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Pre-Surgical Evaluation of Non-Melanoma Skin Cancers Using High-Frequency Ultrasound

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ABSTRACT

Background: High-frequency ultrasound imaging is increasingly used as a noninvasive, accurate, and real-time method to evaluate non-melanoma skin cancers (NMSC). It plays a complementary role in the physical examination and the detection margins of skin cancers.

Objectives: This study investigates the efficacy and accuracy of high-frequency ultrasound as a complementary method to ensure complete elimination of skin cancers with maximum preservation of function and aesthetics, with postoperative confirmation based on histopathological examination.

Patients and Methods: This was a cross-sectional study. Forty-nine skin lesions in forty-seven patients underwent preoperative ultrasound examination using (6-19 MHz) probes. Ultrasound examination included lesion nature, thickness, invasion depths, and the subsequent excision size of the lesion circumferentially and in-depth.

Results: Forty patients had forty–two lesions. Ultrasound had the ability to differentiate skin cancers from fibrosis and to detect subclinical lesions extensions with better clearance of malignancy.

Conclusion: High-frequency ultrasound can provide additional information for preoperative evaluation of non-melanoma skin cancers with maximum preservation of function and aesthetics in addition to be a valuable non radiating tool for postoperative follow up for NMSC after surgical excisions to determine the presences or absence of early recurrence before skin ulceration.

Key words: High-frequency ultrasound, Non-melanoma skin cancers

INTRODUCTION

Skin cancers such as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are referred to as "non-melanoma skin cancer" (NMSC). The most efficient course of action for the majority of NMSCs is surgical excision with a safety margin [(1)].

A special non-invasive and non-radiating medical imaging method for examining skin malignancies is ultrasound. Lesion size in three dimensions; (length, width, and depth), morphology, inner structure, homogeneity, foci of calcifications or necrosis, location, and extension can all be determined with the aid of imaging techniques. Planning surgical excision with a free safety margin is greatly aided by the rich anatomic information offered by sonography [(2)].

A wide range of frequencies are used by transducers in contemporary digital ultrasound systems. High frequency ultrasound (HFUS), which has a frequency range of 6 to 18 MHz, is a relatively new method that can clearly define deeper structures and skin layers. By precisely defining the tumor margins for surgical excision and aiding in the early diagnosis of recurrence, HFUS can characterize lesions in the submillimeter range (down to 0.1 mm), reducing the rate of recurrence [(3)].

To avoid incomplete excision, the need for re-intervention, and to prevent functional and cosmetic defects, the assessment of tumor margins is crucial in the surgical planning of cutaneous cancers, especially in tumors that mainly involve the head and neck, face, and sun-exposed regions [(4)].

The most frequent type of skin cancer detected is basal cell carcinoma (BCC), which appears on ultrasonography as heterogeneous hypoechoic lesions with irregular contours and dense focal internal echoes (Figures 1A, B, and C), while squamous cell carcinoma (SCC) has a major tendency to local recurrence and frequent lymph node involvement. The tumor growth causes infiltration of the adjacent tissue and erosion of the underlying layers such as cartilage and bones.

On ultrasonography, it appears as homogeneous hypoechoic lesions with irregular margins (Figures 2A, B, and C) [(5)].

