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ABSTRACT

X-ray tomography, a non-destructive technique, provides three-dimensional data with a spatial resolution down to the nanometer scale. Therefore, academia and industry as well as patients equally benefit from improvements in preparative work, data acquisition and analysis. Since 1997, the conference on *Developments in X-ray Tomography* has set the benchmark in the dissemination of knowledge related to the dedicated instrumentation, the developments in software for reconstruction, the artefact removal and the data analysis as well as to the wide range of applications. The paper summarizes some aspects analyzing the previous volumes and the contributions in the current volume.

Keywords: Hard X rays, computed tomography, phase tomography, microtomography, nano-tomography, synchrotron radiation, non-destructive three-dimensional characterization, multi-modal imaging

1. INTRODUCTION

X-ray tomography belongs to the non-destructive techniques for the three-dimensional characterization of a wide variety of objects. It provides the three-dimensional data with an isotropic spatial resolution down to the nanometer scale. Therefore, the technique plays a vital role in academia, industry, and clinics. The applications range from quality control in watch industry via unique object visualization in palaeontology to the characterization of the human hard and soft tissues in health and disease. This broad palette of applications in many fields (mechanical engineering, museum sciences, biology and medicine) requires further technical improvements such as (i) the highly efficient detectors with an increasing number of pixels, dynamic range and single photon counting capability, (ii) the detection beyond the conventional attenuation contrast, and (iii) the implementation of X-ray optics to reach a spatial resolution of 10 nm and below.

A key challenge is to quantitatively evaluate the datasets with sizes in the GB- and even TB-range in an automatic fashion. Dedicated features have to be identified, segmented, and measured concerning their shape and size. The rigid and non-rigid registration algorithms support the quantification of changes and the comparison of objects. Consequently, computational sciences are not only a prerequisite to reconstruct the data in an efficient manner and to eliminate artefacts, but also to develop and integrate powerful tools for three-dimensional image analysis. Machine learning approaches have been applied to data reconstruction and image analysis. In the future, machine learning will play an increasing role in the field of hard X-ray tomography [1].

2. RETROSPECTS INTO TWO DECADES DEVELOPMENTS IN X-RAY TOMOGRAPHY

2.1 Authors of the proceedings papers

The authors of the contributions are experts from many fields including physics and chemistry, mechanical and electrical engineering, mathematics and computer sciences, medicine and dentistry, biology and geology, etc. Therefore, the papers often include a general introduction for a broad audience. Nevertheless, the papers also contain many essential details. Therefore, the proceedings can be regarded as a bargain box for all scientists working in this fascinating area.

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A simple analysis of the proceedings papers published since 1997 demonstrates that Felix Beckmann is the most frequent author with impressive 62 authorships followed by Ge Wang with 52 authorships. The author of this paper is listed in 45 papers. The author's former doctoral student and current post-doc Georg Schulz has 29 authorships followed by Hengyong Yu (28) and Stuart R. Stock (27). More than 15 proceedings papers in this conference series are from Hans Deyhle (24), Julia Herzen (21) and Alexander Sasov (20). This analysis indicates that the frequent authorships originate from the user facilities at the synchrotron radiation sources, the power users of these set-ups, the computational scientists working on the efficient reconstruction algorithms, and the suppliers of CT-systems.

2.2 Chronological development of the proceedings papers

U. Bonse, one of the pioneers in the field, initiated the conference series on *Developments in X-ray Tomography* in 1997. The first related innovative ideas, however, he already published in 1965 [2]. The first three conferences had a reasonable size with about 30 conference papers each, see Figure 1. After further three years, the number raised to about 80, an amount already difficult to handle. Therefore, the standard CT-instrumentation, as used in the clinics, was not further advertised by the Program Committee members under the leadership of S.R. Stock. Since 2008, the number of manuscripts stayed constant and ranged between 40 to 60, see green-colored squares. Also, this year, a two-and-a-half-day program was offered. The current volume demonstrates that the large majority of the 53 contributions could be published.

