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Integrating Imaging Bioinformatics in Ophthalmology

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Abstract: Imaging informatics collates the multitude of information into data; allowing research to occur, driving data quality, and ultimately improving patient care. Imaging informatics increases the efficiency of imaging workflows by enhancing productivity and making information accessible to multiple users simultaneously. Consistency of critical data is essential for marrying information together through the process, to save the radiologist time, for consistency, billing, and research.

Abbreviations:

radiology information system (RIS)

hospital information system (HIS)

picture archive and communication system (PACS)

vendor neutral archive (VNA)

health level 7 (HL7)

“Fast Healthcare Interoperability Resources” or FHIR

Integrating the Healthcare Enterprises (IHE)

Digital Imaging and Communications in Medicine (DICOM)

Clinical Document Architecture) CDA)

Continuity Of Care Documents (CCD)

Modality Performed Procedure Step (MPPS)

Storage Commitment (SC)

Patient Identifier (PID)

unique identifiers (UIDs)

Information Object Definitions (IODs)

protected health information (PHI)

Clinical Document Architecture (CDA)

Continuity of Care Document (CCD)

Study Content Notification (SCN)

AI Artificial intelligence

ML Machine learning

CML Conventional machine learning

DL Deep learning

SVM Support vector machine

RF Random forest

DT Decision tree

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ANN Artificial neural network

RNN Recurrent neural network

CNN Convolutional neural network

OCT Optical coherence tomography

ASP Anterior segment photographs

AS-OCT Anterior segment optical coherence tomography

IVCM In vivo confocal microscopy

LASEK Laser-assisted epithelial keratomileusis

LASIK Laser in situ keratomileusis

SMILE Small incision lenticular extraction

DMEK Descemet membrane endothelial keratoplasty

AUC Area under the receiver operating characteristic curve

LASSO Least absolute shrinkage and selection operator

LR logistic regression

RANSAC RANdom SAmple Consensus

MRF Material recovery facilities

MG Meibomian gland

MGD Meibomian gland dysfunction

mAP Mean average precision

GAN Generative adversarial network

CNF Corneal nerve fiber

DC Dendritic cell

AUPRC Area under precision-recall curve

I. Introduction

The advancement of computer science and the availability of big data has enabled the emergence of artificial intelligence, which has led to a technological revolution significantly affecting many aspects of our daily life [1–4]. The application of AI in the field of medicine is expanding rapidly [5], mainly due to the advancement of machine learning (ML) that can be utilized for the analysis of medical images and patient data, diagnosis of diseases, and prediction of treatment outcomes [6]. ML is a paradigm of AI that systematically allows computer algorithms to adapt according to a large amount of raw input data and make predictions or determinations using the learned patterns [1,7,8]. The method can be roughly divided into conventional machine learning (CML) and deep learning (DL) [8]. CML algorithms, such as the support vector machine (SVM), random forest (RF), decision tree (DT), and linear regression and logistic regression, generally do not involve large neural networks [8] and have been applied for the construction of predictive algorithms for the diagnosis or classification of diseases based on data from medical records or population-based studies [9]. DL has usually been applied for the analysis of multimedia datasets, including images, sound, and videos [7,8], and involves large neural networks composed of multiple neuron-like layers of algorithms, such as artificial neural networks (ANNs), recurrent neural networks (RNNs), and convolutional neural networks (CNNs) [7,8].

In ophthalmology, AI has initially been applied for the analysis of fundus photographs and optical coherence tomography (OCT) images; thus, previous studies have mostly focused on the integration of AI into the diagnostic approach of posterior segment diseases, such as diabetic retinopathy, glaucoma, macular degeneration, and retinopathy of prematurity [5,10–14]. However, as DL algorithms can be utilized for the analysis of imaging the data of anterior segment structures, such as anterior segment photographs (ASPs), anterior segment OCT (AS-OCT) images, specular microscopy, corneal topography, in vivo confocal microscopy (IVCM), infrared meibography, and tear interferometry [2], AI is also expected to assist in the diagnosis and monitoring of various anterior segment diseases. Recently, many studies have been conducted on the application of AI in various anterior segment diseases [2].