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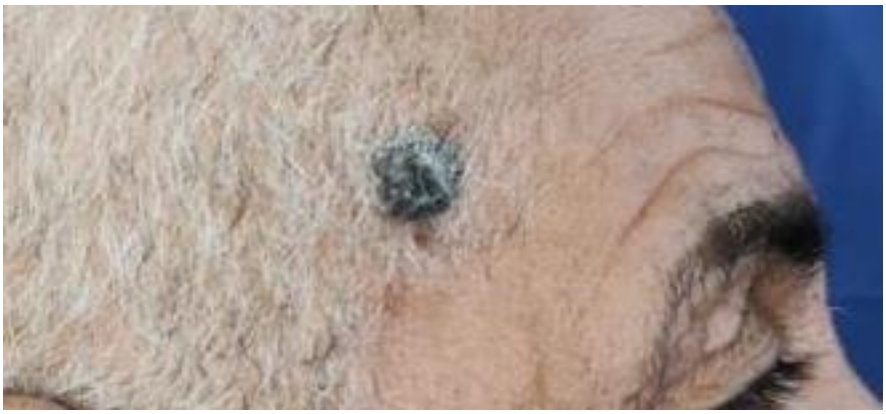
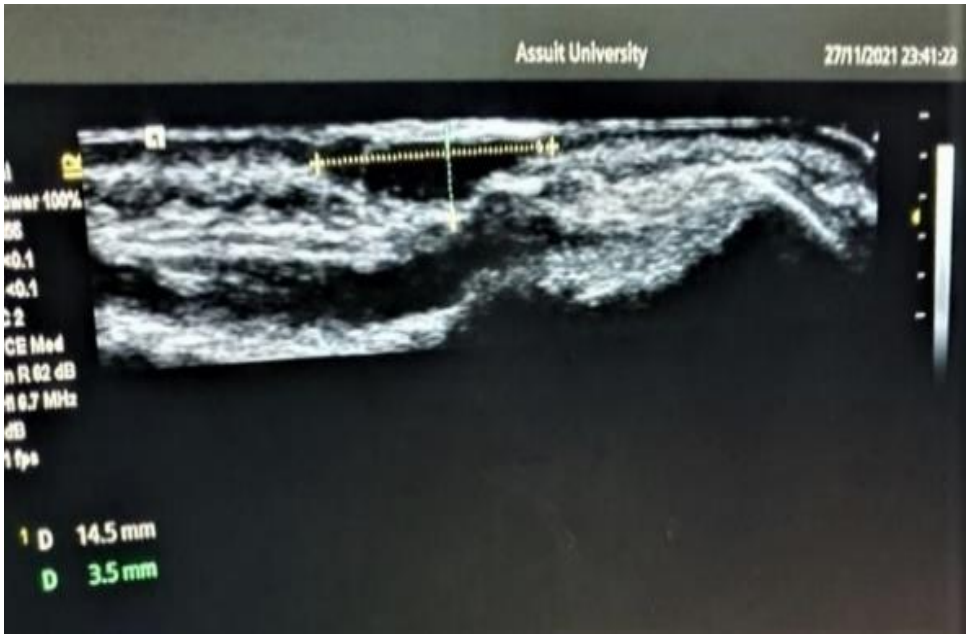
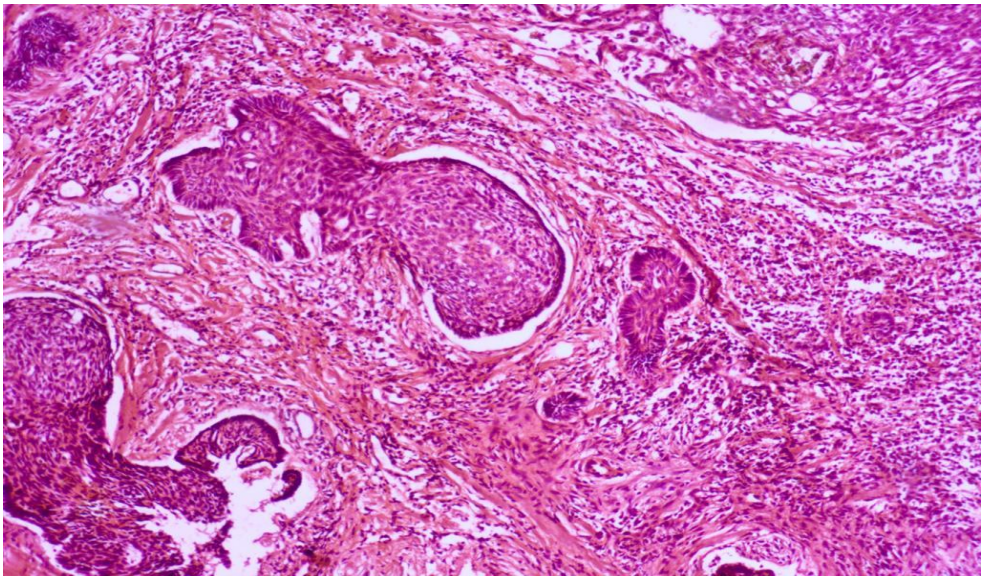


