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## 1 Abbreviations

| Abbreviation | Full Form |
|--------------|-----------|
| aBMD         | areal Bone Mineral Density |
| ALL          | Acute Lymphoblastic Leukaemia |
| ALN          | Alendronat |
| ALP          | Alkaline Phosphatase |
| BGLD         | Blood Glucose Lowering Drugs |
| BMD          | Bone Mineral Density |
| BMDD         | Bone Mineralisation Density Distribution |
| BMSi         | Bone Material Strength index |
| BMU          | Basic Multicellular Units |
| BP           | Bisphosphonate |
| BRIL         | Bone-Restricted IFITM-like |
| BV/TV        | Bone Volume per Trabecular Volume |
| Ca           | Calcium |
| CaMean       | mittlere Ca-Konzentration |
| CaPeak       | häufigste auftretende Ca-Konzentration |
| CaWidth      | Peak-Breite der Knochenmineralisationsdichteverteilung |
| CC           | Chronic Complications |
| CD           | Crohn's Disease |
| CKD          | Chronic Kidney Disease |
| CKD-MBD      | Chronic Kidney Disease–Mineral Bone Disorder |
| CLSM         | Confocal Laser Scanning Microscopy |
| CML          | N-((Carboxymethyl)lysine |
| COL1A1       | Collagen Type I alpha 1 |
| COL1A2       | Collagen Type I alpha 2 |
| CRISPR/Cas   | Clustered Regularly Interspaced Short Palindromic Repeats/ CRISPR-associated |
| CT           | Computertomographie |
| DMT2         | Diabetes Mellitus Type 2 |
| DNA          | Deoxyribonucleic Acid |
| DXA          | Dual Energy X-Ray Absorptiometry |
| ECM          | Extracellular Matrix |
| FESEM        | Field Emission Scanning Electron Microscope |
| FGF23        | Fibroblast Growth Factor 23 |
| FH           | Femoral Head |
| FLS          | Fracture Liaison Service |
| FTIR         | Fourier Transform Infrared |
| FTIRI        | Fourier Transform Infrared Imaging |
| FWF          | Fonds zur Förderung der wissenschaftlichen Forschung (Austrian Science Fund) |
| Fx           | Fracture |
| GAG          | Glycosaminoglycan |
| HbA1c        | Hämoglobin A1 (Glykierung) |
| HF           | Hip Fracture |
| HPP          | Hypophosphatasia |
| HRT          | Hormonal Replacement Therapy |
| IBD          | Inflammatory Bowel Disease |
| IFITM5       | Interferon Induced Transmembrane Protein 5 |
| IgG4-RD      | Immunoglobulin G4 – Related Disease |
| IL-10        | Interleukin 10 |
| ko           | Knockout |
| KRN23        | Burosumab |
MAP2K1  dual specificity mitogen-activated protein kinase kinase 1
MC3T3-E1  Mouse Osteoblastic Cell Line
MDS  Myelodysplastic Syndromes
MFx  Morphometric Fracture
MMC  Mineral/Maturity/Crystallinity
MSCs  Mesenchymal Stem Cells
NIH  National Institutes of Health
OI  Osteogenesis imperfecta
OLCN  Osteocyte Lacuna Canaliculi Network
OLS  Osteocyte Lacunae Section
OPG  Osteoprotegerin
OVX  Ovariectomised
PEDF  (also SERPINF1) Pigment Epithelium-Derived Factor
PEN  Pentosidine
PHEX  Phosphate Regulating Endopeptidase Homolog, X-Linked
PLS3  Plastin 3
PMMA  Polymethyl Methacrylate
PPI  inorganic Pyrophosphate
PTH  Parathyroid Hormone
Pyd  Pyridinoline
qBEI  quantitative Backscattered Electron Imaging
RANKL  RecetRANKLptor Activator of NFkappa-B Ligand
RD  Rescue Diet
RNA  Ribonucleic Acid
ROD  Renal Osteodystrophy
SAM  Scanning Acoustic Microscope
SASAM  Saarland Scanning Acoustic Microscopy
SAXS  Small Angle X-Ray Scattering
SEM  Scanning Electron Microscope
SHAM  Placebo Surgery
sHPT  secondary Hyperparathyroidism
T2DM  Type 2 Diabetes Mellitus
TA  Tissue Age
TMV  Turnover Mineralisation Volume
TPTD  Teriparatide
WNT1  Wnt family member 1
WT  Wild type
XLH  X-Linked Hypophosphatemia
ZOL  Zoledronic Acid
2 Overview of the Institute

The Ludwig Boltzmann Institute of Osteology (LBIO) was founded in 1991 through a partnership agreement between Austrian Workers' Compensation Board (AUVA), Vienna Health Insurance Fund (WGKK) – now Austrian Social Health Insurance Fund (OEGK) and Ludwig Boltzmann Gesellschaft (LBG) at the Hanusch Hospital and the Trauma Centre Meidling, with Prof Klaus Klaushofer, MD, serving as the Scientific and Administrative Head until the end of 2018. As from 1 January 2019, he was succeeded by Assoc.Prof Jochen Zwerina, MD. A Board oversees the scientific and administrative activities of the LBIO with Board members representing the partner institutions (AUVA, OEGK, LBG). Special emphasis was placed on the organisation and performance of multidisciplinary basic and clinical research in bone and mineral metabolism with the main focus on translational medicine. Thus, the LBIO serves as the scientific core centre within a multidisciplinary clinical network located at the two hospitals targeting diagnosis and treatment of bone and joint diseases.

2.1 Mission Statement

LBIO's mission is to achieve the highest level of scientific excellence through basic and clinical research, as well as the training of young scientists in clinical and experimental Osteology and the gender-neutral development of their careers.

LBIO's goal is the improvement of patient care. Towards this goal, the study of bone is undertaken at all hierarchical levels through a combination of techniques, unique worldwide.

The aim is the elucidation of the mechanisms underlying the basic function of bone, and musculoskeletal diseases, leading to the discovery and development of effective strategies for diagnosis, prevention, and treatment.

To achieve the stated goal, LBIO basic scientists and clinicians in tandem with scientists of the Department of Biomaterials of the Max Planck Institute of Colloids and Interfaces, Potsdam, Germany, as well as national and international collaborators and industry, are utilizing in partnerships the globally unparalleled LBIO expertise and available combination of analytical approaches to study bone at all hierarchical levels. The existing combination of instrumental capabilities allows analyses to be performed from a clinical, cell & molecular biology, physical chemical, and material science perspective.
2.2 Organisation

External Organisation

Board members:
GD Mag. Alexander Bernart (President) (Allgemeine Unfallversicherungsanstalt)
FBL Erol Holawatsch, MSc (Vice President) (Österreichische Gesundheitskasse)
Obmann Alois Bachmeier (Österreichische Gesundheitskasse)
ÄD Dr. Roland Frank (Allgemeine Unfallversicherungsanstalt)
Ing. Martin Heimhilcher (Österreichische Gesundheitskasse)
Dr. Johannes Pflug (Wirtschaftskammer Wien)
Senator Prof. Mag. Dr. Günther Schön (Wirtschaftskammer Wien)
ÄD Dr. in Elisabeth Zwettler (Österreichische Gesundheitskasse)

Representatives of the Ludwig Boltzmann Society:
Mag. Claudia Lingner (Geschäftsführerin)
Dr. Peter Mayrhofer (Bereichsleiter Medizin & Life Sciences)
Internal Organisation

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Sonja Jäger
Stamatis Rokiti

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Martina Behanova
Julia Feurstein
Jerome Fleger
Judith Haschka
Marlis Huber

Cell Biology
Thomas Dechat
Johanna Besold
Norbert Hassler
Lejla Mastalic
Silvia Spitzer

Biostatistics
Martina Behanova

Support Facilities

Institute Director
Jochen Zwerina

Orthopaedics & Traumatology Consultant
Roland Frank

Administration
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Basic Science Consultant
Peter Fratzl

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3 Co-operations

3.1 Partners

Allgemeine Unfallversicherungsanstalt und Traumazentrum Wien Meidling

Österreichische Gesundheitskasse

Hanusch-Krankenhaus

Ludwig Boltzmann Gesellschaft

3.2 Ongoing scientific co-operations

Barmherzige Schwestern Hospital Vienna, II Medical Department, Vienna Austria (Prof. Heinrich Resch, Dr. Zora Messner)

Clinic Donaustadt, Institute for Pathology and Microbiology, Vienna, Austria (Dr. Richard Arnhold)

Clinical Hospital of the Federal University of Parana, Department of Internal Medicine, Curitiba, PR, Brazil (Dr. Carolina Moreira-Kulak)

Columbia University, Division of Endocrinology, New York, USA (Prof. Elizabeth Shane, prof. David Dempster)

Creighton University School of Medicine, Department of Endocrinology, Omaha, USA (Prof. Robert R. Recker)

Eli Lilly and Company, Indianapolis, USA (Prof Fernando Marin, Prof Imre Pavo, Dr Liandong Ma, Dr Kathleen Taylor)

Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bone and Extracellular Matrix Branch, Bethesda, USA (Dr. Wayne Cabral, Dr. Joan Marini)

Friedrich-Alexander University Erlangen-Nuremberg, Department of Internal Medicine 3, Erlangen, Germany (Prof. Georg Schett, Dr. David Simon)

Governing Body of Social Security Institutions, Vienna, Austria (Argumentation Group)

Harvard School of Dental Medicine, Boston, USA (Prof. Beate Lanske)

Helsinki University Central Hospital and University of Helsinki, Department of Pediatrics, Helsinki, Finland (Prof. Outi Mäkitie, Dr. Pauliina Utriainen)

Image Biopsy Lab GmbH, Vienna, Austria (DI Richard Ljuhar, Mag. Philip Meier)

Indiana University-Purdue University, Department of Biomedical Engineering, Indianapolis, USA (Prof. David Burr)

Institute of Molecular Biotechnology, Vienna, Austria (Dr. Ulrich Elling, Dr. Arabella Meixner)

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Julius Maximilian University Würzburg, Medical Clinic II, Würzburg, Germany (Prof. Franziska Jundt)
Karolinska Institute, Department of Biosciences and Nutrition, Stockholm, Sweden (Prof. Maria Eriksson)

Keio University School of Medicine, Japan (Dr. Koichi Matsuo)

Kepler University Hospital, Department of Paediatrics and Adolescent Medicine, Linz, Austria (Prof Wolfgang Höglerr)

Leiden University Medical Center, Department of Endocrinology, Leiden, The Netherlands (Prof. Sokrates Papapoulos)

Ludwig Boltzmann Institute for COPD and Respiratory Epidemiology, Vienna, Austria (Assoc.Prof. Sylvia Hartl)

Ludwig Boltzmann Institute for Experimental and Clinical Traumatology, Vienna, Austria (Prof. Johannes Grillari)

Max-Planck-Institute of Colloids and Interfaces, Department of Biomaterials, Potsdam, Germany (Prof. Peter Fratzl, Dr. Richard Weinkamer)

Mayo Clinic, Department of Biochemistry and Molecular Biology, Rochester, USA (Dr. Roman Thaler)

McGill University Shriners Hospital for Children, Genetics Unit, Montreal, Canada (Prof. Frank Rauch, Prof. Francis H. Glorieux)

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Medical University of Vienna, Department of Medical Biochemistry, Max Perutz Labs, Vienna, Austria (Prof. Roland Foisner)

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Medical University of Vienna, Department of Paediatrics and Adolescent Medicine, Vienna, Austria (Prof. Gabriele Häusler)