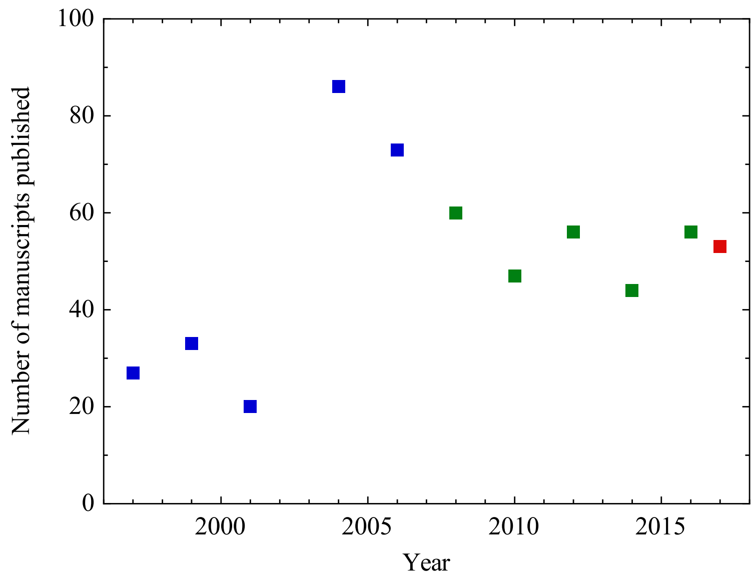

Figure 1. In 1997, the conference series on *Developments in X-ray tomography* was initiated by U. Bonse. He successfully chaired the conference for five times. The blue-colored squares show the number of manuscripts published in the proceedings. Subsequently, S.R. Stock chaired the conference (between 2008 and 2016) for five times. The number of manuscripts ranged between 40 to 60, see green-colored squares. This year, 53 contributions are in the program (red-colored square).

3. PUBLICATIONS IN HIGH-RESOLUTION TOMOGRAPHY

3.1 Analysis from 2008 and 2016

From 2008 to 2016, Stock searched for relevant terms in the databases PubMed, Web of Science, and Compendex [3-6]. He pointed out that there have been a surprisingly small number of duplications between the three databases. Consequently, the interested researchers have to consult more than one database to reasonably cover the field. Stock indicated that the reason behind has been the incredible number of journals, where the relevant papers could be found. Consequently, the experts in the field of high-resolution X-ray tomography have to invest much more time to reasonably cover the state-of-the art than specialists in other fields. Participation at the conference series in *Developments of X-ray*

Tomography and the usage of the related Proceedings volumes can, therefore, be a valuable starting point for a thorough literature search.

3.2 Choice of keywords

Stock used some key words, such as "microCT", to determine the number of publications in the field. He frequently uses "microCT" in the keywords of his publications. A simple search in SCOPUS, a publisher's database, which recently also covers a broad range of journals and proceedings of other publishers, and only indirectly considered by Stock, however, shows that already the change from "microCT" to "micro CT" (with space) gives a different result. One could also use terms, such as "micro computed tomography", and finds that the most cited experts are not the same. For example, Swiss scientists seem to prefer the term "micro computed tomography" in the title, the keywords and the text of their abstracts.

4. SELECTION OF KEYWORDS

4.1 Search for a common term

The considerations, given above, advise us to agree on a common term in our wording (keywords) and to replace the currently used terms, including "microCT", "micro CT", and "micro computed tomography", by an appropriately chosen abbreviation. This conference may initiate discussions on this important issue.

4.2 Temporal evolution of citation numbers

The usage of rather general terms, such as "CT" AND "x-ray" and "microCT", indicate that the number of publications per year is rather constant – as is the community. Therefore, one may hypothesize a static behavior in our field or some kind of saturation. Other colleagues, including the SPIE officers, prefer pointing out that such a static behavior guarantees continuity and a stable interest of the broad community. This opinion correlates with the generally high quality of the proceedings papers in the volumes of the *Developments in X-ray Tomography* series.

Using some other keywords, such as "CT" AND "nano", however, we can find an increasing number during the last few years. The members of the Program Committee hope that such areas of increasing interest have been identified and represented in the present volume.

It is worth mentioning that the number of publications in the field of high-resolution X-ray tomography was always significantly higher in the years, when the conference took place, also because of the papers of the proceedings volumes.

