iBiomat: Imaging Biological and Soft Matter

Report of Contributions

Contribution ID: **1** Type: **oral**

Imaging intra-breath cyclic changes in pulmonary blood volume: effect of ventilator settings

Rationale: Despite the importance of dynamic changes in the regional distributions of gas and blood during the breathing cycle for lung function in the mechanically ventilated patient, no quantitative data on such cyclic changes is currently available.

Methods: We used a novel gated synchrotron CT-imaging with K-edge subtraction technique to quantitatively image regional lung gas (Vg), tissue density and blood volume (Vb) in 6 anaesthetized, paralyzed and mechanically ventilated rabbits with normal lungs. Images were repeatedly collected during ventilation and steady-state inhalation of 50% Xe, or iodine infusion. Data were acquired in a dependent and non-dependent image level, at an end-expiratory pressure of 0 (ZEEP) and 9 cmH2O (PEEP), and a VT of 6 (VT1) or 9 ml/kg (VT2) at an I:E ratio of 0.5 or 1.7 by applying an end-inspiratory pause (EIP).

Results: A video showing dynamic decreases in Vb during inspiration is presented. Vb decreased with PEEP (p=0.006; p=0.036 vs. VT1-ZEEP and VT2-ZEEP, respectively) and showed larger oscillations in the dependent image level , while a 45% increase in VT did not have a significant effect. End-inspiratory Vb minima were reduced by an EIP (p=0.042, p=0.006 in non-dependent and dependent levels, respectively). Normalized regional gas to blood volume ratio increased upon inspiration.

Conclusions: Our data demonstrate for the first time, within-tidal cyclic variations in regional pulmonary blood volume. The quantitative matching of regional gas and blood volume improved upon inspiration under ZEEP, suggesting a possible link between cyclic changes in regional gas and blood distribution and previously-described PaO2 oscillations, under controlled ventilation.

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Track Classification: Medicine, pre-clinical studies

Contribution ID: **2** Type: **oral**

BioXRM: Microtomography of embryos, tissues, cells, and molecules

3D imaging has become a familiar player in developmental and comparative biology, offering ever more realistic views of the native structures of organisms and materials. For morphology-based studies of development and evolution, X-ray microtomography (microCT) is the most suitable method to visualize 3D micromorphology in whole embryos and other intact samples. Contrast-enhanced microCT can produce images with microscopic detail and high contrast among various non-mineralized tissues –histology without sectioning.

The accuracy of any analysis based on 3D images depends first on the quality of the sample, and second on the fidelity of the imaging process. Thus we are refining our methods for fixation, tissue stabilization, and contrast staining of whole samples for microCT imaging. The images generated by microCT are size-calibrated and suitable for quantitative 3D analyses of developmental morphology. We are currently establishing datasets and workflows to measure and model intraspecific variation, asymmetry, and growth during development.

Ongoing work on dual-energy (spectrally-sensitive, "two-color") microCT has demonstrated simultaneous imaging of different tissues or materials, e.g. skeletal hydroxyapatite amid counterstained soft tissues, and selective labeling and imaging of melanocytes (pigment cells) in whole animals. We are extending this work to 3D localization and quantification of molecular probes in counterstained whole embryos. Further collaborative work is aimed at imaging cultured and regenerating tissues within artificial scaffolds and incorporating novel biomarkers such as nanoparticles.

Digital volume images are inherently shareable, and we have recently published the first new (millipede) species description to be based partly on its cybertype –a set of virtual specimens made from microCT images of the physical type material for the species. We have also made a developmental atlas of the squid Euprymna scolopes available online, and we are currently creating a high-resolution 3D atlas of Sprague-Dawley rat development as a basis for analyzing mutations, experimental perturbations, and for quantitative comparisons with other species.

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Track Classification: Zoology

Contribution ID: **4** Type: **oral**

Multiscale imaging of mammalian teeth

Teeth are three-dimensional consisting of highly mineralized tissues. Both the formation of tooth shape during development and the structural details of mature dental tissues are active topics of research. We have used phase-contrast holotomography synchrotron imaging to study mineralized dental ultrastructure with voxel resolutions down to 25 nanometres. The resulting details uncovered provide novel insights into the structural and developmental bases of mineralized tissues. The 3D models obtained from the synchrotron data help to direct laboratory investigations on developing teeth using confocal microscopy. Conversely, developmental biology data combined with X-ray imaging on gene expression patterns can be used to direct the use of synchrotron imaging in the study of developing organs.