Figure 1: (A) Basal cell carcinoma on RT temple, seen as a pigmented nodular lesion with rolled-in edge

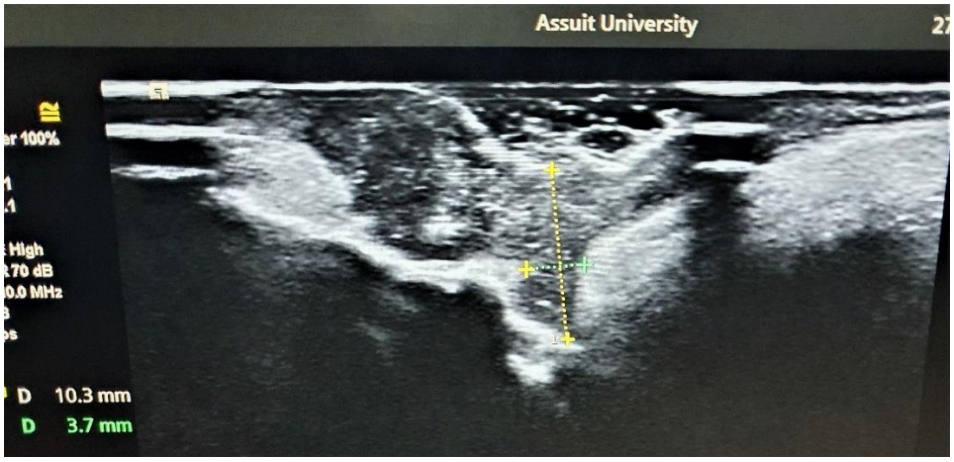


(B) High frequency ultrasound shows an irregular, hypoechoic, heterogeneous lesion in the dermis, with posterior shadowing

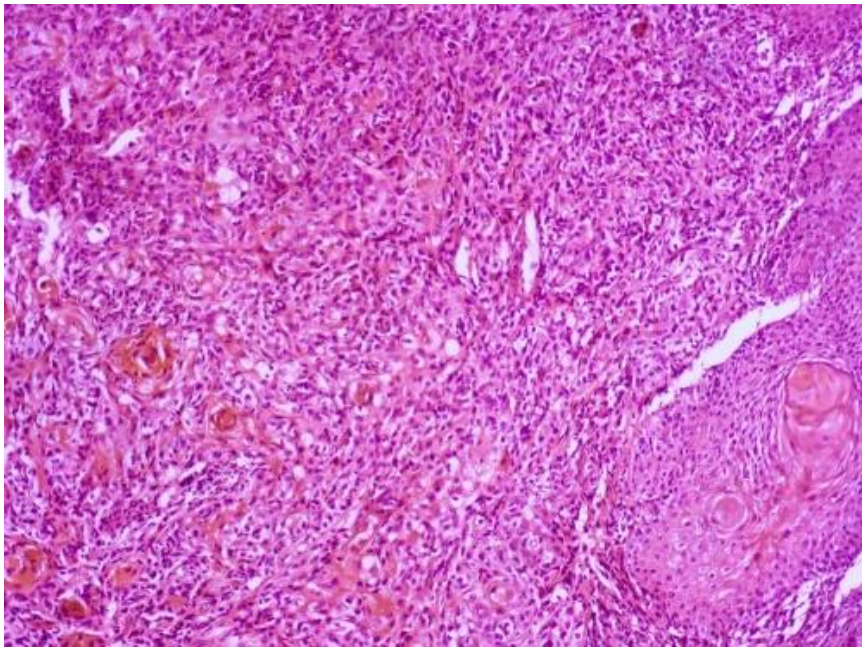


(C) Basal cell carcinoma, Hematoxylin & eosin 20x

Figure 2: (A) Invasive squamous cell carcinoma at the inner canthus of LT eye infiltrating the adjacent tissue with the erosion of underlying structure.