5. RECENT ADVANCES IN HIGH-RESOLUTION X-RAY TOMOGRAPHY

5.1 Instrumentation

Four-dimensional tomography measurements of live animals generally contain movement artifacts. Cardiac and breathing gating are powerful approaches to obtain reasonable data. A. Sasov *et al.* demonstrate that retrospective gating, based on the images, waives physiological monitoring and, thus, simplifies the data acquisition [7].

The combination of CT-techniques among themselves and CT-techniques with other methods including neutron tomography allows for unpreceded insights into materials. Here, one may acquire the data simultaneously [8] or use registration tools for data alignment [9]. Based on precise registration or simultaneous data acquisition [8], joint histograms can be generated, which help to identify components impossible by one technique alone [10].

Recently, the spatial resolution of hard X-ray tomography data has been improved to well below 100 nm by means of dedicated X-ray optics. The related effective pixel sizes are already one order of amplitude smaller than the optical wavelength, i.e. a three-dimensional dataset becomes three orders of magnitude larger than the related serial sections. T. Salditt *et al.* have taken advantage of waveguide optics to image heart tissue at nanometer scale [11]. H. Takano *et al.* developed a full-field phase tomography microscope taking advantage of a conventional X-ray source, which enables the visualization of 50 nm-wide lines [12].

The ptychographic tomography also provides information on nanostructures and seem to become a user experiment soon. At the nano-imaging beamline ID16A, European Synchrotron Radiation Facility (ESRF), Grenoble, France, near- and far-field ptychography has been successfully implemented [13].

The users with specific and challenging tasks more and more often take advantage of phase-contrast approaches, especially the single-distance phase retrieval at synchrotron radiation facilities, as this approach is simple and provides submicron resolution easily. Grating-based tomography, which belongs to the most recent phase tomography methods, is in common use both at synchrotron radiation facilities as well as in the laboratories of the specialists [14, 15]. For example, very recently single- and double-grating phase tomography setups have been compared in detail [16, 17].

Laboratory sources, in some cases with liquid metal jet anodes [14], are now available in some leading research teams and reach better and better performance. Based on the collision of laser light with relativistic electrons, a Thomson scattering X-ray source has been realized to generate quasi-monochromatic pulses in the hard X-ray regime. Using such a source for computed tomography, one eliminates beam hardening and can easily relate the reconstructed linear attenuation coefficients to the composition of the specimen [18].

X-ray diffraction has been used as the signal for tomographic reconstruction. It provides a cross-sectional map of the crystallographic phases and related abundance. Diffraction tomography has been developed over the last decade using monochromatic X rays and area detectors. S.R. Stock *et al.* report tomographic reconstruction with polychromatic radiation and an energy-sensitive detector array [19].

In order to precisely determine the local X-ray absorption values in tomography data, the choice of the detector and related software tools is essential. U.L. Olsen *et al.* successfully corrected detector response artifacts, which can reach 20 % in spectral tomography [20]. In order to incorporate spectroscopic information into hard X-ray tomography, energy-discriminating CdTe detectors have been built [21].

Real-time control systems for tomography experiments perform routines to provide feedback to the user, that ranges from instant monitoring of the data acquisition to fast reconstruction [22].

5.2 Algorithms

The development of software for the wide variety of challenges in the field of X-ray tomography, i.e. simulations, noise quantification and filtering, data reduction, missing information, artefact compensation and the fast-growing field of machine/deep learning, is a vital part of the scientific activities. One can always find experts in computational sciences within the leading teams active in the field of X-ray tomography. Because of the huge data sizes and the complexity of the problems as well as the application potential, dedicated knowledge in mathematics, computer vision including programming, and physics is a prerequisite for the success in reliable reconstruction and extracting meaningful quantities such as average pore sizes and shapes.

For spectral computed tomography, an algorithm in the projection domain has been proposed [23], which allows materials decomposition of the object of interest such as a mouse.