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Track Classification: Developmental biology & Palaeontology

Contribution ID: **6** Type: **oral**

Synchrotron tomography reveals life history and physiology of the earliest mammals

Palaeontological applications of synchrotron techniques such as tomography and spectroscopy have offered a new dimension to palaeobiological studies, revealing what extinct animals ate, the long believed unknowable colour of ancient animals from insects to dinosaurs, and the life histories of animals from the earliest tetrapods to the first humans. Despite recent discoveries and analyses revolutionising our knowledge of Mesozoic mammals (the early mammals living alongside dinosaurs for the first 2/3 of mammalian evolutionary history), little is known about their physiology or life history. Were they warm-blooded, how long did they live, and how active were they? To address this we used synchrotron tomography to measure the lifespan of fossil mammals using growth rings in tooth root cementum, analogous to tree growth rings. Maximum lifespan is highly correlated with many aspects of physiology such as maximum growth and basal metabolic rates.

Traditional cementum growth ring analysis requires destructive thin sectioning of teeth. Since large sample sizes are needed for population maximum lifespan estimates, this is not allowed in valuable fossil material. Tomography allows non-destructive imaging of whole root volumes instead of single slices, improving understanding of cementum ring formation and increasing percentages of successfully counted specimens. Sub-micron scale phase contrast synchrotron tomography is required for its high sensitivity and signal:noise ratios, due to the small size of growth rings and low density-differences between dark/light rings.

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Track Classification: Developmental biology & Palaeontology

Contribution ID: **8** Type: **oral**

Using Artificial Intelligence and Big Data to Accelerate and Improve Medical Imaging

The diagnosis and treatment of lung cancer has been drastically improved by new imaging methods which generate large number of images where single spots can drastically influence the diagnosis and treatment. For physicians this means a long time must be spent carefully reading images. 4Quant (an ETH Spinoff) together with the University Hospital Basel have demonstrated the potential to radically reduce the reading time without sacrificing quality by using Big Data and Deep Learning approaches. We present the work we have done towards a computer aided staging of Non-Small Cell Lung Cancer (NSCLC) on a group of over 2000 patients.

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Track Classification: Sample preparation and Image analysis

Contribution ID: **9** Type: **oral**

Small-Angle X-ray Scattering (SAXS): From Solutions to Imaging.

Small-angle X-ray scattering (SAXS) probes structures in the size-range of one to several hundred nanometers. Raster scanning a sample through a focused X-ray beam allows to record SAXS pattern spatially resolved. The information extracted from each scattering pattern can be used to construct images with different contrasts. Bragg peaks arising from characteristic distances in the sample, such as the repetition distance of myelin sheets in brain, provide a selective contrast for their density distribution. Besides density also orientation of ultrastructure can be retrieved from the SAXS pattern, for example the orientation of collagen fibrils in bone. The technique is mainly advantageous for hierarchical samples, since information about nanostructures can be obtained in macroscopic samples of several millimeter of even centimeters. The method can also be combined with computed tomography to study the inside of three-dimensional samples.

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Track Classification: Spectroscopy, soft X-rays and scattering imaging

Contribution ID: **10** Type: **oral**

Live animal imaging & radiation therapy methods at the synchrotron

Synchrotrons provide users with unique imagining and therapeutic methods. They provide very high flux, with flat energy spectrum and quasi-coherent beam. At the same time synchrotrons are very different from clinical machines: beam is parallel and has limited size, its position is fixed and sample, together with the required live support and diagnostic equipment, has to be rotated or scanned across the beam. Scan times maybe much longer due to higher resolution and the vital signs triggering requirements. They don't normally provide a turn-key operation.

Synchrotron have proven however to be powerful tools for visualization of soft tissue as well as for functional imaging and novel therapy methods.

Phase-sensitive imaging methods exploit differences in the refractive index of tissue to enhance the contrast and imaging can be done at higher energies. They offer improved contrast sensitivity, especially when imaging respiratory system, tissue engineering samples (scaffolds) and other low contrast tissue samples such as cartilage. The high energy X-rays ensure lower radiation dose for the animals, and the high brightness reduces total time required for experiment, which is extremely important for live animal experiments and longitudinal studies. Monochromatic light provides unique options for techniques such as K-Edge Subtraction, used to visualize bone growth and development, and imaging is not affected by the beam hardening artifacts.

There are two main programs that use X-rays for cancer treatment trials: Synchrotron Stereotactic Radiation Therapy (SSRT), which uses the finely tuned monochromatic beam for localized dose delivery enhancement within the tumor mass, and micro-beam (MRT) radiation therapy, based on the spatial fractionation of high dose-rate, low energy X-rays, which promise significant advantages over conventional clinical techniques for some diseases if successfully transferred to clinical practice.

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Track Classification: Small animal imaging and therapy

Contribution ID: **11** Type: **not specified**

Coherent nano-imaging

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