Medical University of Vienna, Institute of Medical Genetics, Vienna, Austria (Assoc.Prof. Franco Laccone)

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Orthopaedic Hospital Vienna-Speising, Department of Pediatric Orthopaedics, Deformity Correction, Neuroorthopaedics and Adult Foot and Ankle Surgery, Vienna, Austria (Prof. Rudolf Ganger, Dr. Ali Al Kaissi)

Orthopaedic Hospital Vienna-Speising, II Orthopaedic Department, Vienna, Austria (Assoc.Prof. Jochen Hofstätter)

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University of California, Molecular Biology Institute, Los Angeles, USA (Dr. Stephen Young)
University of Liège, Mechanics of Biological and Bioinspired Materials Laboratory, Liège, Belgium (Prof. Davide Ruffoni)
University of Veterinary Medicine Vienna, Institute of Pathophysiology, Vienna, Austria (Prof. Reinhold Erben)
University of Vienna, Computational Physics Group, Vienna, Austria (Prof. Christoph Dellago)
## 4 Infrastruktur/Methods

| TECHNIQUE                                                                 | OUTCOME                                                                                                                                                                                                                                                                                                                                 |
|---------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Light Microscopy/Histomorphometry                                         | Structural parameters, parameters of static bone formation and resorption, dynamic bone formation. Pathohistological diagnostic evaluation of bone biopsies in collaboration with the Department of Pathology at the Hanusch Hospital.                                                                                                         |
| Confocal Laser Scanning Microscopy (CLSM)                                 | 3-D fluorescence imaging of labelled bone tissue, cellular structures & cytoskeletal architecture. Imaging of resorption lacunae in in-vitro assays.                                                                                                                                                                                                  |
| qBEI (quantitative backscattered electron imaging)                        | Bone mineral density distribution (BMDD) in a spatially resolved manner at the μm-range.                                                                                                                                                                                                                                                                                                                   |
| EDX (energy dispersive X-ray micro-analysis)                             | Elemental composition of bone (sensitivity of quantification 0.1%)                                                                                                                                                                                                                                                                                                                                     |
| HR-BEI (high-resolution backscatter electron imaging)                     | Visualisation of bone matrix in nm-range (limit 4nm)                                                                                                                                                                                                                                                                                     |
| Scanning SAXS (Small-angle X-ray scattering) in coop. with Prof Fratzl    | Information of bone mineral crystallites characteristics in a spatially resolved manner at the nanometer range.                                                                                                                                                                                                                           |
| Nanoindentation in coop. with Prof Fratzl                                | Spatial distribution of elastic properties of bone composite.                                                                                                                                                                                                                                                                              |
| SASAM (Saarland scanning acoustic microscopy)                             | Spatially resolved acoustic properties of bone material at the μm-range.                                                                                                                                                                                                                                                                                                                             |
| FTIRI (Fourier transform infrared imaging)                                | Spatial distribution of mineral crystallite maturity and collagen cross-links ratio at the 6.3 μm spatial level.                                                                                                                                                                                                                           |
| ATR-FTIR (Attenuated total reflectance Fourier transform infrared)        | Attenuated total reflectance FTIR spectroscopy coupled to a flow-through chamber for real-time analysis of extracellular matrix in *in situ* cell cultures.                                                                                                                                                                                          |
| RAMAN                                                                    | Spatial distribution of mineral characteristics at the 0.6-1 μm spatial level. Mineral crystallite and collagen fibre orientation Nanoporosity Spatial distribution of pyridinoline collagen cross-link content Lipids, AGEs, Pyrophosphate, Proteoglycans                                                                                                                                 |
| Micro-computed tomography (micro-CT) instrument shared with Prof Grillari| Architecture/structure of mineralised bone sample                                                                                                                                                                                                                                                                                      |

The methods used in the Cell Biology unit comprise various cell culture techniques (e.g. cultivating cell lines as well as primary cells and stem cells, cell differentiation, cell transfection, genome editing using the CRISPR/Cas9 system, immunofluorescence microscopy) and molecular biology and biochemical techniques (e.g. cloning, expression analyses using quantitative RT-PCR and Affymetrix microarray analysis, Western Blot, immunoprecipitation, chromatin immunoprecipitation, expression and purification of recombinant proteins).
5 Closed projects and published manuscripts

5.1 Impact microindentation measurements correlate with cortical bone material properties measured by Fourier transform infrared imaging in humans

Bone Material Strength index (BMSi) measured by Impact Microindentation is generally lower in subjects with fragility fractures independently of BMD values. We recently reported that in humans, BMSi values are strongly associated with material properties of subperiosteal mineralized bone surface (local mineral content, nanoporosity, pyridinoline content). In the present study we investigated the relationship of BMSi with material properties of the whole bone cortex, by analyzing thin sections of iliac crest biopsies (N = 12) from patients with different skeletal disorders and a wide range of BMD with or without fractures, by Fourier transform infrared imaging (FTIRI). The calculated parameters were: i) mineral and organic matrix content and their ratio (MM), ii) mineral maturity/crystallinity (MMC) and iii) the ratio of pyridinoline (Pyd) and divalent collagen cross-links (XLR). Results were expressed as images, which were converted to histogram distributions. For each histogram the characteristics recorded were: mean value, mode (most often occurring value), skewness, and kurtosis and their association with BMSi values was examined by correlation analysis. BMSi values were significantly correlated only with MM mean and mode values (r = 0.736, p = 0.0063, and r = 0.855, p = 0.0004, respectively), and with XLR mode values (r = -0.632, p = 0.0274). The results of the present study demonstrate that BMSi values are strongly associated with MM, a metric that corrects the mineral content for the organic matrix content, and may also depend on organic matrix quality. These and our previous observations strongly suggest that BMSi assesses material properties of cortical bone.

Bone 137:115437 IF 4.147 (1528)

5.2 Galectin-9 reflects the Interferon signature and correlates with disease activity in systemic autoimmune diseases

Response To: 'Biomarkers: To Be or Not to Be' by Yavuz and Rönnblom.

Ann Rheum Dis 79(1):e9 IF 16.102 (1529)

5.3 Newly formed and remodeled human bone exhibits differences in the mineralization process

During human skeletal growth, bone is formed via different processes. Two of them are: new bone formation by depositing bone at the periosteal (outer) surface and bone remodeling corresponding to a local renewal of tissue. Since in remodeling formation is preceded by resorption, we hypothesize that modeling and remodeling could require radically different transport paths for ionic precursors of mineralization. While remodeling may recycle locally resorbed mineral, modeling implies the transport over large distances to the site of bone apposition. Therefore, we searched for potential differences of size, arrangement and chemical composition of mineral particles just below surfaces of modeling and remodeling sites in femur midshaft cross-sections from healthy children. These bone sites were mapped using scanning synchrotron X-ray scattering, Raman microspectroscopy, energy dispersive X-ray analysis and quantitative backscattered electron microscopy. The results show clear differences in mineral particle size and composition between the sites, which cannot be explained by a change in the rate of mineral apposition or accumulation. At periosteal modeling sites, mineral crystals are distinctly larger, display higher crystallinity and exhibit a lower calcium to phosphorus ratio and elevated Na and Mg content. The latter may originate from Mg used for phase stabilization of mineral precursors and therefore indicate different time periods for mineral transport. We conclude that the mineralization process is distinctively different between modeling and remodeling sites due to varying requirements for the transport distance and, therefore, the stability of non-crystalline ionic precursors, resulting in distinct compositions of the deposited mineral phase. STATEMENT OF SIGNIFICANCE: In growing
children new bone is formed either due to apposition of bone tissue e.g. at the outer ridge of long bones to allow growth in thickness (bone modeling), or in cavities inside the mineralized matrix when replacing tissue (bone remodeling). We demonstrate that mineral crystal shape and composition are not the same between these two sites, which is indicative of differences in mineralization precursors. We suggest that this may be due to a longer mineral transport distance to sites of new bone formation as compared to remodeling where mineral can be locally recycled. Acta Biomater 104:221-30 IF 7.242 (1530)

5.4 Somatic SMAD3-activating mutations cause melorheostosis by up-regulating the TGF-β/SMAD pathway

Melorheostosis is a rare sclerosing dysostosis characterized by asymmetric exuberant bone formation. Recently, we reported that somatic mosaicism for MAP2K1-activating mutations causes radiographical "dripping candle wax" melorheostosis. We now report somatic SMAD3 mutations in bone lesions of four unrelated patients with endosteal pattern melorheostosis. In vitro, the SMAD3 mutations stimulated the TGF-β pathway in osteoblasts, enhanced nuclear translocation and target gene expression, and inhibited proliferation. Osteoblast differentiation and mineralization were stimulated by the SMAD3 mutation, consistent with higher mineralization in affected than in unaffected bone, but differing from MAP2K1 mutation-positive melorheostosis. Conversely, osteoblast differentiation and mineralization were inhibited when osteogenesis of affected osteoblasts was driven in the presence of BMP2. Transcriptome profiling displayed that TGF-β pathway activation and ossification-related processes were significantly influenced by the SMAD3 mutation. Co-expression clustering illuminated melorheostosis pathophysiology, including alterations in ECM organization, cell growth, and interferon signaling. These data reveal antagonism of TGF-β/SMAD3 activation by BMP signaling in SMAD3 mutation-positive endosteal melorheostosis, which may guide future therapies. J Exp Med 217:e20191499 IF 11.743 (1531)

5.5 Cardiovascular events associate with diabetes status rather than with early basal insulin treatment for the prevention of post-transplantation diabetes mellitus

Post-transplantation diabetes mellitus (PTDM) is a common complication after solid organ transplantation. Although some results on the impact of PTDM on cardiovascular disease and its related mortality are not in full agreement, most of the evidence is in favour of PTDM and impaired glucose tolerance (IGT) predicting mortality. We aimed at exploring the occurrence of cardiovascular events (CVEs) in (kidney) transplant patients who participated in the randomized, controlled Treat-to-target Trial of Basal Insulin in Posttransplant Hyperglycemia (TIP). The present analysis consisted of performing a follow-up study visit on all available TIP study participants from October 2015 to March 2016, assessing the occurrence of CVEs, specifically myocardial infarction, coronary angioplasty/artery bypass graft surgery, valve replacement, congestive heart failure, peripheral artery disease and stroke. We then divided our patients by the initial study group (basal insulin treatment versus standard-of-care control) and by glycaemic status during the study oral glucose tolerance tests (OGTTs). In conclusion, early basal insulin therapy after kidney transplantation had no beneficial effect on CVEs compared with previous standard of anti-hyperglycaemic care post-transplantation, despite clearly improved glycaemic control during the study period. Nephrol Dial Transplant 35:544-6 IF 4.531 (1532)
5.6 Skeletal phenotype/genotype in progressive pseudorheumatoid chondrodysplasia

Axial and extra-axial deceleration in function and progressive joint pain with subsequent development of antalgic gait associated with swellings, and stiffness of the joints with loss of the physiological spine biomechanics were the natural history in this group of patients. Clinical and radiological phenotypes have been analysed carefully to further understand the aetiology behind. Seven patients (three children around the age of 9-11 and one child of 17 years old). Three adults aging 25, 30, 33 and 40 years old were seen and examined. The paediatric group of patients were initially diagnosed with myopathy followed later by juvenile rheumatoid arthritis in other institutions. Clinical and imaging documentation were collected in our departments, followed by mutation screening, was carried out by bidirectional sequencing of the WISP3 gene.