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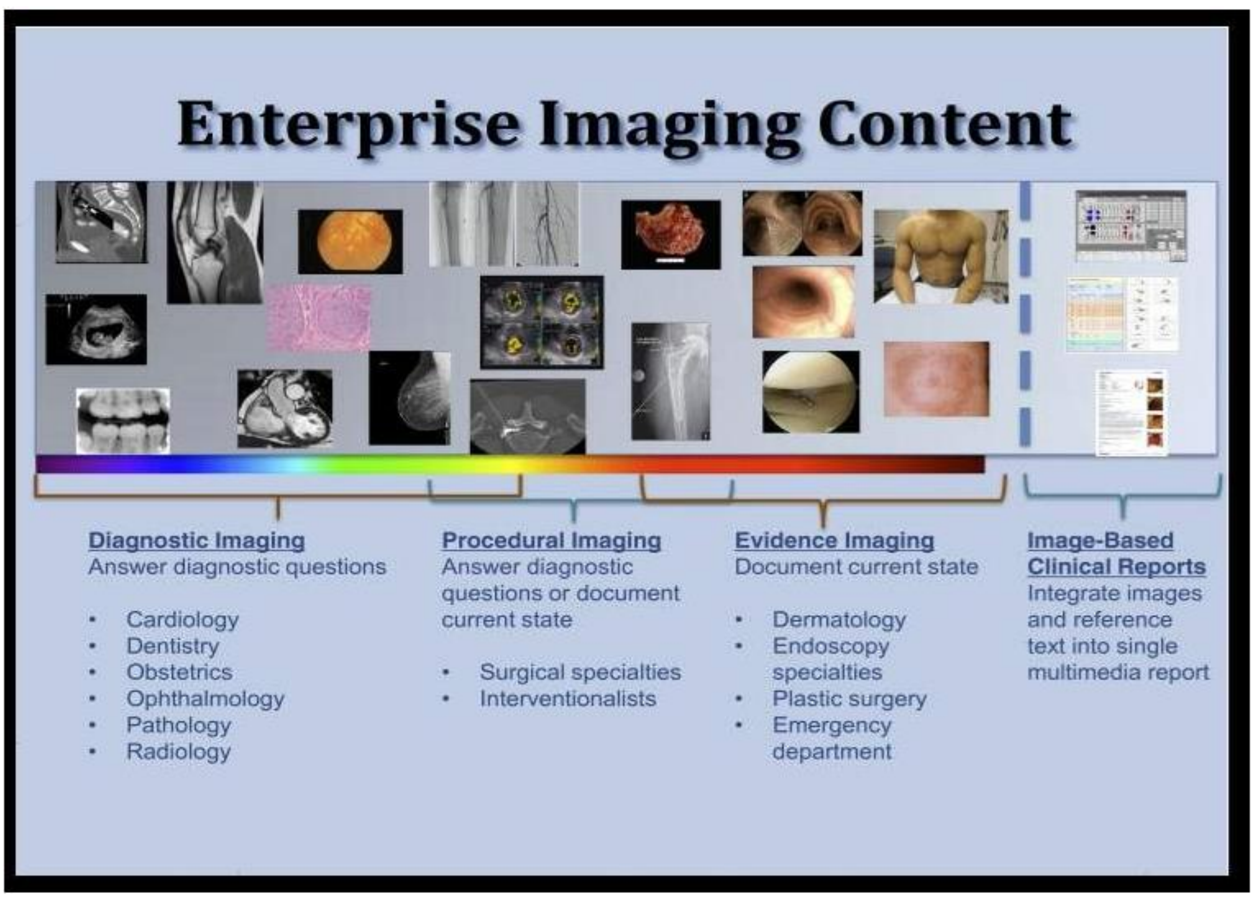
In modern medicine, each medical specialty obtains and consumes images during their delivery of care. These images allow providers of all specialties to better understand the diseases afflicting their patients. Unfortunately, current electronic health records focus only on textual/numeric data and largely avoid imaging data. The enterprise imaging community aims to build the imaging pillar of an electronic health record, raising awareness for the role of imaging and advocating for change.

Enterprise Imaging Community defines enterprise imaging as "a set of strategies, initiatives and workflows implemented across a healthcare enterprise to consistently and optimally capture, index, manage, store, distribute, view, exchange, and analyze all clinical imaging and multimedia content to enhance the electronic health record [15].

Medical images, whether still or in video format, can be acquired for one of three purposes: diagnosis, documentation/evidence, or procedural guidance. Diagnostic imaging is defined as "imaging obtained to elicit a differential diagnosis or confirm a clinical suspicion [15]." Examples of diagnostic imaging include abdomen/pelvis CT obtained in the assessment of right lower quadrant abdominal pain, echocardiogram obtained to assess cardiac function, and whole slide pathology obtained to provide a histologic tumor diagnosis.

