Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/17258
DOI URL: http://dx.doi.org/10.21474/IJAR01/17258

RESEARCH ARTICLE

ULTRA HIGH-FREQUENCY ULTRASOUND - AN EMERGING IMAGING DIAGNOSTIC TECHNIQUE FOR ORAL MUCOSAL LESIONS

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Manuscript Info

Manuscript History
Received: 15 May 2023
Final Accepted: 19 June 2023
Published: July 2023

Key words:-
Oral Mucosal Lesions, Conventional Ultrasonography, Ultra High Frequency Ultrasound (UHFUS)

Abstract

In day-to-day practice, we give diagnosis of oral soft tissue lesions like oral lichen planus, pemphigus vulgaris, mucous membrane pemphigoid (MMP), leukoplakia, erythroplakia by history, clinical examination, and histological findings. But imaging modalities are never used for the diagnostic purpose of the above-mentioned lesions, though conventional ultrasonography (US) has been routinely used for the evaluation of various pathologies of maxillofacial region with frequency ranging from 3-15 MHz. Ultra-high frequency ultrasound (UHFUS) is an emerging ultrasonographic technique which uses higher frequency ranging from 30-100 MHz (mainly 70 MHz), this limits the depth of penetration upto 10mm from surface and increases the resolution of images upto 30 µm. UHFUS usesintraoral ultrasonographic machine with 70 MHz probe for scanning two acquisitions i.e., B-mode and C-mode. Biomarkers used for diagnosis are growth pattern, epithelial thickness, echogenicity and vascularization. Thus, clinicians can give confirmatory diagnosis of oral mucosal lesions prior to histology. This article provides overview of imaging principles, underlying technology and in particular focuses on the emerging role of UHFUS in Oral medicine and diagnosis.

Introduction:-

Oral medicine and diagnosis practice is lacking in the confirmatory diagnostic support for oral mucosal lesions and mostly depends on histopathology. We are currently diagnosing oral mucosal lesions like leukoplakia, erythroplakia, oral lichen planus, pemphigus vulgaris, mucous membrane pemphigoid, etc. through history taking, clinical examination, and histological findings.[1,2,3,4,5]Using an imaging technique for the investigation of oral mucosa and their alterations become very big support to the clinical diagnosis.[6]

Conventional ultrasonography (US) is very useful diagnostic imaging technique for evaluation of swellings of the head and neck like tumours, cysts etc, detection of pathologies of salivary gland[7] and to evaluate calculi of the duct of salivary glands, detection of the relationship of the vasculature structures and vascularity of masses with the addition of colour flow Doppler imaging, assessment of blood flow in the carotids and carotid body tumours. Ultrasound is also used for evaluation of depth of invasion (DOI) of oral cancer preoperatively. [8,9] and ultrasound-guided fine needle aspiration (FNA) biopsy. It is used as a tool for diagnosis,assessment of severity, and for

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evaluation of prognosis of OSMF.[14]In ultrasonography each lesion is described according to shape, margins, echogenicity, homogeneity, presence of necrosis/calcifications, and posterior echo. That's why conventional ultrasound (US) becomes very useful imaging tool in the diagnosis of head and neck swellings, salivary gland diseases[7] etc. Frequency used for conventional ultrasonography is ranging from 3-12 MHz.It is well-known that an increase in the frequencies of ultrasound leads to lowerdepth of penetration, but also provides higher resolution of the image.

Therefore,ultra-high frequency ultrasound (UHFUS) is the new emerging diagnostic imaging technique which can be used for the diagnosis of oral mucosal lesions and could become promising imaging technique for the study of oral mucosal superficial epithelium and related alterations. [6,10]As this technique provides high-resolution images of superficial structures, Oral medicine and diagnosis is a recently introduced field of application for this imaging technique. Intraoral application of this imaging focuses on study of normal anatomy as well as oral diseases.

History:-
In the mid-90s high-frequency techniques were introduced, that too in the preclinical setting, where the applications ranged from embryological development to response to chemotherapy in animal models. Later in the beginning of the 2000s,UHFUS entered the clinical setting. Initial applications of UHFUS, dermatology and angiology were predominantly involved, where conventional US technique was already available and widely employed. But later on,the development of more performing UHFUS made it possible to obtain micromillimetre resolution of small structures and a very big achievement in medical field. At present, UHFUS is used for imaging of dermatological, vascular, musculoskeletal and small parts applications.