Clinical and radiological phenotypic studies confirmed the diagnosis of progressive pseudorheumatoid chondrodysplasia. A constellation of abnormalities such as early senile hyperostosis of the spine (Forestier disease), osteoarthritis of the hips showed progressive diminution and irregularities of the hip joint spaces associated with progressive capital femoral epiphyseal dysplasia and coxa vara have been encountered. Loss-of-function homozygous mutations (c.667T>G, p.Cys223Gly) and (c.170C>A, p.Ser57*) in the WISP3 gene were identified in our patients.

The definite diagnosis was not defined via vigorous myopathic and rheumatologic investigations. Detailed clinical examination and skeletal survey, followed by genotypic confirmation, were our fundamental pointers to rule out the false diagnosis of juvenile rheumatoid arthritis and rheumatoid polyarthritis in the adult group of patients. We wish to stress that the clinical/radiological phenotype is the baseline tool to establish a definite diagnosis and to guide the geneticist toward proper genotype. Key Points:

- Joint pain and difficulties in walking/climbing the stairs are characteristic features encountered in early childhood. False diagnosis of juvenile rheumatoid arthritis can be made at this point.
- False positive-like muscular wasting resembling myopathy results in ensuing vigorous troublesome investigations.
- Flattened vertebral bodies associated with defective ossification of the anterior end plates are characteristic features of progressive pseudorheumatoid chondrodysplasia.
- Joint expansions, which are usually accompanied by narrowing of the articular ends of the appendicular skeletal system, show a clear radiological phenotype of pseudorheumatoid chondrodysplasia.

Clin Rheumatol 39:553-60 IF 2.394 (1533)

5.7 Primary external stenting of an autogenous brachial-basilic upper arm transposition

High-volume shunt flow after arteriovenous fistula (AVF) creation for hemodialysis can cause high-output heart failure. We used the Frame™ (Vascular Graft Solutions Ltd., Tel Aviv, Israel) external support, a stent, to limit vein dilatation and consecutive high-volume shunt in a 62-old female who underwent brachial-basilic upper arm transposition. After maturation, the shunt was used for dialysis and showed a plateauing flow volume 3 months after the operation. This case illustrates the safety and feasibility of this intervention when performed during AVF formation.

Ann Vasc Surg 65:288.e1-4 IF 1.125 (1534)

5.8 Impact microindentation assesses subperiosteal bone material properties in humans

Impact microindentation (IMI) is a Reference Point Indentation technique measuring tissue-level properties of cortical bone in humans in vivo. The nature, however, of the properties that can affect bone strength is incompletely understood. In the present study we examined bone material properties in transiliac bone biopsies obtained concurrently with measurements of Bone Material
Strength index (BMSi) by IMI in 12 patients with different skeletal disorders and a wide range of BMD, with or without fractures (8 males, 4 females, mean age 48±12.2 (SD) years, range 15-60 years). IMI was performed in the mid-shaft of the right tibia with a hand-held microindenter (OsteoProbe). Cancellous and cortical bone mineralization density distributions (BMDD) were measured in the entire biopsy bone area by quantitative backscattered electron imaging. Raman measurements were obtained right at the outer edge of the cortex, and 5, 50, 100, 500μm inwards. The calculated parameters were: i) Mineral and organic matrix content as well as the mineral / matrix ratio. ii) Nanoporosity. iii) Glycosaminoglycan content. iv) Pyridinoline content. v) Maturity/crystallinity of the apatite crystallites. There was no relationship between BMSi values with any measurement of mineral content of whole bone tissue (BMD, BMDD) or maturity/crystallinity of bone mineral. On the other hand, a positive correlation between BMSi and local mineral content, and an inverse correlation between BMSi and nanoporosity at the mineralized subperiosteal edge of the sample and at 5μm inwards was found. A positive correlation was also observed between BMSi and pyridinoline content at the same locations. These results indicate that local mineral content, nanoporosity and pyridinoline content at the subperiosteal site in the transiliac bone biopsy are linked to the BMSi values measured in the tibia. As both high porosity at the nano level and low pyridinoline content of the bone matrix can negatively impact bone strength, our findings suggest that BMSi most likely assesses subperiosteal bone material properties.

Bone 131:115110 IF 4.147 (1535)

5.9 A high coordination of cross-links in fiber bundles prevents local strain concentrations

We investigate the influence of the coordination of cross-links on the plastic (i.e., permanent) deformation in cross-linked fiber bundles. Yield strain and strength as well as the resilience are studied as a function of cross-linker and grafting density. It is found that classical twofold coordinated cross-links lead to a pronounced strain concentration in the system, while cross-links with higher coordination allow for a more homogeneous load transfer through the system. This results in inferior mechanical properties related to plastic behavior in the first system compared to the latter. Particularly, in twofold coordinated systems, the resilience shows a nonmonotonic behavior with respect to cross-linker density. This means that inserting always more and stronger cross-links do not necessarily improve the mechanical performance of a material. These findings may help to interpret experimental findings on the fracture energy in hydro-gels cross-linked with zinc ions.

Comput Mater Sci 184:109849 IF 2.863 (1536)

5.10 Clinical and genetic heterogeneity in six Tunisian families with horizontal gaze palsy with progressive scoliosis: a retrospective study of 13 cases

Background: Horizontal Gaze Palsy with Progressive Scoliosis (HGPPS) is a rare autosomal recessive congenital disorder characterized by the absence of conjugate horizontal eye movements, and progressive debilitating scoliosis during childhood and adolescence. HGPPS is associated with mutations of the ROBO3 gene. In this study, the objective is to identify pathogenic variants in a cohort of Tunisian patients with HGPPS and to further define ROBO3 genotype-phenotype correlations. Methods: Thirteen Tunisian patients from six unrelated consanguineous families all manifesting HGPPS were genetically investigated. We searched for the causative variants for HGPPS using classical Sanger and whole exome sequencing. Results: Four distinct homozygous mutations were identified in ROBO3 gene. Two of these were newly identified homozygous and non-synonymous mutations, causing effectively damage to the protein by in silico analysis. The other two mutations were previously reported in Tunisian patients with HGPPS. Mutations were validated by Sanger sequencing in parents and affected individuals. Conclusion: To the best of our knowledge, this is the largest ever reported cohort on families with HGPPS in whom ROBO3 mutations were identified. These molecular findings have expanded our knowledge
of the ROBO3 mutational spectrum. The relevance of our current study is two-fold; first to assist proper management of the scoliosis and second to protect families at risk.

*Front Pediatr* 8:172  IF 2.349  (1537)

### 5.11 Detection and imaging of gadolinium accumulation in human bone tissue by micro- and submicro-XRF

Gadolinium-based contrast agents (GBCAs) are frequently used in patients undergoing magnetic resonance imaging. In GBCAs gadolinium (Gd) is present in a bound chelated form. Gadolinium is a rare-earth element, which is normally not present in human body. Though the blood elimination half-life of contrast agents is about 90 minutes, recent studies demonstrated that some tissues retain gadolinium, which might further pose a health threat due to toxic effects of free gadolinium. It is known that the bone tissue can serve as a gadolinium depot, but so far only bulk measurements were performed. Here we present a summary of experiments in which for the first time we mapped gadolinium in bone biopsy from a male patient with idiopathic osteoporosis (without indication of renal impairment), who received MRI 8 months prior to biopsy. In our studies performed by means of synchrotron radiation induced micro- and submicro-X-ray fluorescence spectroscopy (SR-XRF), gadolinium was detected in human cortical bone tissue. The distribution of gadolinium displays a specific accumulation pattern. Correlation of elemental maps obtained at ANKA synchrotron with qBEI images (quantitative backscattered electron imaging) allowed assignment of Gd structures to the histological bone structures. Follow-up beamtimes at ESRF and Diamond Light Source using submicro-SR-XRF allowed resolving thin Gd structures in cortical bone, as well as correlating them with calcium and zinc.

*Sci Rep* 10:6301  IF 3.998  (1538)

### 5.12 Network architecture strongly influences the fluid flow pattern through the lacunocanalicular network in human osteons

A popular hypothesis explains the mechanosensitivity of bone due to osteocytes sensing the load-induced flow of interstitial fluid squeezed through the lacunocanalicular network (LCN). However, the way in which the intricate structure of the LCN influences fluid flow through the network is largely unexplored. We therefore aimed to quantify fluid flow through real LCNs from human osteons using a combination of experimental and computational techniques. Bone samples were stained with rhodamine to image the LCN with 3D confocal microscopy. Image analysis was then performed to convert image stacks into mathematical network structures, in order to estimate the intrinsic permeability of the osteons as well as the load-induced fluid flow using hydraulic circuit theory. Fluid flow was studied in both ordinary osteons with a rather homogeneous LCN as well as a frequent subtype of osteons-so-called osteon-in-osteons-which are characterized by a ring-like zone of low network connectivity between the inner and the outer parts of these osteons. We analyzed 8 ordinary osteons and 9 osteon-in-osteons from the femur midshaft of a 57-year-old woman without any known disease. While the intrinsic permeability was 2.7 times smaller in osteon-in-osteons compared to ordinary osteons, the load-induced fluid velocity was 2.3 times higher. This increased fluid velocity in osteon-in-osteons can be explained by the longer path length, needed to cross the osteon from the cement line to the Haversian canal, including more fluid-filled lacunae and canaliculi. This explanation was corroborated by the observation that a purely structural parameter-the mean path length to the Haversian canal-is an excellent predictor for the average fluid flow velocity. We conclude that osteon-in-osteons may be particularly significant contributors to the mechanosensitivity of cortical bone, due to the higher fluid flow in this type of osteons.

*Biomech Model Mechanobiol* 19:823-40  IF 2.527  (1539)
5.13 Substitution of murine type I collagen A1 3-hydroxylation site alters matrix structure but does not recapitulate osteogenesis imperfecta bone dysplasia

Null mutations in CRTAP or P3H1, encoding cartilage-associated protein and prolyl 3-hydroxylase 1, cause the severe bone dysplasias, types VII and VIII osteogenesis imperfecta. Lack of either protein prevents formation of the ER prolyl 3-hydroxylation complex, which catalyzes 3Hyp modification of types I and II collagen and also acts as a collagen chaperone. To clarify the role of the A1 3Hyp substrate site in recessive bone dysplasia, we generated knock-in mice with an α1(I)P986A substitution that cannot be 3-hydroxylated. Mutant mice have normal survival, growth, femoral breaking strength and mean bone mineralization. However, the bone collagen HP/LP crosslink ratio is nearly doubled in mutant mice, while collagen fibril diameter and bone yield energy are decreased. Thus, 3-hydroxylation of the A1 site α1(I)P986 affects collagen crosslinking and structural organization, but its absence does not directly cause recessive bone dysplasia. Our study suggests that the functions of the modification complex as a collagen chaperone are thus distinct from its role as prolyl 3-hydroxylase.

Matrix Biol 90:20-39 IF 8.572 (1540)

5.14 Regional and gender differences in population-based oral health insurance data

Objective: Early dental monitoring contributes substantially to good oral health in children. However, little is known on whether children from different geographical regions and gender are equally reached with current preventive and curative oral health strategies. The aim of our study therefore was to explore regional and gender differences in a population-based oral health dataset of Austrian children up to the age of 14.

Materials and methods: We extracted the first electronically available health insurance data of children aged up to 14 years on dental services within a 4-year observation period in Austria and performed a separate analysis in up to 6-year-old children. In addition, we used a smaller randomly selected sample dataset of 3000 children as the large numbers would result in significant, but very small effects.