Images obtained for documentation/evidence purposes are defined as those "images captured primarily for documentation of a patient's current state [15]." Examples of documentation/evidence photos include photographs of the skin showing the current state of infection, a video showing a patient's gait after diagnosis of Parkinson's disease, and photographs in the emergency room showing the effect of trauma. Forensic images are a special type of document/evidence images obtained to be used as a part of legal proceedings.

Finally, procedural images are images "obtained before, during, and after surgical and percutaneous invasive procedures. These images are intended to establish relevant procedure anatomy, guide a surgical approach, document timestamps of salient procedure events using modality-generated metadata, or confirm post-procedure conditions such as stent deployment [15]." Examples of procedural images include ultrasound images obtained during a renal biopsy, fluoroscopic images obtained during orthopedic hardware placement, and photographs obtained during arthroscopic knee surgery.



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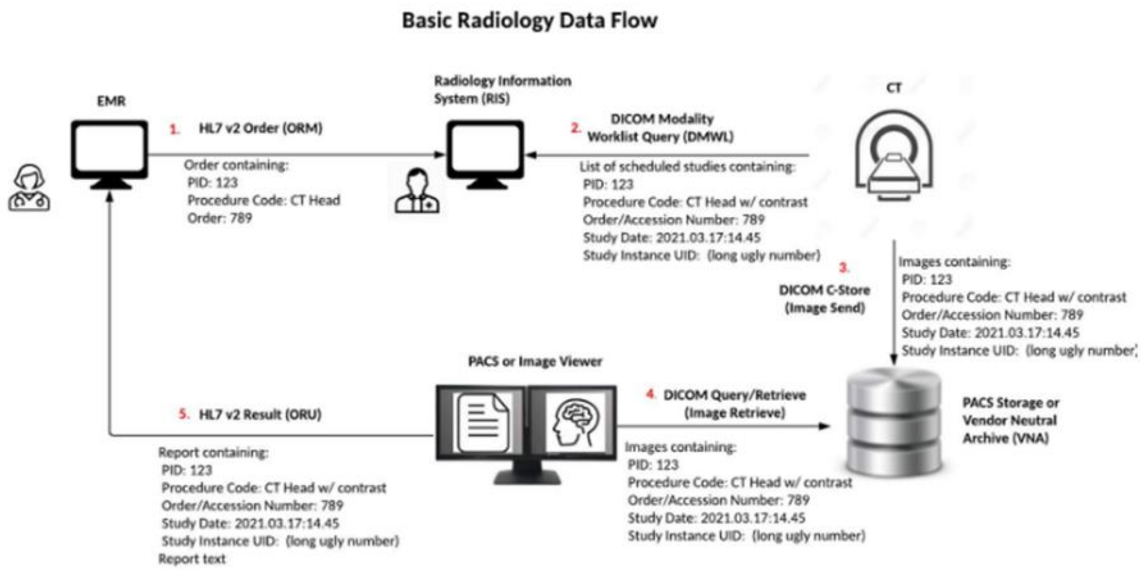
Roth CJ, Lannum LM, Persons KR. A Foundation for Enterprise Imaging: HIMSS-SIIM Collaborative White Paper. J Digit Imaging. 2016 Oct;29(5):530-8.1-

The next component of enterprise imaging to explore are the "strategies, initiatives, and workflows." These terms represent the work needed to plan, design, implement, and support enterprise imaging. Governance is crucial for each of these steps as imaging informaticists must balance the needs of the organization with those from each specialty.

Finally, the verbs to "capture, index, manage, store, distribute, view, exchange, and analyze [15]" represent all of the actions that must be accounted for when developing, implementing, and supporting an enterprise imaging program.



II. Healthcare Information and Management Systems Society (HIMSS)

The Digital Imaging and Communications in Medicine (DICOM) Standard is the digital backbone of modern radiology. Universally supported by radiology and cardiology equipment (and, increasingly, radiotherapy, ophthalmology, dental, pathology, dermatology, veterinary, and other imaging specialties), the Standard is designed to cover routine clinical practices from scheduling exams, to acquiring, storing, processing, displaying, reporting, and distributing images and related data.

