records and a Master degree in Physical Acoustics.

Contact

For additional information and application, contact Guillaume Renaud (guillaume.renaud@upmc.fr - 01 44 41 49 71). Applications should include a CV, a motivation letter, and a list of references.