(B) High frequency ultrasound shows irregular, hypoechoic, heterogeneous lesions invading the dermis and subcutaneous layers, with loss of normal cutaneous architecture



(C) Squamous Cell Carcinoma, Hematoxylin & eosin 20x

The purposes of this study were;
A) to assess the ultrasonographic features,
B) to measure the unknown lesion depth, and
C) to determine the diagnostic accuracy of HFUS technology in the excision and reconstruction of non-melanoma skin lesions.

PATIENTS AND METHODS

A cross-sectional study was conducted at Assiut University Hospital, Egypt, between January 2018 and March 2020.

Forty-nine lesions in forty-seven patients were enrolled in this study, who presented with a clinical suspicion of non-melanoma skin lesions. Scanning by ultrasound with (MyLabSeven; Esaota, Genova, Italy) imaging system using (an SL2325) linear probe with high frequency (6-19 MHz) after the application of thick layer of US gel and measuring both lateral margins and deep margin in millimeters was performed.

Safety margins were determined with subsequent surgical excision of the lesion based on ultra-sonographic evaluation with a surgical margin of approximately 3 to 5 mm, depending on the location and limits of the margins and defect followed by histopathological evaluation of the resected specimens after being marked for orientation and fixed with 10% formaldehyde solution and stained with hematoxylin and eosin and examined using light microscopy to define structural morphology and to ensure complete elimination of lesions.

Ethical approval:

This work was conducted in accordance with the Code of Good Practice and the guidelines of Declaration of Helsinki and being approved by the Medical Ethics Committee of the Faculty of Medicine at Assiut University. Informed consent was obtained from each patient.

Statistical analysis

Data were collected and analyzed by using SPSS (Statistical Package for the Social Sciences, version 20, IBM, and Armonk, New York).

Quantitative data were expressed as mean ± standard deviation (SD) and range. Nominal data were given as a number (n) and percentage (%). Diagnostic accuracy of ultrasound in the prediction nature of the lesion and assessment of the safety margin was determined by the receiver operator characteristics curve. Level of confidence was kept at 95% and hence, P value was considered significant if < 0.05.

RESULTS

The most frequently affected sites were the nose (23.80%), cheek (21.40%), and eyelid (11.9%). Other affected areas are summarized at table (1).

Table 1: Affected sites in the studied patients

Site of the lesion	
Nose	10 (23.80%)
Cheek	9 (21.40%)
Eyelid	5 (11.90%)
Leg	3 (7.10%)
Lip	3 (7.10%)
Scalp	3 (7.10%)
Temporal area	2 (4.80%)
Forehead	2 (4.80%)
Others areas	5 (11.9%)

Data expressed as frequency (percentage)

It was found that mean length, width, and thickness of the lesions in the ultrasound (US) study are shown in table (2).

Table 2: Lesions characteristics in the ultrasound study of the studied patients

	N= 42
Length (mm)	18.94 ± 9
Range	5.70-37.40
Width (mm)	15.67 ± 8.33
Range	5.10-45.10
Thickness (mm)	4.68 ± 2.56
Range	1.10-13.70

Data expressed as mean ± SD, and range

Five patients had lesion margins larger than 50 mm and could not be assessed by ultrasonographic probe in single view, and two patients were failed to follow up because of death. Therefore, the final sample comprised 42 lesions in 40 patients as two patients have two lesions. Based on clinical evaluation; there were 35 (83.3%), 4 (9.5%) and 3 (7.1%) lesions of basal cell carcinoma, squamous cell carcinoma, and basosquamous carcinoma respectively.

According to safety margins including the lesion based on ultrasound evaluation of the lesions, mean safety margin was 28.69 ± 22.09 mm with range between 5 and 120 mm.