Multi-modal imaging is increasingly essential for advanced diagnosis and therapy. Therefore, the simultaneous data acquisition using hybrids of CT/SPECT/MRI is in the focus of research activities. These hardware developments have to go along with algorithm evaluation. Recently, MRI-modulated nuclear data for simultaneous image reconstruction of both emission and transmission parameters were studied [24]. The authors present numerical results that show the feasibility of reconstructing concentration and attenuation data through a head phantom with radio-labeled regions.

Energy-resolving detectors are essential parts of spectral tomography systems. The channels of the detector store the number of photons within a certain energy range. The counted photons in each energy channel, however, is low and, thus, the noisy radiographs suffer from low contrast. Because the multi-channel radiographs originate from the same object at the selected photon energies, there is a strong correlation among these radiographs. Very recently, scientists took advantage of the redundant information by weighted block-matching and three-dimensional filtering. The approach does not only incorporate the spatial correlation within each channel, but also exploits the spectral correlation among the channels. The advances through the proposed method are evaluated on preclinical data with success [25]. Such a detector has also been the basis of the study by Kheirabadia *et al.* [26]. They have analyzed data from a tomographic setup employing the MultiX detector, that records projection data in 128 energy bins covering a photon energy range from 20 to 160 keV. They have reduced the dimensionality of the projection data prior to reconstruction, which is, for example, important for fast security inspection.

In order to reduce the dose and to shorten the acquisition time, sparse-view tomography is a valuable method. Compressed sensing is regarded as suitable to reconstruct these undersampled data. Ueda *et al.* compare the standard total variation regularization and a nonlinear smoothing filter to design the regularization term in X-ray sparse-view phase tomography and provide results with numerically simulated data [27]. The nonlinear filter-based compressed sensing outperforms the total variation regularization in terms of textures and smooth intensity changes [27]. Undersampled data have a dedicated impact on noise level, artifacts, and spatial resolution, as quantitatively demonstrated by Mohan [28]. Abascal *et al.* [29] discussed how sparse reconstruction methods could improve the data quality in dynamic tomography studies.

Low-dose X-ray tomography has attracted a considerable interest for diagnoses. Currently, the related software developments focus on vendor-specific sinogram domain filtration and iterative reconstruction algorithms. Inspired by deep learning approaches, Chen *et al.* [30] have combined the auto-encoder, deconvolution network, and shortcut connections into the residual encoder-decoder convolutional neural network. After patch-based training, the algorithm achieves competitive performance relative to the-state-of-art methods [30].

In our aging society, more and more patients obtain highly X-ray absorbing implants including artificial hips and crowns. These implants often cause severe artifacts in the X-ray images. The existing algorithms on artifact reduction have been extended by Zhang *et al.* [31]. They have developed a convolutional neural network, which combines the information from the original data and the images corrected. Their results demonstrate an improvement of the metal artifact reduction capability by means of the proposed pipeline. Similarly, Gjesteby *et al.* [32] treated the challenge by replacing the artifact-dominated projection data with values from an interpolation scheme or a projection of a prior image. The authors have combined a convolutional neural network with the state-of-the-art normalized artefact reduction to remove the streaks in certain regions. These results indicate that powerful algorithms for artifact reduction will support the tumor location for related therapy planning.

The improved sensitivity of tomography setups often correlates with the occurrence of ring artefacts. Many algorithms for their removal have been introduced. For objects with weak changes, such as tumors with surrounding healthy tissues, their performance is not entirely satisfying. Thalmann *et al.* [33] proposed a pipeline, which finally enables the accurate segmentation of tumors.

Machine learning plays an increasing role in computed tomography. Parkinson *et al.* [34] have deployed a series of tools to automate data processing using machine learning, i.e. reconstruction algorithms, feature-extraction tools, and image classification and recommendation systems for tomography data.

Kaufmann *et al.* [35] have compared approaches to calculate the phase from Talbot-Lau interferometer measurements using the phase-stepping approach. Besides the Fourier coefficient method, they have proposed the application of a linear fitting technique and the Taylor series expansion.

Even simple monochromatic absorption tomography becomes nonlinear, when the source and detectors elements are considered as areas. Lionheart and Coban have shown that the nonlinearity is significant in fast tomography systems as used for inspection of flow in pipes [36]. They have described an iterative reconstruction algorithm.

