How synchrotrons are accelerating research to help the fight against caries within global health

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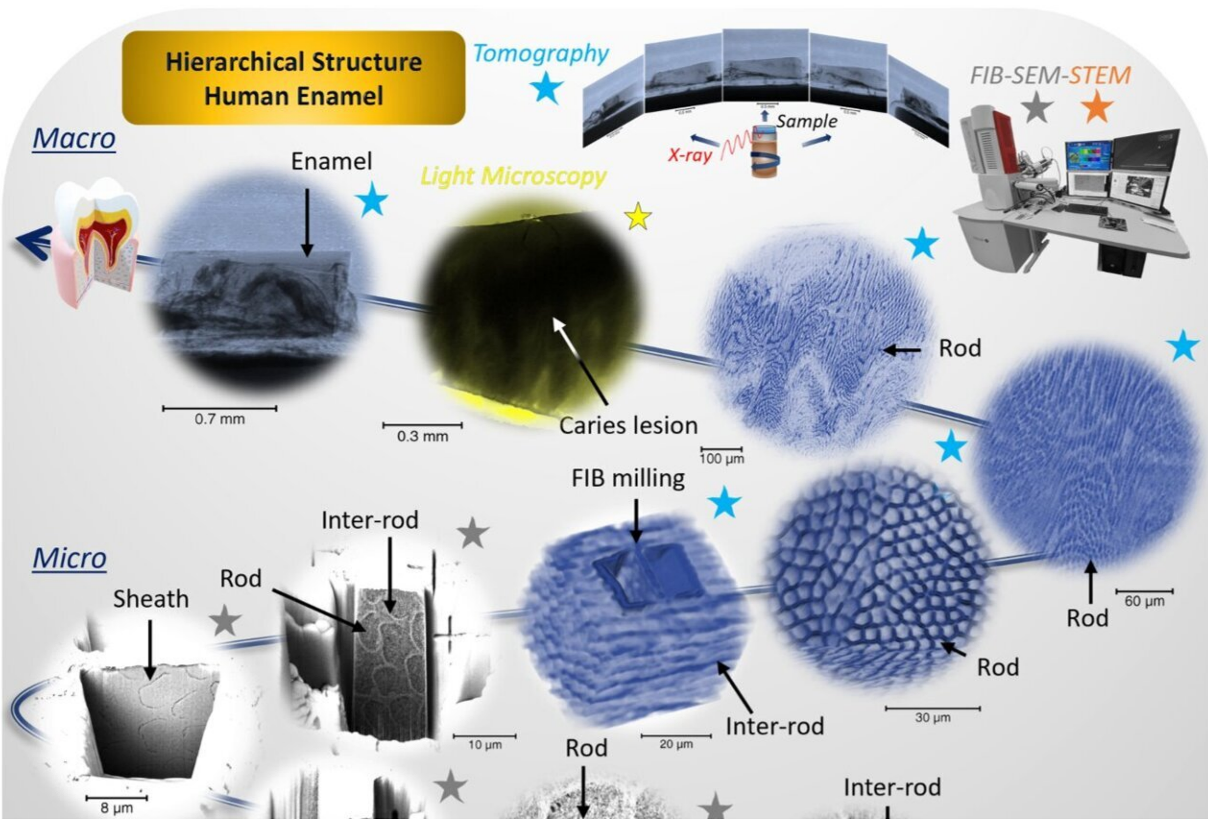

Hierarchical structure human enamel. Credit: Professor Alexander Korsunsky, Trinity College, Oxford

A team of scientists from the University of Oxford and the University of

Birmingham has just published one of the most comprehensive multi-disciplinary reviews covering nearly 40 years of discoveries and advancements in the study of enamel and its demineralization (caries). The review reveals how synchrotron radiation facilities have enabled new insights into dental tissue function and degradation at different scales.

Caries remains a debilitating condition that lacks adequate prevention and treatment demanding further research to find innovative ways to overcome its detrimental impact on global health. The disease had a global prevalence of around 2.3 billion in 2017 (in permanent teeth). In addition to the clinical effects of pain and discomfort, aesthetic issues and eventually tooth loss, it constitutes a huge economic burden, estimated to be billions of U.S. dollars worldwide in painful disruptive treatments.

The team's paper, "Synchrotron X-ray Studies of the Structural and Functional Hierarchies in Mineralised Human Dental Enamel: A State-of-the-Art Review," is published in *Dentistry Journal*. Its strategic aim was to identify and evaluate prospective avenues for analyzing dental tissues and developing treatments and prophylaxis for improved dental health.