Based on the histopathological evaluation; it was found that 8 lesions were benign while 44 lesions were malignant. Also, the types of benign and malignant lesions are shown in table 3, which also shows that only four patients had infiltrated safety margin.

Table 3: Histopathological evaluation among the studied patients

	N= 42
Histopathology	
Benign	8 (19.1%)
Actinic keratosis	2 (4.8%)
Inflammatory lesion	3 (7.1%)
Seborrheic keratosis	2 (4.8%)
Nevus	1 (2.4%)
Malignant	
Basal cell carcinoma	34 (82.9%)
Squamous cell	25 (59.5%)
carcinoma	6 (14.3%)
Basosquamous	3 (7.1%)
Infiltrated safety margin	4 (9.5%)

Data expressed as frequency (percentage)

In the current study, it was found that 8 (19.1%) lesions were falsely diagnosed by clinical assessment to be malignant lesions but based on histopathology, these lesions were proved to be benign in nature.

So, for prediction nature of the lesions, clinical assessment had an overall accuracy of 81%, as illustrated in table (4).

Table 4: Accuracy of clinical assessment in prediction nature of the lesion

Indices	Value
Sensitivity	100%
Specificity	0
Positive predictive value	81%
Negative predictive value	0
Accuracy	81%
Area under curve	0.50
P value	1.00

Ultrasound assessment had 100% sensitivity and 87.5% specificity in prediction of malignant skin lesion as illustrated in table (5).

Table 5: Accuracy of ultrasound assessment in prediction of malignant skin lesion

Indices	Value
Sensitivity	100%
Specificity	87.5%
Positive predictive value	97.1%
Negative predictive value	100%
Accuracy	97.6%
Area under curve	0.94
P value	< 0.001

Ultrasound assessment of safety margin had 75% sensitivity, 63.2% specificity for assessment of safety margin, as illustrated in table (6).

Table 6: Accuracy of ultrasound in assessment of the safety margin of the lesion

Indices	Value
Sensitivity	75%
Specificity	63.2%
Positive predictive value	75%
Negative predictive value	50%
Accuracy	73.8%
Area under curve	0.65
P value	0.223

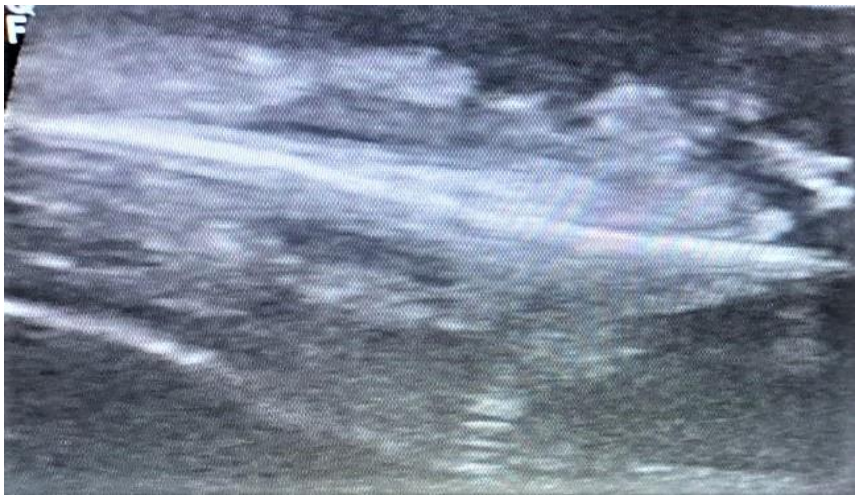
Ultrasound assessment of safety depth had 75% sensitivity, 61% specificity for assessment of safety depth as illustrated in table (7).