Metadata is what turns a bunch of pixels into a medical record. The DICOM metadata captures details about the patient, the order, the procedure performed, and the imaging technique so the image can be properly interpreted.

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Fundamentals Of Precision Medicine and Evidence Based approaches in:

"Orbital Inflammatory Disorders"

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Contents:

1) Overview of Orbital Inflammation/Unmet Needs

Khazaei H, Khazaei D, Ashraf DC, Mikkilineni S, Seethapathy Prasad, Ng JD. Overview of Orbital Inflammation/Unmet Needs. J Ophthalmology 2022, 7(2): 000245. https://doi.org/10.23880/oajo-16000245

Abstract: Diseases of the orbit and periorbital eye tissues manifest in a wide variety of clinical presentations. Space occupying lesions in the orbit include infections, inflammations, vascular malformations, and malignancies. The significant variation in presentations is due to the complex anatomy of the orbit and the heterogeneous nature of the multiple disease processes that present themselves as orbital inflammatory processes. Additionally, although specific disease entities often show similar patterns of orbital tissue involvement, there is still a spectrum of clinical presentations within disease processes, which furthermore overlap with other inflammatory etiologies. This heterogeneity creates a significant challenge in determining specific diagnoses and subsequently instituting timely medical and surgical management of patients with orbital inflammation. Despite advances in imaging, physical examination, and laboratory tests, a biopsy is often needed for diagnosis and to guide treatment. Unfortunately, the biopsy is too often read as non-specific or idiopathic inflammation, a term that gives minimal guidance to the patient or to the clinician. There is clearly a need for developing more specific and sensitive clinical diagnostic testing.

2) Spectrum of orbital inflammatory Disorders

Dr. Hadi M Khazaei, Dr. G. Seethapathy. Spectrum of orbital inflammatory Disorders
ISSN (online): 2582-8940 Volume: 03 Issue: 02 April-June 2022 Page No: 35-38 DOI: https://doi.org/10.54660/Ijmabhr.2022.3.2.3(International Journal of Medical and All Body Health Research)

Abstract: Knowledge of the incidence and distribution of inflammatory responses can help clinicians understand orbital disorders, and establish standard protocols for appropriate treatments, including those conditions that warrant immediate attention. The orbital compartment contains a variety of tissues arranged in a fashion reminiscent of Pandora's box. These tissues can be independently involved in a plethora of disorders which can impose a number of sight-threatening risks. Many prior studies of these matters have laid a foundation for understanding the approximate incidence of various orbital pathologies.

3) The potential of tear proteomics for diagnosis and management of orbital inflammatory disorders including Graves' ophthalmopathy

Hadi Khazaei, Danesh Khazaei, Rohan Verma, John Ng, Phillip A. Wilmarth, Larry L. David, James T. Rosenbaum. The potential of tear proteomics for diagnosis and management of orbital inflammatory disorders including Graves' ophthalmopathy. Experimental Eye Research 213 (2021) 108813

Abstract

Background: Orbital compartments harbor a variety of tissues that can be independently targeted in a plethora of disorders resulting in sight-threatening risks. Orbital inflammatory disorders (OID) including Graves' ophthalmopathy, sarcoidosis, IgG4 disease, granulomatosis with polyangiitis, and nonspecific orbital inflammation constitute an important cause of pain, diplopia and vision loss. Physical examination, laboratory tests, imaging, and even biopsy are not always adequate to classify orbital inflammation which is frequently deemed "nonspecific". Tear sampling and testing provide a potential "window" to the orbital disease process through a non-invasive technique that allows longitudinal sampling as the disease evolves.

Using PubMed/Medline, we identified potentially relevant articles on tear proteomics published in the English language between 1988 and 2021. Of 303 citations obtained, 225 contained empirical data on tear proteins, including 33 publications on inflammatory conditions, 15 in glaucoma, 15 in thyroid eye disease, 1 in sarcoidosis (75) and 2 in uveitis (77,78). Review articles were used to identify an additional 56 relevant articles through citation search. In this review, we provide a short introduction to the potential use of tears as a diagnostic fluid and tool to investigate the mechanism of ocular diseases. A general review of previous tear proteomics studies is also provided, with a focus on Graves' ophthalmopathy (GO), and a discussion of unmet needs in the diagnosis and treatment of orbital inflammatory disease (OID). The review concludes by pointing out current limitations of mass spectrometric analysis of tear proteins and summarizes future needs in the field.