Team leader Professor Alexander Korsunsky, Professor and Fellow Emeritus at Trinity College, Oxford, explains, "Understanding the mechanism of caries development requires tracing the pathways of the biological, chemical, and structural processes that unfold progressively from the microbial and crystal level up to the macroscopic scale. This necessarily engenders the need to visualize and understand tissue organization and function, along with its interaction with the microbial and chemical environment, through static and dynamic studies. Synchrotron-based studies offer unique tools for this purpose, due to the versatile interaction of X-ray photons with the organic and inorganic tissue components."

Hard dental tissues possess a complex hierarchical structure that is particularly evident in enamel, the most mineralized substance in the human body. Its complex and interlinked organization at the Ångstrom (crystal lattice), nano-, micro-, and macro-scales is the result of evolutionary optimization for mechanical and functional performance: hardness and stiffness, fracture toughness, thermal and chemical resistance. Understanding the physical-chemical-structural relationships at each scale requires the application of appropriately sensitive and resolving probes.

"Currently, about 50 synchrotron facilities worldwide are contributing an outstanding amount of research work along with the continuous improvement of analytical approaches. This is due to the fact that synchrotron X-ray techniques offer the possibility to progress significantly beyond the capabilities of conventional laboratory instruments, i.e., X-ray diffractometers, and electron and atomic force microscopes. The last few decades have witnessed the accumulation of results obtained from X-ray scattering (diffraction), spectroscopy (including polarization analysis), and imaging (including ptychography and tomography)," adds Dr. Cyril Besnard, the lead author of the research.

The first section of the review briefly covers the structure of the enamel (and dentin), describes dental caries disease and its causative factors, including the nature and organization of biofilm and its effects on the enamel, and discusses the existing strategies for remineralization. The second section provides an overview of synchrotron facilities, followed by a description of the application of synchrotron methods to dental tissue studies: diffraction (scattering), imaging (including tomography and ptychography), and spectroscopy.

"The modern synchrotron, like the UK's Diamond Light Source, offers the versatility of utilizing customized experimental setups, which can be categorized based on the type of detector and relevant setup; the energy in use, either soft or hard X-rays (in vacuum or air or liquid); the presence of magnetic fields or temperature control; and the type of monitoring process (static or dynamic analysis) and equipment. The continuous development of synchrotron facilities, techniques, and devices, means that the future will be bright for the research into mineralized tissues," comments Dr. Igor Dolbnya, senior beamline scientist on the B16 Test beamline at Diamond.

The review summarizes studies using synchrotron techniques for structural, imaging, and chemical analyses. The utility of these methods is emphasized in terms of bringing new insights, and the benefits of the combined use of multiscale correlative techniques. Diamond's facilities and beamlines have been used extensively by the authors to study dental tissue and are covered in the review. It is a great example of a multi-disciplinary approach on one research topic as the team used beamlines spread over four different science groups at Diamond.

Many recent studies are summarized in the review with details and knowledge from state-of-the-art analysis, which could be implemented in future studies. For example, to elucidate the phenomenon of caries and explore avenues such as the 3D structure of the nanocrystallites, the motion of atoms occurring during demineralization, the in situ process of demineralization by acid from the bacteria using multimodal imaging, in the time, space and energy domains.

The researchers state that these techniques can be applied to design and implement new studies for enamel remineralization and to develop novel biomimetic materials and strategies to repair enamel and dentin.

"Synchrotron-based analyses have led to major advances in the structure, and hence mechanical properties, of dental tissues. This includes the caries process, and other dental fields, aiming to improve quality of life.

However, there are still open research questions that warrant further investigation. Continuously building on current research will help us to better understand the changes in diseased tissue structure and, in turn, its management," concludes Dr. Adrian Mancuso, Diamond's director of Physical Sciences.

The review also highlights the importance of the applications and approaches carried out on the research of other materials. The knowledge gathered from these approaches can often be transferred to dental caries research, to bring new research opportunities and connect methods and analytical results to other research applications. The authors believe this comprehensive review will be of interest to a wide network of researchers and clinicians in the field of cariology and pharmaceutical industries, as well as industries which could benefit from the knowledge transfer of technologies including pharmaceutical industry, corrosion studies, biomedical engineering, and nanodentistry.

More information: Cyril Besnard et al, Synchrotron X-ray Studies of the Structural and Functional Hierarchies in Mineralised Human Dental Enamel: A State-of-the-Art Review, *Dentistry Journal* (2023). DOI: 10.3390/dj11040098

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