

Communication

Detection of 2-Hydroxyglutarate by 3.0-Tesla Magnetic Resonance Spectroscopy in Gliomas with Rare IDH Mutations: Making Sense of “False-Positive” Cases

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Abstract: We have previously published a study on the reliable detection of 2-hydroxyglutarate (2HG) in lower-grade gliomas by magnetic resonance spectroscopy (MRS). In this short article, we re-evaluated five glioma cases originally assessed as isocitrate dehydrogenase (IDH) wildtype, which showed a high accumulation of 2HG, and were thought to be false-positives. A new primer was used for the detection of IDH2 mutation by Sanger sequencing. Adequate tissue for DNA analysis was available in 4 out of 5 cases. We found rare IDH2 mutations in two cases, with IDH2 R172W mutation in one case and IDH2 R172K mutation in another case. Both cases had very small mutant peaks, suggesting that the tumor volume was low in the tumor samples. Thus, the specificity of MRS for detecting IDH1/2 mutations was higher (81.3%) than that originally reported (72.2%). The detection of 2HG by MRS can aid in the diagnosis of rare, non-IDH1-R132H IDH1 and IDH2 mutations in gliomas.

Keywords: 2-hydroxyglutarate; glioma; magnetic resonance spectroscopy; rare IDH mutations; false-positive

1. Introduction

Isocitrate dehydrogenase (IDH)-mutant gliomas produce the oncometabolite 2-hydroxyglutarate (2HG). We previously reported on the reliable detection of 2HG by 3.0-tesla magnetic resonance spectroscopy (MRS) in a cohort of 52 lower-grade glioma patients (WHO grades 2 and 3) [1]. A cutoff of 1.489 mM for 2HG yielded 100% sensitivity and a 72.2% specificity for the detection of IDH1 or IDH2 mutations was reported. A high level of 2HG was detected in 5 of 27 (18.5%) gliomas that were determined to be IDH-wildtype. These were thought to be false-positive results or a failure to detect rare IDH1 or IDH2 mutations by DNA sequencing [1]. The unambiguous detection of 2HG (chemical shift 2.25 ppm) by MRS is difficult because of a spectral overlap with glutamate (Glu; 2.43 ppm), glutamine (Gln; 2.34 ppm), and gamma-aminobutyric acid (GABA; 2.28 ppm). Recently, the tumor recurred in one of the five patients, and the patient underwent a second surgery. An analysis of IDH1/2 mutations using Sanger sequencing revealed an IDH2 mutation. In the current study, we re-evaluated IDH1 and IDH2 status in the remaining “false-positive”

Hydroxyglutarate Detection By Magnetic Resonance

Lee Roy Morgan, Feyzi Birol Sarica



Hydroxyglutarate Detection By Magnetic Resonance:

Imaging of Brain Tumors, An Issue of Magnetic Resonance Imaging Clinics of North America Rivka R.

Colen, 2016-10-15 This issue of MRI Clinics of North America focuses on Imaging of Brain Tumors and is edited by Dr Rivka Colen. Articles will include Multiparametric Imaging Analysis MR Spectroscopy Genomics and MicroRNAs in Glioma Metabolomics and Hyperpolarization MRI in Brain Tumors Imaging Genomics in Glioma Radiomics and Big Data in Imaging RANO Criteria and Clinical Endpoints Gliomas The New WHO Brain Tumor Pathological Molecular Classification and Clinical and Radiographic Classifications Liposomal Contrast Agents and Nanoparticles in Brain Tumor Imaging Multiparametric Imaging Analysis Perfusion and more

Diffuse Low-Grade Gliomas in Adults Hugues Duffau, 2017-07-03 The second edition of this well received volume has been revised and updated to reflect the advances in pathological classification and molecular epidemiology of diffuse low grade gliomas DLGG in adults and offers an updated review on individualized therapies. This book presents the latest research pertaining to the diagnosis genetics therapy and management of DLGGs. It extensively covers recent research on the natural history of DLGGs and their interaction with the brain and reviews the new diagnostic and therapeutic strategies which increase survival and quality of life of the patient. New topics covered are the management of DLGGs during pregnancy functional rehabilitation of patients with DLGG and the onco functional balance in DLGG among others. The reader will have the opportunity to gain insight in both clinical and basic science aspects of this type of tumor and learn about the application of novel imaging techniques such as diffusion tensor imaging. Edited by a leading expert in the field and authored by a team of recognised specialists this book is a valuable resource for medical oncologists neuro oncologists and neurologists

Functional Neuroradiology Scott H. Faro, Feroze B.

