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Opinion

In Vivo Visualization of Oxidative Stress: Prospects and Perspectives of Hydrogen Peroxide–Based VDMP CEST Imaging in Ophthalmic Diseases Research

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Abstract

Oxidative stress is a common pathological pathway in various ocular diseases; however, effective methods for visualizing and detecting intracellular oxidative stress in living subjects remain lacking. In this study, our team developed a visualization technique based on VDMP-CEST technology, optimizing pulse sequence parameters to achieve in vivo imaging of oxidative stress by exploiting the relative stability of hydrogen peroxide. This method demonstrates high sensitivity toward fast-exchanging molecules and holds promise as a new imaging tool for the diagnosis, treatment, and research of oxidative stress-related ocular diseases.

Keywords: Ophthalmic diseases; Oxidative stress; Hydrogen peroxide; Variable delay multi-pulse chemical exchange saturation transfer

Abbreviations: ROS: Reactive oxygen species; ELISA: Enzyme-linked immunosorbent assays; GSH: Glutathione; GSSG: Oxidized glutathione; H_2O_2: Hydrogen Peroxide; VDMP CEST: Variable delay multi-pulse chemical exchange saturation transfer; CW-CEST: Continuous-wave CEST

Opinion

Oxidative stress refers to a pathological process in which the dynamic balance between reactive oxygen species (ROS) production and antioxidant defense systems within the body is disrupted, leading to excessive accumulation of ROS. This overabundance attacks biological macromolecules such as lipids, proteins, and nucleic acids, resulting in cellular structural damage and functional impairment. The eye, characterized by high oxygen consumption, intense metabolic activity, continuous exposure to light, and relatively weak endogenous antioxidant reserves, is one of the most vulnerable organs to oxidative damage [1]. In ophthalmic diseases, oxidative stress has been established as a common core pathogenic mechanism underlying various conditions, including age-related macular degeneration, cataract, glaucoma, diabetic retinopathy, and thyroid-associated ophthalmopathy [2].

Although the critical role of oxidative stress in the onset and progression of ocular diseases is widely recognized, there remains a lack of non-invasive, quantitative, and real-time imaging techniques capable of detecting intracellular oxidative stress in living subjects.

Current assessment methods primarily rely on ex vivo analysis of tissue or bodily fluid samples, such as fluorescent probe staining, enzyme-linked immunosorbent assays (ELISA), and measurement of glutathione/oxidized glutathione (GSH/GSSG) ratios. These approaches are limited in their ability to reflect real-time changes in the redox status of the eye during disease progression, thereby constraining their clinical translation potential.

Among the ROS family, hydrogen peroxide (H_2O_2) holds a unique biological position: it acts as a second messenger involved in regulating physiological processes such as cell proliferation, differentiation, apoptosis, and innate immune responses [3]; conversely, under pathological conditions, abnormal accumulation of H_2O_2 can deplete antioxidant molecules (e.g. GSH) and catalyze the formation of highly reactive hydroxyl radicals via the Fenton reaction, thereby exacerbating oxidative damage [4]. Compared with superoxide anions and hydroxyl radicals, H_2O_2 exhibits relatively stable chemical properties, making it a more suitable representative molecule for monitoring oxidative stress levels in vivo [5].

Recently, our research team developed a method based on variable delay chemical exchange saturation transfer (VDMP-CEST) magnetic resonance imaging, enabling non-invasive, high-sensitivity visualization of H_2O_2 in vivo through optimized pulse numbers and inter-pulse spacing. Compared with conventional continuous-wave CEST (CW-CEST) techniques, VDMP-CEST improves signal-to-noise ratio and specificity for H_2O_2 detection [6,7], offering a promising imaging tool for in vivo monitoring of oxidative stress-related diseases. Currently, the application of VDMP-CEST in ophthalmology is still in the preclinical validation stage. With the increasing availability of ultra-high-field MRI systems (7T and above), along with ongoing optimization of imaging sequences and post-processing algorithms, this technology holds great promise as an effective means for assessing intravitreal oxidative stress status, thus providing objective reference data for both clinical management and scientific research of oxidative stress-related eye diseases.

Acknowledgement

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Conflict of Interest

None.

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