Results: In a total of 130,895 children, of whom 77,173 children (59%) were up to the age of six, we detected an east-west gradient: The eastern regions of Austria showed an older age at first contact and a higher number of dental services. A child aged up to 6 years who needed more than four dental services had a likelihood of 40% to be from Vienna, Austria's capital city located in the east. The smaller random sample did not show significant gender differences.

Conclusions: Even in regions with a high density of dentists, such as Vienna, we obviously did not reach young children in the same extent as in other regions.

Clin Oral Investig 24:2331-9 IF 2.812 (1541)

5.15 Alterations of bone material properties in adult patients with X-linked hypophosphatemia (XLH)

X-linked hypophosphatemia (XLH) caused by PHEX mutations results in elevated serum FGF23 levels, renal phosphate wasting and low 1,25-dihydroxyvitamin D. The glycosphosphoprotein osteopontin, a potent inhibitor of mineralization normally degraded by PHEX, accumulates within the bone matrix. Conventional therapy consisting of supplementation with phosphate and vitamin D analogs is burdensome and the effects on bone material poorly characterized. We analyzed transiliac bone biopsies from four adult patients, two of them severely affected due to no diagnosis and no treatment until adulthood. We used light microscopy, qBEI and FTIRI to study histology, histomorphometry, bone mineralization density distribution, properties of the organic matrix and size of hypomineralized periosteocytic lesions. Non-treatment resulted in severe osteomalacia, twice the amount of mineralized trabecular volume, multiple osteon-like perforations, continuity of lamellae from mineralized to unmineralized areas and distinctive patches of woven bone. Periosteocytic lesions were larger than in treated patients. The latter had nearly normal osteoid
thicknesses, although surface was still elevated. The median calcium content of the matrix was always within normal range, although the percentage of lowly mineralized bone areas was highly increased in non-treated patients, resulting in a marked heterogeneity in mineralization. Divalent collagen cross-links were evident independently of the mineral content of the matrix. Broad osteoid seams lacked measurable pyridinoline, a mature trivalent cross-link and exhibited considerable acidic lipid content, typically found in matrix vesicles. Based on our results, we propose a model that possibly integrates the relationship between the observed mineralization disturbances, FGF23 secretion and the known osteopontin accumulation in XLH.

J Struct Biol 211:107556 IF 3.071 (1542)

5.16 Increased FGF-23 levels are linked to ineffective erythropoiesis and impaired bone mineralization in myelodysplastic syndromes

Myelodysplastic syndromes (MDS) are clonal malignant hematopoietic disorders in the elderly characterized by ineffective hematopoiesis. This is accompanied by an altered bone microenvironment, which contributes to MDS progression and higher bone fragility. The underlying mechanisms remain largely unexplored. Here, we show that myelodysplastic NUP98-HOXD13 (NHD13) transgenic mice display an abnormally high number of osteoblasts, yet a higher fraction of nonmineralized bone, indicating delayed bone mineralization. This was accompanied by high fibroblast growth factor-23 (FGF-23) serum levels, a phosphaturic hormone that inhibits bone mineralization and erythropoiesis. While Fgf23 mRNA expression was low in bone, brain, and kidney of NHD13 mice, its expression was increased in erythroid precursors. Coculturing these precursors with WT osteoblasts induced osteoblast marker gene expression, which was inhibited by blocking FGF-23. Finally, antibody-based neutralization of FGF-23 in myelodysplastic NHD13 mice improved bone mineralization and bone microarchitecture, and it ameliorated anemia. Importantly, higher serum levels of FGF-23 and an elevated amount of nonmineralized bone in patients with MDS validated the findings. C-terminal FGF-23 correlated negatively with hemoglobin levels and positively with the amount of nonmineralized bone. Thus, our study identifies FGF-23 as a link between altered bone structure and ineffective erythropoiesis in MDS with the prospects of a targeted therapeutic intervention.

JCI Insight 5:137062 IF 6.014 (1543)

5.17 Inflammatory bowel disease: a nationwide study of hip fracture and mortality risk after hip fracture

Background and aims: With rising rates of inflammatory bowel diseases (IBD) in older adults, management of co-morbidities such as osteoporosis is becoming increasingly important. Hip fracture (HF) is the most serious consequence of low bone mineral quality and is associated with excess risk of mortality. For older IBD patients, there are only limited data available. Therefore, we aimed to assess the association of IBD with HF and all-cause mortality risk after HF among IBD patients older than 50 years.

Methods: In a national database-registered case-control study, 56,821 HF cases aged ≥50 years and 113,718 age-, sex- and region-matched non-hip fracture controls were analyzed between 2012-2016. A history of IBD was assessed from data of Austrian social health insurance funds. Logistic regression and Cox proportional multivariate models were used to test the association of IBD with HF and post-hip fracture mortality risk.

Results: A total of 531 patients were identified with IBD (25.0% men, mean age 81.2 years, SD 9.7). Analysis adjusted for anti-osteoporotic treatment, use of glucocorticoids and selected medications showed that IBD patients had an increased odds of HF (OR 2.22, 95%CI 1.86-2.64). Patients with Crohn's disease (CD) revealed a higher HF odds in contrast to patients with ulcerative colitis (OR 2.91, 95% CI 2.17-3.89 and OR 1.89, 95% CI 1.52-2.35, respectively). Overall mortality risk after HF was higher among female CD patients (HR 1.75, 95%CI 1.28-2.41) than in the general population.
Conclusions: IBD was strongly associated with HF in older patients. Post-hip fracture mortality risk was elevated particularly in women with CD.

*J Crohns Colitis* 14:1256-63  IF 8.658  (1544)

5.18 Heterogeneity of the osteocyte lacuno-canalicular network architecture and material characteristics across different tissue types in healing bone

Various tissue types, including fibrous connective tissue, bone marrow, cartilage, woven and lamellar bone coexist in healing bone. Similar to all bone tissue type, healing bone contains a lacuno-canalicular network (LCN) housing osteocytes that are known to orchestrate bone remodeling in healthy bone by sensing mechanical strains and translating them into biochemical signals. The structure of the LCN is also hypothesized to influence mineralization processes. Hence, the aim of the present study was to visualize and correlate spatial variations in the LCN topology with mineral characteristics, within and at the interfaces of the different tissue types that comprise healing bone. We applied a correlative multi-method approach to visualize the LCN architecture and quantify mineral particle size and orientation within healing femoral bone in a mouse osteotomy model (26 weeks old C57BL/6 mice). This approach revealed structural differences across several length scales during endochondral ossification within the following regions: calcified cartilage, bony callus, cortical bone and the transition zone between the cortical region and callus that developed during 21 days after the osteotomy. In this transition zone, we observed a continuous convergence of mineral characteristics and osteocyte lacunae shape as well as discontinuities in the lacunae volume and LCN connectivity. The bony callus exhibits a 34% higher lacunae number density with 40% larger lacunar volume compared to cortical bone. The presented correlations between LCN architecture and mineral characteristics improves our understanding of how bone develops during healing and may indicate a contribution of osteocytes to bone (re)modeling.

*J Struct Biol* 212:107616  IF 3.071  (1545)

5.19 No role of osteocytic osteolysis in the development and recovery of the bone phenotype induced by severe secondary hyperparathyroidism in vitamin D receptor deficient mice

Osteocytic osteolysis/perilacunar remodeling is thought to contribute to the maintenance of mineral homeostasis. Here, we utilized a reversible, adult-onset model of secondary hyperparathyroidism to study femoral bone mineralization density distribution (BMDD) and osteocyte lacunae sections (OLS) based on quantitative backscattered electron imaging. Male mice with a non-functioning vitamin D receptor (VDRΔΔ) or wild-type mice were exposed to a rescue diet (RD) (baseline) and subsequently to a low calcium challenge diet (CD). Thereafter, VDRΔΔ mice received either the CD, a normal diet (ND), or the RD. At baseline, BMDD and OLS characteristics were similar in VDRΔΔ and wild-type mice. The CD induced large cortical pores, osteomalacia, and a reduced epiphyseal average degree of mineralization in the VDRΔΔ mice relative to the baseline (-9.5%, p < 0.05 after two months and -10.3%, p < 0.01 after five months of the CD). Switching VDRΔΔ mice on the CD back to the RD fully restored BMDD to baseline values. However, OLS remained unchanged in all groups of mice, independent of diet. We conclude that adult VDRΔΔ animals on an RD lack any skeletal abnormalities, suggesting that VDR signaling is dispensable for normal bone mineralization as long as mineral homeostasis is normal. Our findings also indicate that VDRΔΔ mice attempt to correct a calcium challenge by enhanced osteoclastic resorption rather than by osteocytic osteolysis.

*Int J Mol Sci* 21:7989  IF 4.556  (1546)
5.20 Bone tissue material composition is compromised in premenopausal women with type 2 diabetes

Type 2 diabetes mellitus (T2DM) patients are at an increased risk of fracture despite normal to high bone mineral density (BMD) values. In this cross-sectional study we establish bone compositional properties in tetracycline labelled iliac crest biopsies from premenopausal women diagnosed with T2DM (N=26). Within group comparisons were made as a function of tissue age (TA), presence of chronic complications (CC), glycosylated hemoglobin (HbA1c) levels, and morphometric fracture (MFx). We also compared these data at actively trabecular bone forming surfaces against sex- and age-matched healthy controls (N = 32).

The bone quality indices determined by Raman microspectroscopic analysis were: mineral / matrix (MM), tissue water content (nanoporosity; NanoP), mineral maturity / crystallinity (MMC), and glycosaminoglycan (GAG), pyridinoline (Pyd), N-(Carboxymethyl)lysine (CML), and pentosidine (PEN) content. Within the T2DM group, at the oldest tissue, CML and PEN contents were significantly elevated in the cancellous compared to cortical compartment. The outcomes were not dependent on MFx. On the other hand, both were significantly elevated in patients with CC, as well as those with HbA1c levels > 7%. At actively forming surfaces, the cortical compartment had higher NanoP compared to cancellous. Still within the T2DM group, patients with MFx had significantly elevated MM and GAGs compared to the ones that did not. At actively forming trabecular surfaces, compared to healthy women, T2DM patients had elevated GAGs content and MMC.

The results of this study indicate increased AGEs in those with poor glycation control and chronic complications. Additionally, T2DM patients had elevated MMC and decreased GAGs content compared to healthy controls. These alterations may be contributing to the T2DM inherent elevated fracture risk and suggest a role for hyperglycemia on bone quality.

Bone 141:115634 IF 4.147 (1547)

5.21 Fractal-based analysis of bone microstructure in Crohn's disease: a pilot study

Crohn's disease (CD) is associated with bone loss and increased fracture risk. TX-Analyzer™ is a new fractal-based technique to evaluate bone microarchitecture based on conventional radiographs. The aim of the present study was to evaluate the TX-Analyzer™ of the thoracic and lumbar spine in CD patients and healthy controls (CO) and to correlate the parameters to standard imaging techniques. 39 CD patients and 39 age- and sex-matched CO were analyzed. Demographic parameters were comparable between CD and CO. Bone structure value (BSV), bone variance value (BVV) and bone entropy value (BEV) were measured at the vertebral bodies of T7 to L4 out of lateral radiographs. Bone mineral density (BMD) and trabecular bone score (TBS) by dual energy X-ray absorptiometry (DXA) were compared to TX parameters. BSV and BVV of the thoracic spine of CD were higher compared to controls, with no difference in BEV. Patients were further divided into subgroups according to the presence of a history of glucocorticoid treatment, disease duration > 15 years and bowel resection. BEV was significantly lower in CD patients with these prevalent risk factors, with no differences in BMD at all sites. Additionally, TBS was reduced in patients with a history of glucocorticoid treatment. Despite a not severely pronounced bone loss in this population, impaired bone quality in CD patients with well-known risk factors for systemic bone loss was assessed by TX-Analyzer™.