4) THE EFFECT OF LOCAL ANESTHETICS ON TEAR PROTEOMICS

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Experimental Eye Research 213 (2021) 108813**-** Supplement Section

The procedures and methods employed for tear collection are an important first step which can dramatically affect tear analysis results.

5) Overview of Orbital Ultrasonography

Khazaei H, Khazaei D, Ashraf D, Mikkilineni S, Ng JD. Overview of Orbital Ultrasonography. Ann Ophthalmol Vis Sci. 2022; 5(1): 1028.

Abstract: Ultrasonography contains a wide selection of clinical indications. For instance, when examining a patient with ocular discomfort or pain, clinicians will use ultrasound to ensure a diagnosis of inflammation, orbital myositis, or dacryoadenitis. Imaging is often used to identify retrobulbar tissue, as well as the extraocular muscles, in patients with symptoms and suspected soft tissue enlargement secondary to Graves' disease.

There are various forms of diseases that involve the orbit and therefore the discussion of those disorders are often organized in line with the etiology (e.g., infection, inflammation, neoplasm) or by anatomic location.

6) Orbital Ultrasonography for measuring meaningful orbital inflammatory responses

Khazaei H, Khazaei D, Ashraf DC, Mikkilineni S, John D Ng. Orbital Ultrasonography for Measuring Meaningful Orbital Inflammatory Responses. Ann Ophthalmol Vis Sci. 2022; 5(2): 1030.

Abstract: Ultrasound being a portable imaging device that is capable of making fast regional estimates of body composition, is an attractive assessment tool in instances when other methods are limited (risks of contrast in MRI and or radiation in CT scan). Furthermore, much of the research suggests that it is reliable, reproducible, not only an accurate means of diagnosing Thyroid Associated Orbitopathy (TAO) pathology and predicting its clinical course, but as a way to follow the course of the disease and the response to treatment as well.

The available imaging modalities in the evaluation and management of TAO are varied, each one having advantages, disadvantages, and particular utilities. Orbital US is a widely used technique that may quantify extraocular muscle enlargement and inflammation (topographic, quantitative and kinetic echography), with the added benefits of ease, low cost, high accessibility, short exam time, and lack of radiation. The disadvantages of orbital US include poor visualization of the posterior orbit, inaccuracy in measurements, and investigator dependence.

The purpose of this review is to explain the technical principles of the ultrasound method, explain the procedures for taking a measurement and interpreting the results, evaluate the reliability and validity of this method for measuring meaningful orbital inflammatory responses, highlight the advantages and limitations of ultrasound in orbital inflammatory disorders.

7) Assessment of disease activity of Graves' using Orbital Ultrasonography

Hadi Khazaei. M.D., M.S., M.C.R.*, Khazaei D, Ashraf D, Mikkilineni S, Ng J Casey Eye Institute, Oregon Health & Science University, Portland, Oregon, 97239, USA *Corresponding author

International Journal of Research and Scientific Innovation (IJRSI) |Volume IX, Issue X, October 2022|ISSN 2321-2705 DOI: 10.51244/IJRSI.2022.91004

Abstract: Orbital ultrasound also has a wide range of clinical indications. For example, following examination of a patient with ocular discomfort or pain, clinicians can use ultrasonography to help confirm a diagnosis of scleritis, orbital myositis, or dacryoadenitis. Clinicians can use ultrasonography to evaluate retrobulbar tissue, including the extraocular muscles, in a patient with exophthalmos and suspected soft tissue expansion secondary to Graves' disease.

Although imaging can help narrow the range of diagnoses to consider, images are only useful in that they reveal patterns and locations of tissue involvement which may statistically be more common in certain disease entities.

8) Time Gain Compensation in Orbital Ultrasonography

Dr. Hadi M Khazaei, Dr. G Seethapathy. Time gain compensation in orbital ultrasonography

Volume: 03 Issue: 03 July-September 2022 Received: 20-06-2021; Accepted: 05-07-2021 Page No: 17-20 DOI: https://doi.org/10.54660/Ijma bhr.2022.3.3.2(International Journal of Medical and All Body Health Research)

Abstract: Time gain compensation (TGC) is a setting applied in diagnostic ultrasound imaging to account for tissue attenuation. By increasing the received signal intensity with depth, the artifacts in the uniformity of a B-mode image intensity are reduced. The purpose of TGC is to normalize the signal amplitude with time, compensating for depth.