In dentistry, both extraoral and intraoral applications of US are there. Extraoral applications mainly focus on the characterization of oral and maxillofacial swellings of various origin, while intraoral applications mostly involve the study of malignant lesions in terms of tumor thickness and depth of invasion.[6]For the intraoral study of lesions, US frequencies ranging between 10 and 15 MHz have been used with wide differences in terms of resolution and depth of penetration of the US beam. This explained that 10 MHz frequencies can reach up to 60 mm below the surface with a 0.15 mm axial resolution, while 15 MHz frequencies just arrive at 40 mm with a 0.10 mm axial resolution. After observing this the introduction of UHFUS for diagnostic imaging of oral cavity with 70 MHz frequency which can reach upto 10 mm from the surface with 30 µm axial resolution may provide a solution to the need.Recently, UHFUS application in oral medicine is becoming progressively more and more relevant.[11]

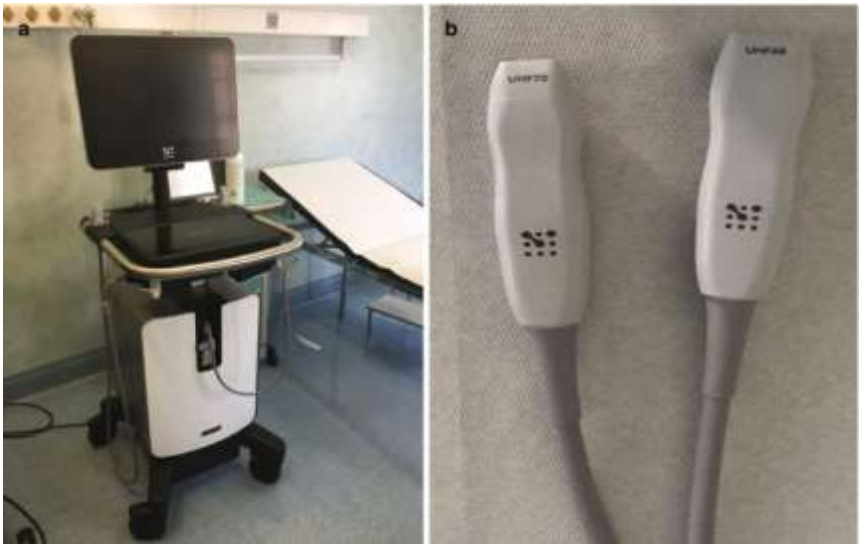
Principle Of Ultra High-Frequency Ultrasound (UHFUS):-
Frequency is inversely proportional to the depth of penetration, but with this it provides higher resolution images. UHFUS is a recently introduced ultrasonographic technique involving the use of ultrasound frequencies between 30 and 100 MHz, thus providing high spatial resolution (pixel size as small as 30 µm) at the expense of the depth of penetration, which is limited to 10 mm from the surface when using frequencies of 70 MHz.[12] Therefore, ultra-high frequency ultrasound (UHFUS) could become a valuable instrument for the study of oral superficial structures. UHFUS has proven to allow correlation between US images and histology with high specific value, in particular being able to discriminate healthy and pathological tissues, with accuracy comparable to biopsy.The possibility of obtaining high-resolution images has thus expanded UHFUS applications to human studies in several medical and dental fields. [11,12]

Acquisition Of UHFUS:-
UHFUS uses an ultrasonographic machine with an intraoral probe mainly of 70 MHz.The probe is covered with plastic cover to avoid cross infection. Ultrasonographic gel is used as interference or couplant and applied on probe and on plastic cover. Gel is used to avoid artefacts caused by plastic cover.[12]

Two acquisitions i.e., B mode and C mode, taken to evaluate any mucosal lesion. So, every lesion is scanned twice, and acquisitions are taken with the probe placed perpendicular to the mucosal surface.These acquisitions are always taken using a standardized protocol with keeping the parameters of gain, time gain compensation, dynamic range, mechanical index, and thermal index constant. Gain is set at 31 and 38 dB so that differences in echo- structure is enhanced.[6,13]

B mode is the brightness mode which is used to analyze the epithelium thickness, growth pattern and echogenicity of the lesion.Axial and longitudinal acquisitions of B-mode images are taken for diagnosis of mucosal lesions.[13]

C mode is the colour doppler mode which is used to analyze the intensity and direction of the blood flow. This is with a setting scale of +/- 1.9 cm/sec to detect blood vessels with a low flow rate.[13]



Ultrasonographic Machine With probe of 70 MHz

Image Analysis:-
The scans taken are viewed in DICOM format images and processed. Lesion analysis is done by following biomarkers:
growth pattern, mucosal thickness, echogenicity, and vascularization [10]

Growth pattern :-
Depending upon the development of lesion this growth pattern is classified into
two types: -
Flat/Endophytic and Exophytic.
1) Flat/Endophytic:- Lesions which are upto or below the epithelial surface.
2) Exophytic:- Lesions which are above the epithelial surface.

Mucosal thickness :-
Epithelial thickness is the distance between epithelial surface and the lower margin of submucosa. These values are compared with normal mucosal thickness given below and accordingly classified as increased, normal, decreased, or varied.[10]
Values of normal mucosal thickness:-
1. Tongue :- mucosa 0.4 and submucosa 0.5 mm.
2. Buccal mucosa :-mucosa 0.5 mm and submucosa 1.2 mm
3. Gingiva :- 1.2 mm
4. Lip :- mucosa 0.3 mm and submucosa 0.9 mm
5. Palate :- 2.5 mm

Echogenicity :-
Echogenicity is given after retrieving gray value distribution. ROI (region of interest) is selected. Then gray value of each pixel in that ROI is taken between 0-255. 0 is the black pixel and 255 is white pixel. The processing software automatically retrieve the mean gray value of that ROI and this is compared with the normal gray value of mucosa. And after comparing, that lesion is defined as hypoechoic, hyperechoic and same echogenicity.