J Clin Med 9:4116 IF 3.303 (1548)

5.22 Rheumatic musculoskeletal diseases and COVID-19 a review of the first 6 months of the pandemic

In December 2019, a cluster of severe pneumonia was observed in China, with the subsequent discovery of a new beta-coronavirus (SARS-CoV-2) as the causative agent. The elicited disease COVID-19 is characterized by fever, dry cough, myalgia, or fatigue and has a favorable outcome in the majority of cases. However, in some patients COVID-19 leads to severe pneumonia and sepsis
with subsequent respiratory failure and gastrointestinal, hematological, neurological, and cardiovascular complications. A higher risk of infection is intrinsic to active rheumatic and musculoskeletal diseases (RMD) and the use of biological disease modifying anti-rheumatic drugs (DMARDs). With an increasing number of reports on COVID-19 in RMD patients, we are beginning to appraise their risks. In this review, we summarize the published cases of COVID-19 infections in RMD patients, including patients with inflammatory arthritis and connective tissue diseases as well as anti-phospholipid syndrome and Kawasaki syndrome. Overall, patients with inflammatory arthritis do not seem to be at a higher risk for infection or a severe course of COVID-19. Risk for critical COVID-19 in patients with systemic inflammatory diseases such as SLE or vasculitis might be increased, but this needs further confirmation. Furthermore, we summarize the data on DMARDs used to fight SARS-CoV-2 infection and hyperinflammation.

Front Med (Lausanne) 7:562142 IF 3.421 (1549)

5.23 No evidence for alteration in early secondary mineralization by either alendronate, teriparatide or combination of both in transiliac bone biopsy samples from postmenopausal osteoporotic patients

The influence of treatment with alendronate (ALN), teriparatide (TPTD) or concurrent treatment with both on the human bone matrix mineralization has not yet been fully elucidated. For this purpose we analyzed quadruple fluorochrome labelled transiliac bone biopsy samples (n = 66) from postmenopausal osteoporotic women with prior and ongoing ALN (ALN-Rx arm) or without ALN (Rx-Naïve arm) after 7 months treatment with cyclic or daily TPTD or without TPTD using quantitative backscattered electron imaging and confocal scanning laser microscopy. Additionally to the bone mineralization density distribution (BMDD) of entire cancellous and cortical compartments, we measured the mineralization kinetics, i.e. the calcium concentration between the younger (Ca_DL2) and older double labels (Ca_DL1), and in interstitial bone (Ca_int) in a subset of the biopsy cohort. We found the BMDD from the patients with prior and ongoing ALN generally shifted to higher calcium concentrations compared to those without ALN (average degree of mineralization in cancellous bone Cn.CaMean + 3.1%, p<0.001). The typical BMDD changes expected by cyclic or daily TPTD treatment due to the increased bone turnover/formation, e.g. an increase in low mineralized bone area were not observed. Additionally, we found no influence of treatment with ALN or TPTD or combination thereof on Ca_DL2, Ca_DL1, or Ca_int. Pooling the information from all groups, Ca_DL1 was +5.9% (p<0.001) higher compared to Ca_DL2, corresponding to a mineralization rate of 0.18 wt% Ca per week during the early secondary mineralization process. Our data suggest that the patients in the ALN-Rx arm had more highly mineralized bone matrix than those without ALN due to their lower bone turnover. The reason for the unexpected BMDD findings in the TPTD treated remain unknown and cannot be attributed to altered mineralization kinetics as no differences in the time course of early secondary mineralization were observed between the treatment groups.

Bone Rep 12:100253 (1550)

5.24 Progressive Deformity of the Lower Limbs in a Patient with KID (Keratitis-Ichthyosis-Deafness) Syndrome

Purpose: Progressive deformity of the lower limbs can be encountered in a long list of syndromic associations. The baseline tool in the management of such disorders is to approach to a definite diagnosis.

Methods: We describe a 4-year-old girl who presented with the clinical phenotype and genotype of congenital erythrokeratoderma, keratosis, and sensorineural hearing loss (keratitis-ichthyosis-deafness syndrome) (KID syndrome). She manifested progressive contractures of the knees associated with talipes equinovarus of the feet. The latter deformities were the main reasons behind her severe retardation in acquiring the normal locomotor functions.
Results: The analysis revealed mutations in intron 1 of the GJB2 gene of C.32G>A (p.Gly11Glu) and c.35delG in the compound heterozygous state. The presence in the genotype of the "dominant" mutation c.32G>A (p.Glu11Glu) was compatible with the clinical phenotype of KID syndrome.

Conclusion: Surgical interventions through the extension of the hamstring tendons have been performed successfully via the application of an external distraction apparatus, namely, Volkov-Oganesyan. The latter procedures resulted in total release of her awkward knee contractures. Eventually, the child was able to regain the physiological alignment of her lower limbs and resume walking. To the best of our knowledge, the overall management of this child could be the first in the literature.

Case Rep Orthop 2020:8747392  (1551)

5.25 A detailed analysis of the association between urate deposition and erosions and osteophytes in gout

Objective: To characterize in detail the structural bone changes associated with the deposition of monosodium urate crystals in the first metatarsophalangeal (MTP1) joint in patients with tophaceous gout.

Methods: Twenty patients with tophaceous gout and involvement of the MTP1 joint received both dual-energy computed tomography (DECT) of the feet for the detection of tophi and high-resolution peripheral quantitative computed tomography (HR-pQCT) of the feet for the detection of bone erosions and osteophytes. Demographic and clinical data were collected. Tophi in DECT and erosions and osteophytes in HR-pQCT were overlayed to define their anatomical relation. In addition, the feet of 20 sex- and age-matched healthy controls were scanned to define the normal architecture of the MTP1 joint.

Results: Patients with gout had an increased number and extent of bone erosions and osteophytes compared with their healthy counterparts (erosions: 5 [0-17] vs 1 [1-2], 45.32 mm3 [7.26-550.32] vs 0.82 mm3 [0.15-21.8]; osteophytes: 10.5 [0-26] vs 1 [0-10], 4.93 mm [0.77-7.19 mm] vs 0.93 mm [0.05-7.61 mm]; all P < 0.001). The median tophi volume detected by DECT (0.12 mm3 [0.01-2.53]) was highly associated with the total volume of erosions (r = 0.597, P = 0.005).

Conclusion: Gout patients show increased changes in their bone microarchitecture. The extent of uric acid deposition is positively correlated with the extent of bone loss at the MTP1 joint, highlighting the strong cohesion of inflammation and erosive changes.

ACR Open Rheumatol 2:565-72  (1552)

5.26 Multidisciplinary patient care in X-linked hypophosphatemic rickets: one challenge, many perspectives

X-linked hypophosphatemic rickets (XLH, OMIM #307800) is a rare genetic metabolic disorder caused by dysregulation of fibroblast-like growth factor 23 (FGF23) leading to profound reduction in renal phosphate reabsorption. Impaired growth, severe rickets and complex skeletal deformities are direct consequences of hypophosphatemia representing major symptoms of XLH during childhood. In adults, secondary complications including early development of osteoarthritis substantially impair quality of life and cause significant clinical burden. With the global approval of the monoclonal FGF23 antibody burosumab, a targeted treatment with promising results in phase III studies is available for children with XLH. Nevertheless, complete phenotypic rescue is rarely achieved and remaining multisystemic symptoms demand multidisciplinary specialist care. Coordination of patient management within the major medical disciplines is a mainstay to optimize treatment and reduce disease burden. This review aims to depict different perspectives in XLH patient care in the setting of a multidisciplinary centre of expertise for rare bone diseases.

Wien Med Wochenschr 170:116-23  (1553)
6 Aktivitäten in Wissenschafts-Organisation und Administration

6.1 Kongressorganisation, Tagungsleitungen und Fortbildung

6.1.1 Fortbildung

Das gemeinsame Retreat von LBIO und MPIKG war ursprünglich für Oktober geplant, wird jedoch aufgrund von Covid-19 in einer verkürzten Form als Online-Konferenz stattfinden.

Judith Haschka absolvierte im März die OSTAK Ausbildung "Osteologe DVO" Grundkurs 3 in Göttingen und im September die OSTAK Ausbildung "Osteologe DVO" Virtueller Spezialkurs Knochen aktuell: Osteoporose, Knocheninfektion, Knochenmarködem.

6.1.2 Kongressorganisation

Roland Kocijan hatte den Vorsitz der Session „Praxisnahe osteologische Forschung aus erster Hand“ der Osteologie 2020, die am 5., 6. und 12. September virtuell abgehalten wurde.

6.2 Aktivitäten in nationalen und internationalen wissenschaftlichen Gesellschaften

Jochen Zwerina und Judith Haschka sind Vorstandsmitglieder der Österreichischen Gesellschaft für Knochen und Mineralstoffwechsel (ÖGKM), Roland Kocijan und Nadja Fratzl-Zelman sind Mitglieder des Wissenschaftlichen Beirates.

Jochen Zwerina ist außerdem Mitglied des Editorial Board des Journals für Kochen- und Mineralstoffwechsel.

Martina Behanova ist Mitglied der Österreichischen Gesellschaft für Public Health (ÖGPH) und der Slovak Public Health Association (SAVEZ) sowie des Editorial Board des International Journal of Public Health.

Markus Hartmann ist sowohl Mitglied der Österreichischen (ÖPG) als auch der Amerikanischen (APS) Physikalischen Gesellschaft.

Peter Fratzl ist korrespondierendes Mitglied der Österreichischen Akademie der Wissenschaften und Mitglied der Berlin-Brandenburgischen Akademie der Wissenschaften.

6.3 Tagungsaktivitäten

Die MitarbeiterInnen des Instituts nahmen an zahlreichen nationalen und internationalen wissenschaftlichen Tagungen teil, wie zum Beispiel: Annual European Calcified Tissue Society (ECTS) Congress, Annual Meeting of the American Society for Bone and Mineral Research (ASMBR), IOF-ESCEO und Osteologie – auch wenn diese Tagungen 2020 hauptsächlich virtuell abgehalten wurden.

Details unter 7.1.2 Abstracts (1564 – 1576) und 7.1.3 Invited talks (V588 – V595).

6.4 Lehrtätigkeit

Jochen Zwerina bietet die Vorlesungen „Osteoimmunologie: Experimentelle und klinische Aspekte“ (2 SSt) und „Vaskulitis“ (2 SSt) an der Universität Erlangen an und ist Vortragender bei der Hauptvorlesung „Rheumatologie“.

Markus Hartmann hielt im WS 2019/20 die Vorlesung „Werkstoffmodellierung auf atomarer Ebene“ (2 SSt) und zugehörige Übungen (2 SSt) an der Montanuniversität Leoben (gemeinsam mit David Holec, Montanuniversität Leoben).

Stéphane Blouin und Barbara Misof hielten im WS 2019/20 die Vorlesung „Bone Material Quality (2 SSt) und den Journal Club (Seminar) Orthopädie und Unfallchirurgie (1SSt) an der Medizinische
Universität Wien. Außerdem hielten sie im SS 2020 gemeinsam den Distant Learning Journal Club (Seminar) Orthopädie und Unfallchirurgie (1 SSt).