Table 7: Accuracy of ultrasound in assessment of the safety depth of the lesion

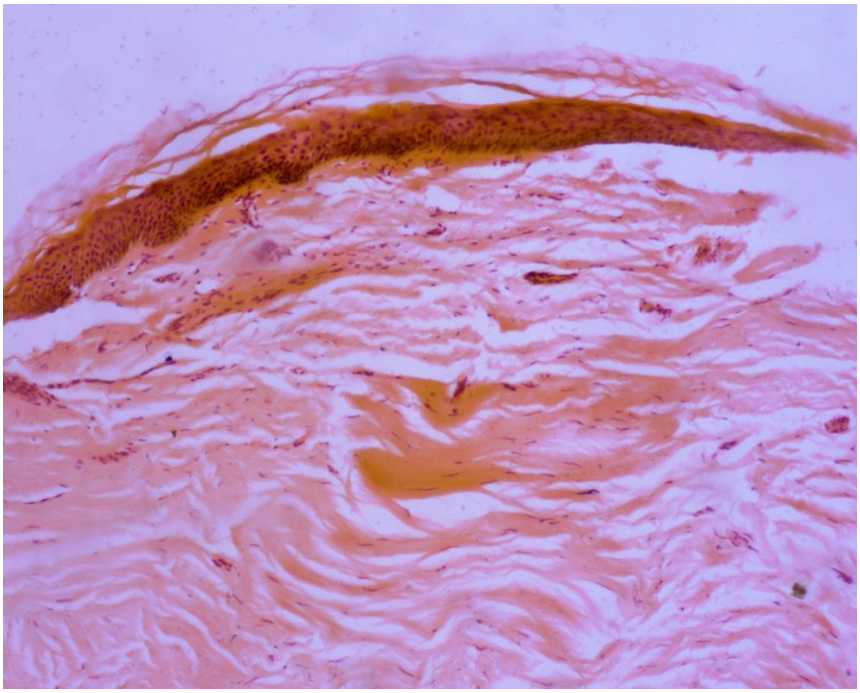
Indices	Value
Sensitivity	75%
Specificity	61%
Positive predictive value	96%
Negative predictive value	16.7%
Accuracy	74%
Area under curve	0.67
P value	0.293

In our study, a case of recurrence was suspected, and differentiation from fibrosis of previous operation was needed. Using HFUS for re-evaluation, we found no infiltration to the epidermis or to the dermis that support the diagnosis of fibrosis from the earlier intervention. This was confirmed by histopathological examination of incisional biopsy of suspected lesion (figures 3A, B, and C).

Figure 3: (A) Postoperative fibrosis of the previous excision of BCC



(B) High frequency ultrasound shows ill- defined, oval-shaped hypoechoic heterogeneous lesion infiltrating the dermis



(C) Fibrosis, Hematoxylin & eosin 20x

Actinic keratosis had an epidermal origin, was clearly defined, was highly superficial, and might be clinically misinterpreted as BCC. Since HFUS displays lesions as hypoechoic lesions with dense echoes and normal dermis, the diagnosis of keratosis was easily suspected which was confirmed by histopathological examination (figures 4A, B, and C).