When the image is displayed, similar materials should have similar brightness, regardless of depth; this is achieved by "Linear-in-dB" Gain, which means the decibel gain is a linear function of the control voltage. Gain is expressed in dB, a logarithmic ratio of the output power relative to the input power. Gain can be calculated by subtracting the input from the output levels when both are expressed in dBm, which is power relative to 1 milliwatt.

The TGC creates uniformity in the brightness of the echoes when used in conjunction with the overall gain. The best approach is to center all the TGC settings before adjusting the overall gain. After adjusting the overall gain, the TGC can then be adjusted to compensate for attenuation at specific depth. Gain is a uniform amplification of the ultrasonic signal that returns to the transducer after it travels through the tissue.

9) ORBITAL Ultrasonography a diagnosis tool in early cellulitis

Hadi Khazaei. M.D., M.S., M.C.R.*, Alireza Mobaseri. M.D, Danesh Khazaei, John D Ng. M.D, M.S, Dr. G. Seethapathy, MS, MRCS, FRCS Ed, FRCOphth. ORBITAL Ultrasonography a diagnosis tool in early cellulitis. International Journal of Research and Scientific Innovation (IJRSI) |Volume IX, Issue VII, July 2022|ISSN 2321-2705

Abstract: The term cellulitis in general parlance refers to nonsuppurative invasive infection (most commonly bacterial) of subcutaneous tissue. Spreading infection, poor localization in addition to cardinal signs of inflammation are the hallmark of cellulitis. Cellulitis can be complicated by spread of infection to the underlying deeper structures with progressive tissue destruction & ulceration with release of bacterial toxins. (1) Orbital cellulitis is an infection of the fat and ocular muscles of the orbit posterior to the orbital septum. It is classically distinguished clinically from pre-septal cellulitis by the presence of pain with eye movement and proptosis on physical examination (1, 2). What makes cellulitis in the preseptal, orbital & retro-orbital soft tissue regions different from generalized cellulitis are the transitional anatomical differences from preseptal (Eyelid skin) to adnexal/orbital to intracranial structures and the presence of well recognized anatomical/surgical sub-compartments. Preseptal cellulitis follows pattern similarities to generalized cellulitis characterized by eyelid edema, eyelid erythema, local rise of temperature and tenderness. Unlike pre-septal cellulitis, orbital cellulitis is considered a medical emergency. If left untreated, it can lead to permanent vision loss, brain abscesses, meningitis, and cavernous sinus thrombosis (3). Though the diagnosis of orbital cellulitis can be made clinically, imaging modalities such as computed tomography (CT) and Orbital Ultrasonography are commonly used to confirm the diagnosis. (4) The present study was designed to provide sequential imaging to visualize the disease progression.

10) Facial Ultrasonography in acquired facial lipoatrophy

Hadi Khazaei M.D., M.S., M.C.R., Danesh Khazaei, Dawn Brundage, Shravani Mikkilineni M.D., Roger A.Dailey M.D., FACS. Facial Ultrasonography in acquired facial lipoatrophy. International Journal of Research and Scientific Innovation (IJRSI) |Volume IX, Issue V, May 2022|ISSN 2321-2705

Abstract: Facial lipoatrophy refers to the loss of adipose tissue and is manifested by flattening or indentation of the convex contours of the face while lipodystrophy is a wider term associated with abnormalities of fat tissue distribution and its metabolism, leading to excessive loss and/or accumulation of adipocytes. Although the management of facial lipoatrophy is very important for a patient's social life and mental health, no treatment framework has been developed due to the unknown nature of the disease manifestation. Early recognition and treatment of the active stage of connective tissue diseases is of essential significance in prevention of subsequent scarring and atrophic lesions. Diagnostic techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and ultrasonography (USG), are used to measure the severity of the lipoatrophy. The present study was designed to provide sequential imaging to visualize the disease progression.