Im Rahmen der „Basic Lectures“ im PhD Programm „Regeneration of Bones and Joints“ hielt Nadja Fratzi-Zelman im WS 2019/2020 an der MUW zwei Journal Clubs (Seminare), einen für „Bones and Joint Regeneration“ (1 SSt) den anderen für „Orthopädie und Unfallchirurgie“ (1 SSt) sowie die Vorlesung „Osteoblasts and Osteocytes: Essentials and Methods“ (2 SSt). Im SS 2020 hielt sie einen distant learning Journal Club (Seminar) für „Bone and Joint Regeneration“ (1 SSt).

Judith Haschka hielt sowohl im WS 2019/2020 sowie im SS 2020 einen Journalclub (Seminar) für „Bones and Joint Regeneration“ (1 SSt).

Roland Kocijan betreute drei Diplomarbeiten: Dr. Stephanie Huber (Determination of Bone Architecture in Patients with Osteogenesis Imperfecta using the Computer Software TX Analyzer) an der MUW, Daniel Kraus (Assessment of Bone Microstructure in Patients with Crohn’s Disease - a cross sectional study using TX Analyzer) an der Karl Landsteiner Privatuniversität für Gesundheitswissenschaften und Amadea Medibach (Complementary & Alternative Medicine in Bone Diseases) an der Sigmund Freud Univeristät Wien.

Thomas Dechat betreute drei Masterstudentinnen (Studium Molekularbiologie) der Uni Wien (eine im Rahmen eines Wahlpraktikums und zwei im Rahmen ihrer Masterarbeit), einen Bachelorstudenten der FH Wiener Neustadt (Studium Biomedizinische Analytik), einen Masterstudenten der FH Biotech Campus Tulln (Studium Biotechnische Verfahren) und eine Masterstudentin im Rahmen eines FemTech-Praktikums.

Ruth Fritsch-Stork hielt im Sommersemester 2020 die Vorlesungen „Autoimmunität und Rheumatologie“ (0,5 SSt) und „Autoimmunität“ (0,5 SSt) sowie das Praktikum „Physikalische Untersuchung des Bewegungsapparates“ (0,5 SSt). Im Wintersemester 2020/2021 dasselbe Programm plus eine Anamnese Blockvorlesung und Klinische Fallbesprechung für den Masterstudiengang (insgesamt jeweils 3 SSt).

Ruth Fritsch-Stork hält den Lehrstuhl für Rheumatologie an der Sigmund Freud Privatuniversität Wien.

6.5 Reviewertätigkeit

Eleftherios Paschalis ist Mitglied der Editorial Boards von Calcified Tissue International und Bone und Associate Editor des Journal of Musculoskeletal and Neuronal Interactions.

Jochen Zwerina ist Mitglied des Editorial Boards von Journal für Knochen- und Mineralstoffwechsel.

Thomas Dechat ist Academic Collection Editor für die Topical Collection "Lamins and Laminopathies" bei Cells.

Stéphane Blouin ist Review Editor von Frontiers in Endocrinology.

Martina Behanova ist Mitglied des Editorial Board des International Journal of Public Health.

Roland Kocijan ist Mitglied des Editorial Board von Osteologie.

Darüber hinaus wurden von MitarbeiterInnen des LBIO Peer Reviews für Therapeutic Advances in Gastroenterology, Journal of Orthopaedic Surgery and Research, Calcified Tissue International, Acta Biomaterialia, Computational Materials Science, Osteoporosis International, Frontiers in Endocrinology, Endocrine Connections, Journal of Bone and Mineral Research, Bone, Therapeutic Advances in Endocrinology and Metabolism, International Journal of Molecular Science, SAGE Open Medical Case Reports, Journal of Biomedical Optics, PLoS One, Nature Scientific Reports, Biotechnology and Biological Sciences Research Council, Journal of Structural Biology, Applied Spectroscopy, Annals of the New York Academy of Sciences, Osteoarthritis and Cartilage,
European Cells & Materials, Journal of Spectroscopy, Journal of the Mechanical Behavior of Biomedical Materials, Journal of Biophotonics, Clinical Orthopaedics and Related Research, Crystal Growth & Design, ACS Biomaterials Science & Engineering, Journal of Raman Spectroscopy and Journal of Cellular Biochemistry.

Stéphane Blouin war Begutachter eines Projektes, das bei der Fondation de l’avenir (Frankreich) eingereicht wurde.

Eleftherios Paschalis begutachtete Projekte für National Institutes of Health (NIH), European Calcified Tissue Society (ECTS), NASA Innovative Advanced Concepts (NIAC), Australian Government National Health & Medical Research Council (NHMRC), Canada Council for the Arts, Killam Program, PSI Foundation, Canada and Amgen Bone Biology Fellowship.

Markus Hartmann fungierte als Gutachter für die Dissertation Computational Methods to Evaluate Gas Adsorption and Small Angle Scattering Data from Hierarchically Porous Materials angefertigt von DI Lukas Ludescher an der Montanuniversität Leoben.

6.6 Beteiligung an Projekten

- Untersuchung von klinischen, serologischen und genetischen Faktoren der IgG4 – Related Disease
    Medizinisch-Wissenschaftlicher Fonds des Bürgermeisters der Bundeshauptstadt Wien, 15069
    Projektleitung: Jochen Zwerina
    01.08.2015 – 14.01.2022

- The Influence of the Coordination of Cross-Links on the Mechanical Properties of Polymers
    FWF P27882-N27
    Projektleitung: Markus Hartmann
    01.09.2015 – 31.08.2020
    Das ursprünglich an der Universität Wien gestartete Projekt wurde mit dem Wechsel von M. Hartmann an das LBIO an dieses übertragen.

- Lamins in Bone
    FFG (FemTech) 875625
    Projektleitung: Thomas Dechat
    01.10.2019 – 31.03.2020

- Occult Bone Disease in Sudden Childhood Death: a Post-Mortem Study
    Kooperation mit Birmingham Women’s & Children’s NHS Foundation Trust
    Projektleitung: Wolfgang Högler
    Projektkoordination LBIO: Nadja Fratzl-Zelman
    01.01.2018 – 31.12.2022

- Bone material properties in transiliac bone biopsies in adult patients with X-linked Hypophosphatemia (XLH) before and after a 48-week treatment with Burosumab
    Kooperation mit Ultragenyx
    Projektkoordination LBIO: Nadja Fratzl-Zelman
    01.09.2019 - 31.08.2020

- Identification and Molecular Genetic Screening of Patients with Hypophosphatasia
    Klinische Studie an der 1. Medizinischen Abteilung im Hanusch-KH
    Projektleitung: Roland Kocijan
    01.08.2019 – 31.07.2022

6.7 Preise und Nominierungen

Ghazal Hedjazi erhielt den ECTS New Investigator Award für den Abstract:
Hedjazi G, Guterman-Ram G, Blouin S, Roschger P, Schemenz V, Wagermaier W, Fratzl P, Zwerina J, Fratzl-Zelman N, Marini JC 2020 Bone tissue in murine atypical type VI osteogenesis imperfecta has changes in vascular pores and matrix organization, plus classic OI hypermineralization.

6.8 Personelle Daten

6.8.1 Neueintritte

Die Studentin Johanna Besold, BSc, die bereits im Vorjahr ein Praktikum am LBIO absolvierte, wurde mit 1. Februar angestellt, um ihre Masterarbeit am LBIO zu erstellen.

Sylvia Weingartner aus der Lungenambulanz des Hanusch-KH wurde von März bis Mai als Vertretung in der Administration angestellt.

Mit Juli verstärkte Dr. Judith Haschka, eine Fachärztin für Innere Medizin, das klinische Team.

Ebenfalls ab Juli wurde Dr. Sonja Jäger aufgenommen, um vor allem an der Entwicklung einer TERS-Raman Methode mitzuarbeiten.

Im Oktober wurde der Student Jerome Fleger angestellt, der für die Befüllung des Biologika-Registers zuständig sein wird.

6.8.2 Austritte

Lejla Mastalic, BSc, beendete ihr FemTech Praktikum am LBIO Ende März.

Dr. Stamatia Rokidi verließ im September das Institut, um sich neu zu orientieren.

6.8.3 Diverses

David Hammermüller, ein Student der Biomedizinischen Analytik an der FH Wiener Neustadt, erstellte von Februar bis Juni seine Bachelorarbeit am LBIO.

Victoria Summerauer, eine Studentin der Biomedizin und Biotechnologie an der Veterinärmedizinischen Universität Wien absolvierte im September ein Praktikum am LBIO.

Die PhD Studentin Dr. Karol Apaza, die im Karl Donath Labor für Hartgewebs- und Biomaterialforschung an der Universitätszahnklinik Wien arbeitet, absolvierte im September ein zweiwöchiges Praxisseminar im LBIO in Meidling.

Claudia Hufnagel, BSc, eine Masterstudentin der Molekularen Biologie, arbeitete weiterhin im Rahmen eines Studiumabschluss-Stipendiums an ihrer Masterarbeit.

Peter Heiser, BSc, Matthias Mähr, BSc und Daniela Gabriel, BSc arbeiteten alle im Rahmen ihrer Masterstudien im LBIO.

PD Dr. Roland Kocijan wurde zum Assoziierten Professor für Klinische Osteologie an der Sigmund Freud Universität berufen.

Dr. Nadja Fratzl-Zelman wurde die Lehrbefugnis als Privatdozentin für Pathophysiologie an der medizinischen Universität Wien erteilt.
7 Publications and oral presentations

7.1 Publications of the year 2020

7.1.1 Original papers

1528. Rokidi S, Bravenboer N, Gamsjaeger S, Chavassieux P, Zwerina J, Paschalis E, Papapoulos S, Appelman-Dijkstra N 2020 Impact microindentation measurements correlate with cortical bone material properties measured by Fourier transform infrared imaging in humans. Bone 137:115437 IF 4.147

1529. van den Hoogen LL, van der Heijden EHM, Hillen MR, Mertens JS, Fritsch-Stork RDE, Radstake TRDJ, van Roon JAG 2020 Galectin-9 reflects the interferon signature and correlates with disease activity in systemic autoimmune diseases. Response to: 'Biomarkers: to be or not to be' by Yavuz and Rönnblom. Ann Rheum Dis 79(1):e9 IF 16.102

1530. Roschger A, Wagermaier W, Gamsjaeger S, Hassler N, Schmidt I, Blouin S, Berzlanovich A, Gruber GM, Weinkamer R, Roschger P, Paschalis EP, Klaushofer K, Fratzl P 2020 Newly formed and remodeled human bone exhibits differences in the mineralization process. Acta Biomater 104:221-30 IF 7.242

1531. Kang H, Jha S, Ivovic A, Fratzl-Zelman N, Deng Z, Mitrea A, Cabral WA, Hanson EP, Lange E, Cowen EW, Katz J, Roschger P, Klaushofer K, Dale RK, Siegel RM, Bhattacharyya T, Marini JC 2020 Somatic SMAD3-activating mutations cause melorheostosis by up-regulating the TGF-β/SMAD pathway. J Exp Med 217(5) pii: e20191499 IF 11.743

1532. Topitz D, Schwaiger E, Frommlet F, Werzowa J, Hecking M 2020 Cardiovascular events associate with diabetes status rather than with early basal insulin treatment for the prevention of post-transplantation diabetes mellitus. Nephrol Dial Transplant 35:544-6 IF 4.531