Mohamed, 2023-05-23 This new edition fully updates and expands Faro and Mohamed's Functional Neuroradiology a gold standard comprehensive introduction to the state of the art functional imaging in neuroradiology including the physical principles and clinical applications of Diffusion Perfusion Permeability MR spectroscopy Positron Emission Tomography BOLD fMRI and Diffusion Tensor Imaging. With chapters written by internationally distinguished neuroradiologists neurologists psychiatrists cognitive neuroscientists and physicists Functional Neuroradiology is divided into 12 major sections including Diffusion and Perfusion Imaging Magnetic Resonance Spectroscopy and Chemical Exchange Saturation Transfer Imaging Multi Modality Functional Neuroradiology BOLD Functional MRI Diffusion Tensor Imaging Presurgical Brain Tumor Mapping Emerging neuroimaging techniques Functional Spine and Hydrocephalus imaging and Neuroanatomical Gray and White matter Brain Atlases. This second edition is fully updated throughout and includes more than 15 new chapters on topics such as Brain tumor Radiogenomics CNS Tumor Surveillance and Functional MR Perfusion Imaging CNS Machine Learning Focused Ultrasound therapy TBI Sports Related Injury and CNS Lymphatic system. By offering readers a complete overview of functional imaging modalities and techniques currently used in patient diagnosis and

management as well as emerging technology Functional Neuroradiology is a vital information source for physicians and cognitive neuroscientists involved in daily practice and research

New Insights into Glioblastoma Carla

Vitorino, Carmen Balana, Célia Cabral, 2023-05-17 New Insights into Glioblastoma Diagnosis Therapeutics and Theranostics provides a compendium of recent diagnostic and therapeutic advances in GBM encompassing a pipeline of compounds and bio nanotechnology strategies that have stood out with potential increased antitumoral activity and capability to cross the blood brain barrier Issues and challenges related to their translation into the clinical practice and their contribution to the increase in survival rates and well being of patients are addressed This is a valuable resource for graduate students oncologists cancer researchers and members of the biomedical field who need to learn more on recent developments on the management of glioblastoma The book is split in three parts Diagnosis focusing on biomarkers and techniques such PET MRI infrared thermography and deep neural networks Therapeutics discussing new chemical entities as natural products and repurposed drugs and new formulation approaches as nanotechnology based and microRNA approaches and Theranostics explaining the role of omics system based approaches and glioblastoma microenvironment Provides guidance towards recent advances of new chemical entities and delivery strategies targeted to glioblastoma Includes overviews to help readers apply information in their research Encompasses summarizing diagrams and real world examples to facilitate comprehension and enhance the applicability of the content

Metabolic Analysis Using Stable Isotopes, 2015-09-21 Metabolic Analysis Using Stable Isotopes the newest volume in Methods in Enzymology continues the legacy of this premier serial with quality chapters authored by leaders in the field This volume covers research methods in metabolic analysis using stable isotopes Continues the legacy of this premier serial with quality chapters on metabolic analysis using stable isotopes Represents the newest volume in Methods in Enzymology providing a premier serial with quality chapters authored by leaders in the field Ideal reference for those interested in the study of metabolism metabolic tracing isotopic labeling and lipogenesis