5.3 Applications

Since the 1990's the user community of hard X-ray tomography has been growing. Most of these users are experts in their individual field, such as geology and anatomy, and are mainly interested in three-dimensional images of suitable quality. Therefore, they rather participate at the workshops organized by the suppliers of the instruments. The participation at the conference series on *Developments in X-ray Tomography* is the exception, since they encounter difficulties in following the discussions on instrumentation and algorithms. Nevertheless, the participants highly appreciate the presence of selected specialists from fields such as dentistry and wood science.

The applications of high-resolution X-ray tomography often relates to hard tissues, metallic implants, and geological materials including rocks, whereby tiny microstructures play an increasing role. The combination with diffraction and scattering enables us not only to measure the density but also to extract information about crystallographic structure as well as grains including their orientation [19]. As one expects, the phase tomography uses the contrast of choice to make visible microstructures within materials composed of elements with low atomic numbers including polymers and embedded human tissues.

Bone exhibits an anisotropic and porous structure at all length scales. The bone morphology has a major impact on the fracture risks in health and disease, e.g. osteoporosis. The number of publications on quantitative three-dimensional data on bone down to the (sub-)cellular scale is increasing. For example, Yu *et al.* have used the recently established nano-tomography system at the beamline ID16A-NI, European Synchrotron Radiation Facility (ESRF), Grenoble, France, to quantify the ultra-structure of human bone [37].

Human brain tissues belong to the most fascinating three-dimensional microstructures, but are mainly imaged by means of two-dimensional histological sections. These sections are especially valuable, as they contain functional information related to the selected staining protocol. A. Khimchenko *et al.* have demonstrated that hard X-ray tomography data can be colored according to selected histological sections [38-40]. The quality of these colorized three-dimensional data can be regarded as realistic and of interest for pathology specialists.

The most common disease worldwide is caries. The diagnosis often relies on X-ray images. It is, therefore, not surprising, that high-resolution X-ray tomography is well established in dental research [41]. In combination with spatially resolved small-angle X-ray scattering, clinically relevant conclusions have been made [42-45].

The morphological changes of degrading implant materials can be easily monitored, as the processes are slow enough to acquire high-resolution data with suitable contrast [46]. Time-dependent phenomena, for example the water transport in selected types of wood, Picea abies, [47] and the separation of polymer blend phases [48] have also a huge socio-economic impact. The precise evaluation of the pore networks is of upmost interest [49].

As hard X-ray tomography is generally non-destructive, it perfectly fits the three-dimensional characterization of unique objects, including the recovery of text from locked 17th-century letters [50], fossils [51] and the extraction of tooth cementum ultrastructure in human archeological teeth [52]. Series of experiments, for example on the cow's inner ear, permit the classification of animals also from former times [53]. The first detailed description of the bony and soft tissues of the hook region of a murine cochlea has been published [54]. It clearly demonstrates that the cochlea's anatomy is perfectly related to the function, i.e. to the acoustic signal recognition in dedicated frequency bands.

In 2016, the international community agreed to essentially decrease the carbon dioxide release to avoid global temperature rise of more than 2 K. Therefore, the capture and storage of carbon through injection of carbon dioxide into rocks became an important task. Hard X-ray tomography by means of laboratory-based systems has been used to study the structural changes of carbonate rocks (chalk) during and after carbon dioxide injection [55]. Such a four-dimensional study can support the experts in choosing the appropriate geological formations and in optimizing the storage process.

Hard X-ray tomography is more and more often applied to measure distances with micrometer precision [56] and characterize pores and their surfaces with errors well below 5 µm in the three-dimensional space [49]. Such measurements will significantly affect the development of international standards.

5.4 Interdisciplinarity

The conference *Developments in X-ray tomography XI* was organized in sessions on instrumentation, algorithms, and applications. Although this choice, already established during previous conferences, seems to be reasonable, it is a complex task to categorize the talks and posters, since most of the papers do not only contribute to one of the three areas. The contributions, however, have in common the subject of X-ray tomography and that generally experts from various fields are part of a given study.

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