Advancing osteoporosis medicine by observing bone microstructure and remodelling using a four-dimensional nanoscope

Berichterstattung

Projektinformationen

4-D nanoSCOPE

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Periodic Reporting for period 3 - 4-D nanoSCOPE (Advancing osteoporosis medicine by observing bone microstructure and remodelling using a four-dimensional nanoscope)

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Zusammenfassung vom Kontext und den Gesamtzielen des Projekts

Osteoporosis (OP) is one of the ten most widespread diseases in both developed and developing countries. In Europe (EU), more than 27 million people suffer from OP (3) and this number is expected to increase - the World Health Organization (WHO) predicts that the number of osteoporotic bone fractures will quadruple within the next 20-30 years due to aging of the population.
This project, 4-D+ nanoSCOPE, aims to revolutionize our knowledge of osteoporosis (OP) based on an increase in understanding of the underlying bone anatomy and scale bridging bone architecture, supporting the development of better treatments by drugs or surgical intervention. In order to do this, a detailed description of bone in three dimensions at various length scales (from macro to nano) is required, as well as a knowledge of how bone structure changes with age and medication. This dynamic monitoring constitutes the 4th dimension, and requires in vivo monitoring of bone remodeling. Additional information on bone morphology and properties will be monitored, including its mechanical strength and composition, from which additional structure/ property relationships can be deduced. However, 4D+ nanoscopy of bone is currently not possible. To achieve this for the first time, a new imaging and diagnostic tool set, consisting of a number of high-risk hardware and software innovations related to pattern recognition, will be developed that goes far beyond the state-of-the-art.
The current poor characterization of the 3-D architecture of bone is first of all due to the limited resolution of standard characterization tools in clinical environments (e.g. 3D quantitative computer assisted, tomographic X-ray or gamma ray imaging (CT)), which permit to distinguish features of at best ~20µm size in mice and ~100µm in humans. On the other hand, bone analysis with sufficiently high resolution to resolve important bone fine structure has been restricted to 3-D synchrotron X-ray analysis, with its costly and limited access. The early recognition of individual changes in scale-bridging bone structure or metabolism is key to allow the timely introduction of measures to prevent of fractures in the elderly.
The 4-D+ nanoSCOPE project has four main objectives:
1. The development of the 4-D+ nanoSCOPE, a high-performance laboratory X-ray microscope (XRM), to allow in vivo bone structure mapping at high resolution – integration of a world first prototype relying on fast read-out detectors, high brilliance sources and data-based machine learning.
2. Creation and implementation of a new machine learning paradigm “precision learning” that effectively combines deep learning and traditional data processing to reduce the number of parameters, the need for training data (and so the number of animal tests), and that makes deep networks interpretable.
3. The systematic collection of 4-D+ nanoSCOPE data of bone microstructure, physicochemical composition and mechanical properties from mouse models of bone loss and bone-active treatments that affect bone remodeling.
4. The substantial improvement of our understanding of bone remodeling dynamics in healthy and osteoporotic bone, enabling fundamentally new methods to assess factors of influence such as hormones and medication, ultimately developing diagnostic methods to predict bone strength and the risk of fractures.

Arbeit, die ab Beginn des Projekts bis zum Ende des durch den Bericht erfassten Berichtszeitraums geleistet wurde, und die wichtigsten bis dahin erzielten Ergebnisse

The COM group considers the publication [#15 from publication list], that showed that learning with known operators reduces maximum error bounds published in Nature Machine Intelligence the most significant achievement. The technical note for the PYRO-NN framework [16] is also one major achievement, which many research groups are currently using for their own projects.
The MAT group: Since the start of the action, the material science group established a close collaboration to Carl Zeiss Microscopy GmbH; especially to the XRM division in Pleasanton, USA. The development of a novel X-ray detector with faster read-out speed through enhanced frame rates was driven by a close exchange, regular meetings, and remote workshops. The XRM has been upgraded successfully in July 2021 with a fast read-out sCMOS camera (Andor) with 40 framerates per second (11 µm pixel size, 95% QE and low noise, vacuum cooled).
The MED Group: Based on their findings with highly advanced techniques established in the ERC, the MED group was able to generate novel models on bone and joint physiology, which have been published in several excellent journals, such as Nature [#25 from publication list]. These models will help to better understand bone pathologies at a new scale in the future.

Fortschritte, die über den aktuellen Stand der Technik hinausgehen und voraussichtliche potenzielle Auswirkungen (einschließlich der bis dato erzielten sozioökonomischen Auswirkungen und weiter gefassten gesellschaftlichen Auswirkungen des Projekts)

The 4-D+ nanoSCOPE project will develop an X-ray microscope with ground-breaking performance (image acquisition for sub-micron resolution over one hundred times faster than currently possible). This will be the first instrument able to image bone structure in detail in living subjects and to track dynamic processes such as blood flow in bone (velocity 1800-3800 µm/sec). The goals of the project anticipate future progress in X-ray source and detector design and performance. The new instrumentation and software will be used to obtain unprecedented information about scale-bridging bone anatomy and dynamics, thereby providing new levels of understanding of osteoporosis and bone diseases.

logo-4d-nanoscope.png

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