In Vivo NMR Spectroscopy Robin A. de Graaf, 2019-03-11 Presents basic concepts experimental methodology and data acquisition and processing standards of in vivo NMR spectroscopy This book covers in detail the technical and biophysical aspects of in vivo NMR techniques and includes novel developments in the field such as hyperpolarized NMR dynamic ¹³C NMR automated shimming and parallel acquisitions Most of the techniques are described from an educational point of view yet it still retains the practical aspects appreciated by experimental NMR spectroscopists In addition each chapter concludes with a number of exercises designed to review and often extend the presented NMR principles and techniques The third edition of In Vivo NMR Spectroscopy Principles and Techniques has been updated to include experimental detail on the developing area of hyperpolarization a description of the semi LASER sequence which is now a method of choice updated chemical shift data including the addition of ³¹P data a troubleshooting section on common problems related to shimming water suppression and quantification recent developments in data acquisition and processing standards and MatLab scripts on the

accompanying website for helping readers calculate radiofrequency pulses Provide an educational explanation and overview of in vivo NMR while maintaining the practical aspects appreciated by experimental NMR spectroscopists Features more experimental methodology than the previous edition End of chapter exercises that help drive home the principles and techniques and offer a more in depth exploration of quantitative MR equations Designed to be used in conjunction with a teaching course on the subject In Vivo NMR Spectroscopy Principles and Techniques 3rd Edition is aimed at all those involved in fundamental and or diagnostic in vivo NMR ranging from people working in dedicated in vivo NMR institutes to radiologists in hospitals researchers in high resolution NMR and MRI and in areas such as neurology physiology chemistry and medical biology **Neuroimaging Techniques in Clinical Practice** Manoj Mannil, Sebastian F.-X.

Winklhofer, 2020-08-11 This book provides a concise overview of emerging technologies in the field of modern neuroimaging Fundamental principles of the main imaging modalities are described as well as advanced imaging techniques including diffusion weighted imaging perfusion imaging arterial spin labeling diffusion tensor imaging intravoxel incoherent motion MR spectroscopy functional MRI and artificial intelligence The physical concepts underlying each imaging technique are carefully and clearly explained in a way suited to a medical audience without prior technical knowledge In addition the clinical applications of the various techniques are described with the aid of illustrative clinical examples Helpful background information is also presented on the core principles of MRI and the evolution of neuroimaging and important references to current medical research are highlighted The book will meet the needs of a range of non technological professionals with an interest in advanced neuroimaging including radiology researchers and clinicians in the fields of neurology neurosurgery and psychiatry **Exploring Cancer Metabolic Reprogramming through Molecular Imaging** Franca Podo, Zaver M.

Bhujwalla, Egidio Iorio, 2017-07-27 The inclusion of oncogene driven reprogramming of energy metabolism within the list of cancer hallmarks Hanahan and Weinberg Cell 2000 2011 has provided major impetus to further investigate the existence of a much wider metabolic rewiring in cancer cells which not only includes deregulated cellular bioenergetics but also encompasses multiple links with a more comprehensive network of altered biochemical pathways This network is currently held responsible for redirecting carbon and phosphorus fluxes through the biosynthesis of nucleotides amino acids lipids and phospholipids and for the production of second messengers essential to cancer cells growth survival and invasiveness in the hostile tumor environment The capability to develop such a concerted rewiring of biochemical pathways is a versatile tool adopted by cancer cells to counteract the host defense and eventually resist the attack of anticancer treatments Integrated efforts elucidating key mechanisms underlying this complex cancer metabolic reprogramming have led to the identification of new signatures of malignancy that are providing a strong foundation for improving cancer diagnosis and monitoring tumor response to therapy using appropriate molecular imaging approaches In particular the recent evolution of positron emission tomography PET magnetic resonance spectroscopy MRS spectroscopic imaging MRSI functional MR imaging fMRI and

optical imaging technologies combined with complementary cellular imaging approaches have created new ways to explore and monitor the effects of metabolic reprogramming in cancer at clinical and preclinical levels. Thus the progress of high tech engineering and molecular imaging technologies combined with new generation genomic proteomic and phosphoproteomic methods can significantly improve the clinical effectiveness of image based interventions in cancer and provide novel insights to design and validate new targeted therapies.