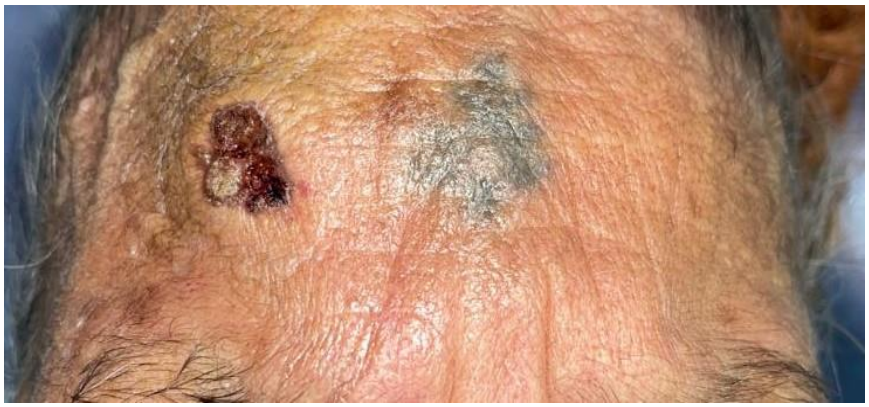
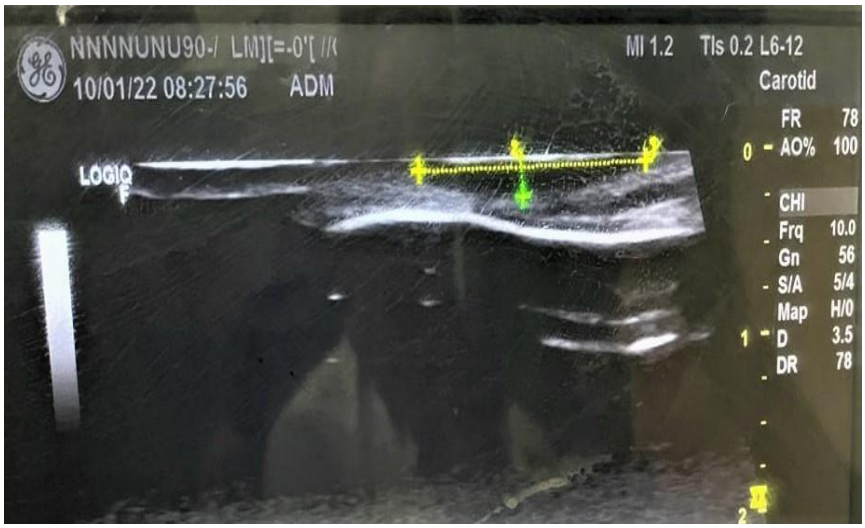
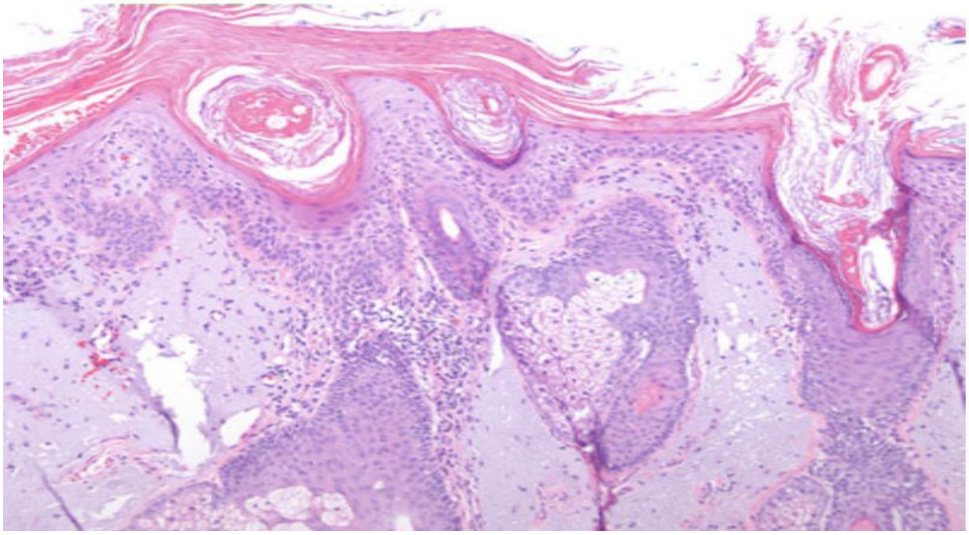


Figure 4: (A) Actinic keratosis with "ulcer" appearance on the forehead.



(B) High frequency ultrasound shows a well-defined, superficial, hypoechoic, heterogeneous lesion beneath the epidermal "entry echo," compressing the underlying dermis



(C) Actinic Keratosis, Hematoxylin & eosin 20x

DISCUSSION

The 42 skin lesions that we investigated all had recognisable ultrasound pictures. We were always able to accurately localize the tumor, evaluate its form, and estimate its thickness before surgery with good histological correlation, which is supported by **Lee** [(6)].