11) Ultrasonography of Lacrimal Gland involvement in systemic Sarcoidosis

Hadi Khazaei. M.D., M.S., M.C.R.*, Danesh Khazaei, Kaneez Abbas, Davin Ashraf, John D Ng. Ultrasonography of Lacrimal Gland involvement in systemic Sarcoidosis. International Journal of Research and Innovation in Applied Science (IJRIAS) |Volume VII, Issue XI, November 2022|ISSN 2454-6194

Abstract: Lacrimal gland lesions generally present as palpable masses in the superolateral aspects of the orbits. Approximately 50% of lacrimal gland masses are inflammatory lesions, 25% are lymphoid lesions or lymphoma, and the other 25% are salivary gland type tumors. Although there are overlaps and exceptions, features such as laterality, portion of gland involvement, presence or absence of bony findings, enhancement pattern, and clinical presentation are valuable in differentiating among lacrimal gland lesions. The 3D ultrasound has been used to define lacrimal gland shape, size, density, structural features the pattern of blood supply, as well as the anatomic and topographic position in the orbit. The study was conducted in the B- and 3D-modes of ultrasonography with color and energy Doppler mapping on both sides

12) Ultrasound Tomography (3D) Triage for Oculofacial emergencies- new paradigms

H. Khazaei, Danesh K., D. Ashraf, Shravani M., John D Ng. Ultrasound Tomography (3D) Triage for Oculofacial emergencies- new paradigms. Journal of Radiology Research and Diagnostic Imaging. 1(1); DOI: 10.0810/ JRRDI.2022/0001

Abstract:

Background: The incidence of ocular trauma has been on the rise for the past few years. This impels the medical community to be more adroit at diagnosing and treating these injuries. An effective way to diagnose different manifestations of ocular trauma involve the use of ultrasound to visualize the anatomical details of the eye and orbit, which is vital for deciding the best management plan.

Aim: To assess the suitability of 3D Ultrasound as a first-line investigation for oculofacial emergencies resulting from projectile and blast injuries.

Methods: In this review article, the focus of discussion will be the accuracy of 3D ultrasound in diagnosing oculofacial injuries and the utility of ultrasound in triage of vision threatening emergencies in austere environments.

Results: Understanding the utility of ultrasound data for diagnosis will assist ophthalmologists in managing ocular trauma more effectively.

Conclusion: We recommend that patients with suspected eye injuries should undergo careful 3D ultrasound examination by appropriately trained ophthalmologists as a part of triage for oculofacial emergencies in austere environments.

13) Ultrasonographic Characteristics of the Facial Nerve in Patient with Bell's Palsy

Khazaei H, Khazaei D, Ashraf D, Mikkilineni S, Ng JD. Ultrasonographic Characteristics of the Facial Nerve in Patient with Bell's Palsy. Ann Ophthalmol Vis Sci. 2022; 5(1): 1029.

Abstract: Peripheral facial paralysis is a diagnostic challenge. Because 10% of the patients referred with a diagnosis of Bell's palsy were found to have a treatable, progressive, or life-threatening lesion, effort should be made to diagnose the cause. Acute facial palsies are mostly "idiopathic" (Bell's palsy) but it is a diagnosis of exclusion, therefore cases of acute acquired, isolated peripheral facial paralysis should be investigated thoroughly.

The purpose of this article is to explain the principles of the ultrasound techniques, outline the procedures, measurements and interpretation of the results, evaluate the reliability and validity of this method for meaningfully measuring inflammatory responses, and to highlight the advantages and limitations of ultrasonography in patients with Bell's palsy.

14) M-Mode ultrasonography in ocular emergencies

Hadi Khazaei. M.D., M.S., M.C.R.*, G. Seethapathy, MS, MRCS, FRCS Ed, FRCOphth , Alireza Mobaseri. M.D., Danesh Khazaei, John D Ng. M.D, M.S(2022).

M-Mode ultrasonography in ocular emergencies International Journal of Research and Scientific Innovation (IJRSI) |Volume IX, Issue IX, September 2022|ISSN 2321-2705

Abstract: M-Mode, or time-motion display, allows a single beam to emit from the ultrasound transducer along a defined track in conjunction with a recorder that captures all motions that occurs along the path. This mode allows high temporal resolution, thus affording the examiner an excellent view of subtle motions. Clinically, this mode is ideal for capturing vessel diameter changes, movement of cardiac valves, and detecting fetal heartbeats.

The use of the M-mode or time-dependent intensity modulated ultrasound technique for ophthalmologic investigations are described here. This technique provides the investigator with a means for monitoring structural changes in the eye during physiologic or pharmacologic experimental conditions, or a combination of both, and is particularly useful in studying optically inaccessible structures. The technique has been used to study accommodation changes in axial length and lens thickness as well as the rate of such changes and to study vascular pulsations and choroidal thickness changes at the rear wall of the eye.