The Frontiers in Oncology Research Topic Exploring Cancer Metabolic Reprogramming Through Molecular Imaging focusses on current achievements challenges and needs in the application of molecular imaging methods to explore cancer metabolic reprogramming and evaluate its potential impact on clinical decisions and patient outcome. A series of reviews and perspective articles along with original research contributions on humans and on preclinical models have been concertedly included in the Topic to build an open forum on perspectives present needs and future challenges of this cutting edge research area.

Brain and Spinal Tumors Lee Roy Morgan, Feyzi Birol Sarica, 2020-01-29 Numerous new concepts and procedures are reviewed and discussed in this book and allude to the transport of drugs to the brain. New radiation concepts are also presented plus management of toxicities associated with both treatment modalities. It is the goal of this book to provide information and data that will be useful for both researchers and practitioners to develop new approaches for the management of CNS malignancies.

Genetic Patterns in Neuroimaging, An Issue of Neuroimaging Clinics Luis Celso Hygino de Cruz, 2014-12-27 Genetic Patterns in Neuroimaging is explored in this important Neuroimaging Clinics issue. Articles include Brain imaging and genetic risk of congenital malformations, Understanding genetics in neuroimaging, Influence of genetics in neuropathology, Building a bridge between genomics and neuroradiology, Systems genetics approaches to neuroimaging phenotypes, Imaging genetic predictions at an individual level, Brain imaging and genetic risk in the pediatric population, Imaging phenotypes in cognitive diseases, Molecular imaging in genetics, Imaging phenotypes in psychiatric disease, Genomics of brain tumor imaging, Neuroimaging and genetic influence in post treatment brain neoplasms, Imaging phenotypes in multiple sclerosis, Genetic markers and influences in cerebrovascular malformations and more.

Imaging Neuroinflammation Cornelia Laule, John D Port, 2023-04-13 Imaging Neuroinflammation provides an overview of the molecular and cellular basis of inflammation and its effects on neuroanatomy, reviews state of the art imaging tools available to measure neuroinflammation and describes the application of those tools to both preclinical animal disease models and human disease. This book is an authoritative reference on imaging neuroinflammation. MRI neuroinflammation, MR Spectroscopy of inflammation, Iron imaging in inflammation and more. Explains how inflammation in the central nervous system impacts tissue microstructure. Presents imaging methods that are useful for assessing neuroinflammation. Describes preclinical models of neuroinflammation. Reviews the role of neuroinflammation in human injury and disease states.

Primary Brain Tumors in Adults: Advances in Mechanistic Understanding, Evaluation, and Management, 2025-07-01 Primary Brain Tumors in Adults: Advances in Mechanistic Understanding, Evaluation and

Management Volume 166 in the Advances in Cancer Research series highlights new advances in the field with this new volume presenting interesting chapters on a variety of timely topics including Molecular drivers in primary brain tumor formation Novel CSF pathways in the glioma DIPG Volumetric analysis in low grade gliomas and other advanced MR imaging techniques Liquid biopsy in the diagnosis of primary brain tumors Intraoperative imaging techniques to improve tumor detection and much more Additional chapters focus on Supramaximal resection in primary brain tumors Radiotherapeutic approaches IMRT re irradiation Molecularly driven therapies in the treatment of primary brain tumors and Changes in the immune microenvironment and immunotherapeutic strategies in the treatment of gliomas Provides the latest information on Primary Brain Tumors in Adults Offers outstanding and original reviews on a range of cancer research topics Serves as an indispensable reference for researchers and students alike