1533. Al Kaisssi A, Kenis V, Jemaa LB, Sassi H, Shboul M, Grill F, Ganger R, Kircher SG 2020 Skeletal phenotype/genotype in progressive pseudorheumatoid chondrodysplasia. Clin Rheumatol 39:553-60 IF 2.394

1534. Kuemmerli C, Habrina D, Puchner S, Laminger F, Werzowa J, Roka S 2020 Primary external stenting of an autogenous brachial-basilic upper arm transposition. Ann Vasc Surg 65:288.e1-288.e4 IF 1.125

1535. Rokidi S, Bravenboer N, Gamsjaeger S, Misof B, Blouin S, Chavassieux P, Klaushofer K, Paschalis E, Papapoulos S, Appelman-Dijkstra N 2020 Impact microindentation assesses subperiosteal bone material properties in humans. Bone 131:115110 IF 4.147

1536. Shabbir H, Hartmann MA 2020 A high coordination of cross-links in fiber bundles prevents local strain concentrations. Comput Mater Sci 184:109849 IF 2.863

1537. Bouchoucha S, Chikhaoui A, Najjar D, Dallali H, Khammessi M, Abdelhak S, Nessibe N, Shboul M, Kircher SG, Al Kaisssi A, Yacoub-Youssef H 2020 Clinical and genetic heterogeneity in six Tunisian families with horizontal gaze palsy with progressive scoliosis: a retrospective study of 13 cases. Front Pediatr 8:172
1538. Turyanskaya A, Rauwolf M, Pichler V, Simon R, Burghammer M, Fox OJL, Sawhney K, Hofstaetter JG, Roschger A, Roschger P, Wobrauschek P, Streli C 2020 Detection and imaging of gadolinium accumulation in human bone tissue by micro- and submicro-XRF. Sci Rep 10:6301
IF 3.998

1539. van Tol AF, Roschger A, Repp F, Chen J, Roschger P, Berzlanovich A, Gruber GM, Fratzl P, Weinkamer R 2020 Network architecture strongly influences the fluid flow pattern through the lacunocanalicular network in human osteons. Biomech Model Mechanobiol 19:823-40
IF 2.527

1540. Cabral WA, Fratzl-Zelman N, Weis MA, Perosky JE, Alimasa A, Harris R, Kang H, Makareeva E, Barnes A, Roschger P, Leikin S, Klaushofer K, Forlino A, Backlund P, Eyre D, Kozloff KM, Marini JC 2020 Substitution of murine type I collagen A1 3-hydroxylation site alters matrix structure but does not recapitulate osteogenesis imperfecta bone dysplasia. Matrix Biol 90:20-39
IF 8.572

1541. Stamm T, Ritschl V, Platzer A, Omara M, Mosor E, Reichardt B, Schmitl L, Behanova M, Bekes K 2020 Regional and gender differences in population-based oral health insurance data. Clin Oral Investig 24:2331-9
IF 2.812

1542. Fratzl-Zelman N, Gamsjaeger S, Blouin S, Kocijan R, Plasenzotti P, Rokidi S, Nawrot-Wawrzyniak K, Roetzer K, Uyanik G, Haeusler G, Shane E, Cohen A, Klaushofer K, Paschalis EP, Roschger P, Fratzl P, Zwerina J, Zwettler E 2020 Alterations of bone material properties in adult patients with X-linked hypophosphatemia (XLH). J Struct Biol 211:107556
IF 3.071

1543. Weidner H, Baschant U, Lademann F, Ledesma Colunga MG, Balaian E, Hofbauer C, Misof BM, Roschger P, Blouin S, Richards WG, Platzbecker U, Hofbauer LC, Rauner M 2020 Increased FGF-23 levels are linked to ineffective erythropoiesis and impaired bone mineralization in myelodysplastic syndromes. JCI Insight 5:137062
IF 6.014

1544. Bartko J, Reichardt B, Kocijan R, Klaushofer K, Zwerina J, Behanova M 2020 Inflammatory bowel disease: A nationwide study of hip fracture and mortality risk after hip fracture. J Crohns Colitis 14:1256-63
IF 8.658

1545. Schemenz V, Gjardy A, Chamasemani FF, Roschger A, Roschger P, Zaslansky P, Helfen L, Burghammer M, Fratzl P, Weinkamer R, Brunner R, Willie BM, Wagermaier W 2020 Heterogeneity of the osteocyte lacuno-canalicular network architecture and material characteristics across different tissue types in healing bone. J Struct Biol 212:107616
IF 3.071

1546. Misof BM, Blouin S, Hofstaetter JG, Roschger P, Zwerina J, Erben RG 2020 No role of osteocytic osteolysis in the development and recovery of the bone phenotype induced by severe secondary hyperparathyroidism in vitamin D receptor deficient mice. Int J Mol Sci 21:E7989
IF 4.556

1547. Rokidi S, Andrade VFC, Borba V, Shane E, Cohen A, Zwerina J, Paschalis EP, Moreira CA 2020 Bone tissue material composition is compromised in premenopausal women with type 2 diabetes. Bone 141:115634
1548. Haschka J, Kraus DA, Behanova M, Huber S, Bartko J, Schanda JE, Meier P, Bahrami A, Zwerina J, Kocijan R 2020 Fractal-based analysis of bone microstructure in Crohn’s disease: a pilot study. J Clin Med 9:4116
IF 3.303

1549. Stradner MH, Dejaco C, Zwerina J, Fritsch-Stork RD 2020 Rheumatic musculoskeletal diseases and COVID-19 a review of the first 6 months of the pandemic. Front Med (Lausanne) 7:562142
IF 3.421

1550. Misof BM, Roschger P, Zhou H, Nieves JW, Bostrom M, Cosman F, Lindsay R, Klausenhofer K, Dempster DW 2020 No evidence for alteration in early secondary mineralization by either alendronate, teriparatide or combination of both in transiliac bone biopsy samples from postmenopausal osteoporotic patients. Bone Reports 12:100253. doi: 10.1016/j.bonr.2020

1551. Kozhevnikov O, Kralina S, Yurasova Y, Kenis V, Kircher SG, Al Kaissi A 2020 Progressive deformity of the lower limbs in a patient with KID (Keratitis-Ichthyosis-Deafness) syndrome. Case Rep Orthop 2020:8747392

1552. Pecherstorfer C, Simon D, Unbehand S, Ellmann H, Englbrecht M, Hartmann F, Figueiredo C, Hueber A, Haschka J, Kocijan R, Kleyer A, Schett G, Rech J, Bayat S 2020 A detailed analysis of the association between urate deposition and erosions and osteophytes in gout. ACR Open Rheumatol 2:565-72

1553. Raimann A, Mindler GT, Kocijan R, Bekes K, Zwerina J, Haeusler G, Ganger R 2020 Multidisciplinary patient care in X-linked hypophosphatemic rickets: one challenge, many perspectives. Wien Med Wochenschr 70:116-23

1554. Kocijan R 2020 Neue Biomarker im Management der Osteoporose. Jatros Orthopädie & Traumatologie Rheumatologie 1/2020:6

1555. Zwerina J, Führlinger S 2020 LBIO – Forschung im Zentrum für musculoskelettale Erkrankungen. J Miner Stoffwechs Muskuloskelet Erkrank 27:90-2

1556. Paschalis E 2020 Knochenqualität und Schwingungsspektroskopie bei Fragilitätsfrakturen. J Miner Stoffwechs Muskuloskelet Erkrank 27:93-7

1557. Misof BM, Fratzl-Zelman N, Blouin S, Hartmann MA 2020 Knochengewebe und -material im gesunden Menschen und bei Krankheit. J Miner Stoffwechs Muskuloskelet Erkrank 27:98-101

1558. Dechat T 2020 Von der Zelle zum Mineral. J Miner Stoffwechs Muskuloskelet Erkrank 27:102-3

1559. Kocijan R, Kritsch D, Feurstein J, Biber N, Brehm A, Distel A, Zwerina J 2020 Die Forschungsgruppe klinische Osteologie – der Link zwischen Klinik und LBIO. J Miner Stoffwechs Muskuloskelet Erkrank 27:104-7

1560. Behanova M 2020 Epidemiologische Daten zu osteoporotischen Frakturen in Österreich. J Miner Stoffwechs Muskuloskelet Erkrank 27:108-10

1561. Rötzer K, Uyanik G 2020 Genetische Analysen in der Osteologie. J Miner Stoffwechs Muskuloskelet Erkrank 27:111-5

1562. Resch H, Zendeli A, Kocijan R 2020 Rheumatoide Arthritis aus der Sicht der Osteologie. Österreichische Ärztezeitung 13/14a, 15. Juli
Publications in print

Müller MM, Schwaiger E, Kurnikowski A, Haidinger M, Ristl R, Tura A, Pacini G, Werzowa J, Hecking M 2021 Glucose metabolism after kidney transplantation: Insulin release and sensitivity with tacrolimus- versus belatacept-based immunosuppression. Am J Kidney Dis 77:462-4 IF 6.618

Grillari J, Mäkitie RE, Kocijan R, Haschka J, Carro Vazquez D, Semmelrock E, Hackl M 2021 Circulating miRNAs in bone health and disease. Bone 145:115787 IF 4.147

Buch S, Sharma A, Ryan E, Datz C, Griffiths WJH, Way M, Buckley TWM, Ryan JD, Stewart S, Wright C, Dongiovanni P, Fracanzani A, Zwerina J, Merle U, Weiss KH, Aigner E, Krones E, Dejaco C, Fischer J, Berg T, Valenti L, Zoller H, McQuillin A, Hampe J, Stickel F, Morgan MY 2021 Variants in PCSK7, PNPLA3 and TM6SF2 are risk factors for the development of cirrhosis in hereditary haemochromatosis. Aliment Pharmacol Ther 53:830-43 IF 7.515

Wienke J, Mertens JS, Garcia S, Lim J, Wijngaarde CA, Yeo JG, Meyer A, van den Hoogen LL, Tekstra J, Hoogendijk JE, Otten HG, Fritsch-Stork RDE, de Jager W, Seyger MMB, Thurlings RM, de Jong EMGJ, van der Kooy AJ, van der Poel WL; Dutch Juvenile Myositis Consortium, Arkachaisri T, Radstake TRDJ, van Royen-Kerkhof A, van Wijk F 2021 Biomarker profiles of endothelial activation and dysfunction in rare systemic autoimmune diseases: implications for cardiovascular risk. Rheumatology (Oxford) 60:785-801 IF 5.606

Kocijan R, Behanova M, Reichardt B, Haschka J, Kocijan A, Zwerina J 2021 Poor adherence to parenteral osteoporosis therapies during COVID-19 pandemic. Arch Osteoporos 16:46 IF 2.017

Fratzl-Zelman N, Wesseling-Perry K, Mäkitie RE, Blouin S, Hartmann MA, Zwerina J, Välimäki VV, Laine CM, Välimäki MJ, Pereira RC, Mäkitie O 2021 Bone material properties and response to teriparatide in osteoporosis due to WNT1 and PLS3 mutations. Bone 146:115900 IF 4.147

Gamsjaeger S, Fratzl P, Paschalis EP 2021 Interplay between mineral crystallinity and mineral accumulation in health and postmenopausal osteoporosis. Acta Biomater 124:374-81 IF 7.242

Paschalis EP, Dempster DW, Gamsjaeger S, Rokidi S, Hassler N, Brozek W, Chan-Diehl FW, Klaushofer K, Taylor KA 2021 Mineral and organic matrix composition at bone forming surfaces in postmenopausal women with osteoporosis treated with either teriparatide or zoledronic acid. Bone 145:115848 IF 4.147