Vascularization :-
Vascularization is analysed in Colour Doppler mode (C mode). It is classified as low, moderate, and severe flow.

So, frame is decided depending upon the lesion location. In this frame if vascularization is <30% of the frame then it is mild vascularization. If the vascularization is between 30-60 % then it is moderate vascularization. And if the vascularization is more >60 % then it is severe vascularization. Blood flow is shown in Colour Doppler mode using the red/blue color coding, with red representing blood motion toward the probe and blue the motion away from the probe.

UHFUS findings of oral mucosal lesions:-

R.Izzetti and S. Vitali studied UHFUS in oral mucosal lesions like oral lichen planus, pemphigus vulgaris, mucous membrane pemphigoid (MMP), leukoplakia, erythroplakia. Patients with clinical and histological diagnosis of these lesions were enrolled in the study. Then lesions were evaluated by means of intraoral UHFUS performed at 70 MHz, using B-mode and C-mode.[10,12,13]

Findings :-

- Oral lichen planus :-

-B mode shows thick mucosal superfacial layer with hypoechoic echogenicity.
-C mode shows mild vascularization.

- Pemphigus vulgaris :-

-B mode shows hypoechoic or anechoic structures within mucosa i.e., intraepithelial localization.
-C mode shows moderate vascularization.

- Mucous membrane pemphigoid (MMP) :-

-B mode shows loss of demarcation of mucosa and submucosa with homogeneity of submucosa.
-C mode shows intense vascularization with aliasing phenomenon.

- Leukoplakia :-

-B mode shows regular echogenicity with mucosal thickening.
-C mode shows moderate vascularization.

- Erythroplakia :-

-B mode shows hyperechogenicity with mucosal thickening.
-C mode shows mild vascularization.

Discussion:-

In oral medicine, oral mucosal lesions like oral lichen planus, pemphigus vulgaris, mucous membrane pemphigoid (MMP), leukoplakia, erythroplakia are diagnosed clinically, with the support of biopsy to obtain histological confirmation. As oral anatomy is very complex and the presentation of oral diseases are variable, which can make diagnosis equivocal, thus it highlights the need for non-invasive diagnostic imaging to support clinical examination.[6,11,12] If we define characteristics of oral mucosa and describe oral anatomy preoperatively this could improve the performance of surgical biopsy and vascular and nervous structures are preserved.[12] Technological advancement with the introduction of UHFUS for clinical use may therefore provide a solution to the need for diagnostic imaging of oral cavity in the diagnostic and surgical phases of the treatment.UHFUS is an effective tool for the investigation of the oral mucosa.Conventional US has been previously employed for the intraoral evaluation of malignant lesions. Although conventional US appears effective in evaluating tumor thickness and depth of invasion of oral cancer, the great variability in terms of frequencies and scan protocols makes it difficult to compare the results obtained. Ultrahigh frequencies overcome the limitations of conventional US because it allows the image of first 10 mm thickness of the mucosa at high resolution.The routine application in the practice of oral medicine can support clinical examination, which to date is mostly employed for the diagnosis of oral lesions, in absence of dedicated diagnostic imaging techniques.[11,12]

However, some limitations are there mostly related to the size and shape of probe for intraoral UHFUS scanning. In particular, the size of the probe affect the performance of intraoral UHFUS examination during scanning of posterior sites of the oral cavity and shape affect during scanning of floor of the mouth.[6] While during palate scanning oblique probe angulation required due to the presence of teeth, which lead to increased measurements for mucosal thickness.Also the limited penetration depth of the US beam allows to scan only the more superficial regions,in particular, 48 MHz frequencies have a depth of penetration of 23.5 mm, while 70 MHz frequencies allow the imaging of the first 10.0 mm below the scanning surface. Additionally, a training period for the operators is usually required to achieve the manual skills to properly manage the probe during the scan and the confidence for an accurate interpretation of the images.Besides these limitations, the study of oral mucosa by means of UHFUS seems

extremely promising, suggesting a potential role in supporting the clinician in the everyday clinical practice of oral medicine.[11]

This unique characteristic has favoured the diffusion of UHFUS in all the fields where the detailed investigation of small anatomy is required.

Conclusion:-

Ultra-high frequency ultrasonography applications involves an increasing number of medical and dental fields. The high spatial resolution and the superb image quality achievable allow to foresee a wider use of this novel technique, which has the potential to bring innovation in diagnostic imaging.[11,13]

The advantages of ultrasonographic techniques in terms of non-invasiveness, repeatability, and relatively low cost make UHFUS the avant-garde in ultrasonography, which has still to be fully explored in all its possibilities. [11,12] Its features give insight into the potential role of UHFUS in the diagnosis, surgical planning, and follow-up of various pathologic conditions in several medical fields. The literature on UHFUS is still evolving, but ultra-high frequencies seem the answer to several clinical problems related to the high-resolution investigation of both normal anatomy and disease processes.

Although further research should be done on larger samples, to have better assess of potential role of UHFUS in the diagnosis of oral lesions.

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