Brain Tumor MRI Image Segmentation Using Deep Learning Techniques Jyotismita Chaki, 2021-11-27 Brain Tumor MRI Image Segmentation Using Deep Learning Techniques offers a description of deep learning approaches used for the segmentation of brain tumors The book demonstrates core concepts of deep learning algorithms by using diagrams data tables and examples to illustrate brain tumor segmentation After introducing basic concepts of deep learning based brain tumor segmentation sections cover techniques for modeling segmentation and properties A focus is placed on the application of different types of convolutional neural networks like single path multi path fully convolutional network cascade convolutional neural networks Long Short Term Memory Recurrent Neural Network and Gated Recurrent Units and more The book also highlights how the use of deep neural networks can address new questions and protocols as well as improve upon existing challenges in brain tumor segmentation Provides readers with an understanding of deep learning based approaches in the field of brain tumor segmentation including preprocessing techniques Integrates recent advancements in the field including the transformation of low resolution brain tumor images into super resolution images using deep learning based methods single path Convolutional Neural Network based brain tumor segmentation and much more Includes coverage of Long Short Term Memory LSTM based Recurrent Neural Network RNN Gated Recurrent Units GRU based Recurrent Neural Network RNN Generative Adversarial Networks GAN Auto Encoder based brain tumor segmentation and Ensemble deep learning Model based brain tumor segmentation Covers research Issues and the future of deep learning based brain tumor segmentation

Rosenberg's Molecular and Genetic Basis of Neurological and Psychiatric Disease Roger N. Rosenberg, Juan M. Pascual, 2020-06-24 Rosenberg's Molecular and Genetic Basis of Neurologic and Psychiatric Disease Sixth Edition Volume Two provides a comprehensive introduction and reference to the foundations and practical aspects relevant to the majority of neurologic and psychiatric disease This updated volume focuses on degenerative disorders movement disorders neuro oncology neurocutaneous disorders epilepsy white matter diseases neuropathies and neuronopathies muscle and neuromuscular junction disorders stroke psychiatric disease and a neurologic gene map A favorite of over three generations

of students clinicians and scholars this new edition retains and expands on the informative concise and critical tone of the first edition This is an essential reference for general medical practitioners neurologists psychiatrists geneticists related professionals and for the neuroscience and neurology research community at large The content covers all aspects essential to the practice of neurogenetics to inform clinical diagnosis treatment and genetic counseling Provides comprehensive coverage on the neurogenetic foundation of neurological and psychiatric disease Presents detailed coverage of genomics animal models and diagnostic methods with new coverage on evaluating patients with biochemical abnormalities or gene mutations Includes new chapters on the pharmacogenomics of epilepsy and the most recent updates in molecular genetics focusing on neurodegenerative and psychiatric diseases [Handbook of Neuro-Oncology Neuroimaging](#) Herbert B. Newton,2022-08-21 With treatment approaches and the field of neuro oncology neuroimaging changing rapidly this third edition of the Handbook of Neuro Oncology Neuroimaging is very relevant to those in the field providing a single source comprehensive reference handbook of the most up to date clinical and technical information regarding the application of neuroimaging techniques to brain tumor and neuro oncology patients This new volume will have updates on all of the material from the second edition and in addition features several new important chapters covering diverse topics such as imaging for the use of Laser Interstitial Thermal Therapy advanced imaging techniques in radiation therapy therapeutic treatment fields response assessment in clinical trials surgical planning of neoplastic disease of the spine and more Sections first overview neuro oncological disorders before delving into the physics and basic science of neuroimaging and great focus on CT and MRI The book then focuses on advances in the neuroimaging of brain tumors and neuroimaging of specific tumor types There is also discussion of neuroimaging of other neuro oncological syndromes This book will serve as a resource of background information to neuroimaging researchers and basic scientists with an interest in brain tumors and neuro oncology Summarizes translational research on brain imaging for brain tumors Discusses limitations of neuroimaging for diagnosis and treatment Presents advanced imaging technologies including CT MRI and PET Contains new coverage on Laser Interstitial Thermal Therapy radiation therapy clinical trials and more [Cancer Metabolomics](#) Shen Hu,2021-04-01 Cancer metabolomics is a rapidly evolving field that aims for a comprehensive dissection of the metabolic phenotypes and functional network of metabolites in human cancers State of the art metabolomics tools have been developed and applied to studying cancer metabolism and developing metabolic targets for improved diagnosis prognosis and therapeutic treatment of human cancers Chapters are written by subject experts in the field of cancer metabolomics with cross disciplinary contributions Coverage includes advanced metabolomics technologies and methodologies including chemical isotope labelling liquid chromatography mass spectrometry capillary ion chromatography mass spectrometry 2 D gas chromatography mass spectrometry capillary electrophoresis mass spectrometry nuclear magnetic resonance spectroscopy shotgun lipidomics tracer based metabolomics microbial metabolomics mass spectrometry imaging for single cell metabolomics and functional