Kirchler C, Husar-Memmer E, Rappersberger K, Thaler K, Fritsch-Stork R 2021 Type I Interferon as cardiovascular risk factor in systemic and cutaneous lupus erythematosus: A systematic review. Autoimmun Rev 17:102794 IF 7.767

Amuno S, Shekh K, Kodzhahinchiev V, Niyogi S, Al Kaissi A 2021 Skeletal pathology and bone mineral density changes in wild muskrats (Ondatra zibethicus) and red squirrels (Tamiasciurus
hudsonicus) inhabiting arsenic polluted areas of Yellowknife, Northwest Territories (Canada): A radiographic densitometry study. Ecotoxicol Environ Saf 208:111721
IF 4.872

Kocijan R, Haschka J, Feurstein J, Zwerina J 2021 New therapeutic options for bone diseases. Wien Med Wochenschr 171:120-5

Haeusler G, Ganger R, Kocijan R, Fratzl-Zelman N 2021 The Vienna Bone and Growth Center care and research in the field of rare diseases. Wien Med Wochenschr 171:85

Mähr M, Blouin S, Misof BM, Paschalis EP, Hartmann MA, Zwerina J, Fratzl-Zelman N 2021 Bone properties in osteogenesis imperfecta: what can we learn from a bone biopsy beyond histology? Wien Med Wochenschr 171:111-9

Kronscläger M, Ruiß M, Dechat T, Findl O 2020 Single high-dose peroral caffeine intake inhibits ultraviolet radiation-induced apoptosis in human lens epithelial cells in vitro. Acta Ophthalmol Oct 30 doi: 10.1111/aos.14641. Online ahead of print
IF 3.362

Al Kaissi A, Ryabykh S, Ochirova P, Bouchoucha S, Kenis V, Shboul M, Ganger R, Grill F, Kircher SG 2020 Arthrogryposis is a descriptive term, not a specific disease entity: Escobar syndrome is an example. Minerva Pediatr Jun 12. doi: 10.23736/S0026-4946.20.05796-5. Online ahead of print
IF 0.863

Al Kaissi A, Ryabykh S, Ochirova P, Kareem AA, Kenis V, Ganger R, Grill F, Kircher GS 2020 The articular and the craniocervical abnormalities are of confusing age of onset in patients with Maroteaux-Lamy disease (MPS VI). Minerva Pediatr Aug 4. doi: 10.23736/S0026-4946.20.05645-5. Online ahead of print
IF 0.863

Hadjizimuratovic B, Mittelbach A, Bahrami A, Zwerina J, Kocijan R 2020 Confluent abscesses in autochthonous back muscles after spinal injections: A case report and narrative review of the literature on low back pain and spinal injections. Wien Med Wochenschr Aug 3. doi: 10.1007/s10354-020-00773-y. Online ahead of print
IF 1.120

Groot N, Kardolus A, Bijl M, Dolhain R, Teng O, Zirkzee E, de Leeuw K, Fritsch-Stork R, Burdorf L, Bultink I, Kamphuis S 2020 Effects of childhood-onset SLE on academic achievements and employment in adult life. J Rheumatol Aug 1;jrheum.191004. doi: 10.3899/jrheum.191004. Online ahead of print
IF 3.634

Vaglio A, Maritati F, Zwerina J 2020 Response to: 'Eosinophilic granulomatosis with polyangiitis can manifest lacrimal and salivary glands swelling by granulomatous inflammation: a potential mimicker of IgG4-related disease' by Akiyama et al. Ann Rheum Dis Jun 26;annrheumdis-2020-218174. doi: 10.1136/annrheumdis-2020-218174. Online ahead of print
IF 16.102

Weigl M, Kocijan R, Ferguson J, Leinfellner G, Heimel P, Feichtinger X, Pietschmann P, Grillari J, Zwerina J, Redl H, Hackl M 2021 Longitudinal changes of circulating miRNAs during bisphosphonate and teriparatide treatment in an animal model of postmenopausal osteoporosis. J Bone Miner Res Feb 17. doi: 10.1002/jbmr.4276. Online ahead of print
IF 5.854

Schanda JE, Huber S, Behanova M, Haschka J, Kraus DA, Meier P, Bahrami A, Zandieh S, Muschitz C, Resch H, Mähr M, Rötzer K, Uyanik G, Zwerina J, Kocijan R 2021 Analysis of bone architecture using fractal-based TX-Analyzer™ in adult patients with osteogenesis imperfecta. Bone Mar 13;147:115915. doi: 10.1016/j.bone.2021.115915. Online ahead of print.
7.1.2 Abstracts

1564. Behanova M 2020 The association between oral antidiabetic medication and hip fracture and post-hip fracture mortality. A nationwide study from Austria. IOF-ESCEO, August 20 - 23, Virtual Event, abstract P1163 and poster presentation

1565. Paschalis EP, Gamsjaeger S, Rokidi S, Dempster D, Zhou H, Shane E, Cohen A, Bilezikian JP, Rubin M, Moreira C, Andreade V, Papapoulos S, Eriksen EF, Klaushofer K 2020 Glycosaminoglycan and Pyridinoline content at forming trabecular surfaces are strongly associated with fracture incidence independent of clinical diagnosis and estimated fracture risk based on BMD. ASBMR, September 11 – 15, Virtual Event, abstract P605 and poster presentation

1566. Gamsjaeger S, Klaushofer K, Paschalis EP 2020 The bone quality index of mineral maturity / crystallinity at forming trabecular surfaces and its potential role in the bone mineral loss evident in postmenopausal osteoporosis. ASBMR, September 11 – 15, Virtual Event, abstract P610 and poster presentation

1567. Zarei A, Fratzl-Zelman N, Do AD, Glassford M, Hannibal M, Esposito PW, Lindstrom K, Zwerina J, Knue M, Talvacchio S, Marini JC 2020 Bone tissue and osteoblasts from X-linked type XVIII OI with defects in regulated membrane proteolysis have distinct features. ASBMR, September 11 – 15, Virtual Event, abstract P809 and poster presentation

1568. Guterman-Ram G, Hedjazi G, Stephan C, Blouin S, Schemenz V, Wagermaier W, Zwerina J, Fratzl P, Kozloff K, Fratzl-Zelman N, Marini JC 2020 New Ifitm5 S42L mouse model for atypical type VI Osteogenesis Imperfecta recapitulates patient phenotype. ASBMR, September 11 – 15, Virtual Event, abstract P805 and poster presentation

1569. Fratzl-Zelman N, Wesseling-Perry K, Mäkitie RE, Blouin S, Hartmann MA, Zwerina J, Välimäki VV, Iaine CM, Välimäki MJ, Pereira RC, Mäkitie O 2020 Bone matrix mineralization increases with age and remains elevated after teriparatide treatment in WNT1 and PLS3 osteoporosis: A transiliac bone biopsy study in children and adults. ASBMR, September 11 – 15, Virtual Event, abstract and oral presentation

1570. Blouin S, Misof BM, Hartmann MA, Berzlanovich A, Gruber GM, Lueger S, Messmer P, Keplinger P, Roschger P 2020 Osteocyte lacunae characteristics in iliac crest bone samples of aged adults. ECTS, October 20 – 24, Marseille, France, abstract P128 and poster presentation

1571. Rokidi S, Bravenboer N, Gamsjaeger S, Chavassieux P, Zwerina J, Paschalis E, Papapoulos S, Appelman-Dijkstra N 2020 Impact microindentation assesses cortical bone material properties in humans. ECTS, October 20 – 24, Marseille, France, abstract P046 and poster presentation

1572. Fratzl-Zelman N, Wesseling-Perry K, Mäkitie RE, Roschger P, Zwerina J, Välimäki V, Laine CM, Välimäki MJ, Pereira RC, Mäkitie O 2020 Bone matrix mineralization increases with age and remains elevated after Teriparatide treatment in WNT1 or PLS3 mutation-related low-turnover osteoporosis: A transiliac bone biopsy stud. ECTS, October 22 – 24, Digital, abstract COP18 and oral presentation

1573. Hedjazi G, Guterman-Ram G, Blouin S, Roschger P, Schemenz V, Wagermaier W, Fratzl P, Zwerina J, Fratzl-Zelman N, Marini JC 2020 Bone tissue in murine atypical type VI
osteogenesis imperfecta has changes in vascular pores and matrix organization, plus classic OI hypermineralization. ECTS, October 22 – 24, Digital, abstract PLO15 and oral presentation

1574. Guterman-Ram G, Hedjazi G, Stephan C, Blouin S, Roschger P, Klaushofer K, Zwerina J, Kozloff KM, Fratzl-Zelman N, Marini JC 2020 New Ifitm5 S42L mouse model for atypical type VI OI connects types V and VI Osteogenesis Imperfecta. ECTS, October 22 – 24, Digital, abstract COP36 and oral presentation

1575. Roschger A, van Tol AF, Thelen M, Seliger A, Yang H, Chan WL, Thiele T, Roschger P, Duda GN, Zaslansky P, Kornak U, Willie BM, Weinkamer R 2020 The effect of a deteriorated architecture of the lacunocanalicular network on the organization and mineralization of the extracellular matrix. ECTS, October 22 – 24, Digital, abstract P048 and poster presentation

1576. Thaler R, Khani F, Denbeigh JM, Sturmlechner I, Zhou X, Pichurin O, Dudakovic A, Zhong J, Lee JH, Natarajan R, Kalajzic I, Deyle DR, Paschalis EP, Misof B, Ordog T, van Wijnen AJ 2020 Vitamin C epigenetically controls osteogenesis and bone mineralization. ECTS, October 22 – 24, Digital, abstract P092 and poster presentation

7.1.3 Invited talks

V588 Behanova M 2020 Evidenz über Mortalität und Refrakturrisiko bei antiresorptiver Therapie von Hüffrakturen in Österreich. Osteologie 2020 (DVO-Kongress), March 12 – 14, Salzburg, Austria, held online September 5, 6 & 12

V589 Kocijan R 2020 Seltene Knochenerkrankungen in der osteologischen Ambulanz. Osteologie 2020 (DVO-Kongress), March 12 – 14, Salzburg, Austria, held online September 5, 6 & 12

V590 Feurstein J 2020 Identifizierung und molekulargenetisches Screening von Patienten mit Hypophosphatasie. Osteologie 2020 (DVO-Kongress), March 12 – 14, Salzburg, Austria, held online September 5, 6 & 12

V591 Haschka J 2020 The osteologic challenge in axial spondyloarthritis. 23. Kongress der tschechischen und slowakischen Gesellschaft für Osteologie, 17 September, cancelled

V592 Kocijan R 2020 Rare bone diseases in the outpatient clinic. 23. Kongress der tschechischen und slowakischen Gesellschaft für Osteologie, 17 September, cancelled

V593 Haschka J 2020 Modern Imaging in Ankylosing Spondylitis. ECTS@HOME Working Group on Rheumatic Diseases, ECTS, 22 – 24 October, cancelled

V594 Haschka J 2020 Junge Patientin mit multiplier Spontanfrakturen – juvenile idiopathische Osteoporose? Österreichisches Osteoporoseforum der ÖGKM, 15. – 17. Oktober, St. Wolfgang, Austria

V595 Zwerina J 2020 EGPA – traditionelle und moderne Therapie. ÖGR Jahrestagung, 26. – 28. November, online Kongress,
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