metabolomics In addition the book highlights new discoveries in cancer metabolism such as hypoxia inducible factor pathway isocitrate dehydrogenase 1 mutation and oncometabolites Finally contributors focus on the translational applications of metabolomics in human cancers such as glioma head and neck cancer and gastric cancer This new volume will be a unique reference source for cancer researchers and promote applications of metabolomics in understanding cancer metabolism

Advanced Imaging Methods in Neuroscience João O. Malva, Jorge Valero, Miguel Castelo-Branco, Alard Roebroek, 2022-01-11 **Neuroimaging, Part I**, 2016-07-12 Neuroimaging Part One a text from The Handbook of Clinical Neurology illustrates how neuroimaging is rapidly expanding its reach and applications in clinical neurology It is an ideal resource for anyone interested in the study of the nervous system and is useful to both beginners in various related fields and to specialists who want to update or refresh their knowledge base on neuroimaging This first volume specifically covers a description of imaging techniques used in the adult brain aiming to bring a comprehensive view of the field of neuroimaging to a varying audience It brings broad coverage of the topic using many color images to illustrate key points Contributions from leading global experts are collated providing the broadest view of neuroimaging as it currently stands For a number of neurological disorders imaging is not only critical for diagnosis but also for monitoring the effect of therapies and the entire field is moving from curing diseases to preventing them Most of the information contained in this volume reflects the newness of this approach pointing to this new horizon in the study of neurological disorders Provides a relevant description of the technologies used in neuroimaging including computed tomography CT magnetic resonance imaging MRI positron emission tomography PET and several others Ideal resource for anyone studying the nervous system from beginners to specialists interested in recent advances in neuroimaging of the adult brain Discusses the application of imaging techniques to the study of brain and spinal cord disease and its use in various syndromes Contains vibrant colorful images to illustrate key points **Advanced Neuroimaging in Brain Tumors, An Issue of Radiologic Clinics of North America, E-Book** Sangam Kanekar, 2021-05-13 This issue of Radiologic Clinics focuses on Advanced Neuroimaging in Brain Tumors and is edited by Dr Sangam Kanekar Articles will include Imaging findings of new entities and patterns in brain tumor IDH mutant IDH wildtype Codeletion and MGMT methylation CT and MR perfusion imaging in neuro oncology Application of diffusion weighted imaging DWI and diffusion tensor imaging DTI in the pre and post surgical evaluation of brain tumor Clinical applications of magnetic resonance spectroscopy MRS in of brain tumors grading and recurrence Cellular and molecular imaging with PET and SPECT in brain tumors Role of Functional MRI fMRI in the presurgical mapping of brain tumor Imaging surveillance of gliomas role of advanced imaging techniques Neoplastic meningitis and paraneoplastic syndrome role of imaging Imaging of neurologic injury following oncologic therapy RadioGenomics of brain tumor Imaging mimics of brain tumors Imaging of tumor syndromes and more **Progress in the Diagnosis and Treatment of Gliomas** Ying Mao, 2024-08-29 This book provides the most current advancements in the medical care of glioma patients accompanied by

clinical cases Clinical implementations of the new multilayered integrated diagnosis of gliomas according to WHO CNS5 are also demonstrated here New adjuvant therapies such as chemotherapy targeted therapy immunotherapy and physiotherapy are discussed in the book The book also covers the applications of genomics and epigenomics of gliomas in clinical practice In essence this book shows the management of gliomas with new treatment modalities which can prolong the overall survival time of patients fighting glioma The translation was done with the help of artificial intelligence The present version has been revised technically and linguistically by the authors in collaboration with a professional translator

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Hydroxyglutarate Detection By Magnetic Resonance Introduction

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