In addition to clinical examination, ultrasound provides additional information to improve surgical excision, particularly in cases of aggressive, high-risk lesions, the presence of nearby, subclinical lesions, or lesions that threaten critical anatomic structures (such as the ears or nose) when cartilage is being removed [(7)].

An exact assessment of the tumor diameters, including thickness (depth), as well as the level of involvement of deeper layers, are all made possible by ultrasound examination. It also allows for the quick, real-time, non-invasive detection of lymph nodes and loco-regional lesions [(8)].

Skin cancers typically appear as homogeneous hypoechoic patches on ultrasonography contrasted with the nearby healthy tissue. Along with measuring lesion borders longitudinally, transversely, and axially, it is also able to determine the involvement of deep layers like muscles, cartilage, and bones. This observation aided the surgeon in making a better reconstructive decision and enhancing the patient's cosmetic outlook [(9)].

In addition, the measurement of tumor thickness was based on the location of greatest invasion (thickness), demonstrating the effectiveness of pre-surgical HFUS evaluation. Some of the tumors reviewed were less than 10 mm in size, demonstrating that small lesions can be accurately identified even if they are asymmetric [(10)].

Using HFUS, the fine structure of the skin lesion may be better shown, and the risk level of lesions with later recurrence risk can be diagnosed, increasing diagnostic accuracy. This is consistent with the findings of **Wang *et al.*** who used preoperative ultrasonography to reveal the characteristics of the lesions to predict the probability of recurrence [(11)].

High-frequency ultrasound is a useful tool for differentiating between benign and malignant tumors since it is quick, easy, safe, promising, reasonably affordable, widely accessible, noninvasive, and readily available. By offering more objective evaluation measures, it can be used in conjunction with a physical examination to help with the diagnosis, management, and monitoring of skin malignancies. The results of **Levy *et al.*** support this [(12)].

LIMITATION

The limitations of HFUS are that;

*The first limitation is consistent with **Wortsman** and **Wortsman**[(13)] 's findings, who stated that HFUS cannot detect lesions that measure less than 0.1 mm in depth, also it cannot detect lesions that are epidermal exclusively.

*Another limitation is that probe length is 4 cm, so lesions that are more than 40 mm in length cannot be shown in a single view, as shown in figure 5 [(13)].

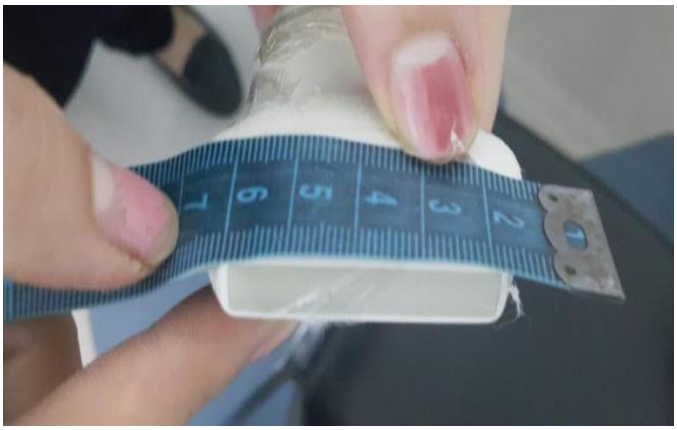


Figure 5: Probe length in cm

*The procedure's drawbacks include the possibility of the lesions being over- or under-estimated, as well as the fact that it is an operator-dependent tool that may require additional diagnostic techniques like CT or MRI [(14)].

* This is consistent with the findings of **Barcaui Ede *et al***., who described underestimate found in ulcerated lesions, overestimation seen in procedures performed previous to the examination, and a relationship between the presence of perilesional hypertrophic glands and nevus/melanoma [(15)].

As large lesions may not be adequately visible on HFUS, we advise using MRI to assess hyperkeratotic or very large squamous cell carcinomas. This is the same recommendation that was made by **Mandava *et al***. in 2013 [(16)].

CONCLUSION

The preoperative examination of skin malignancies can be improved with the use of high-frequency ultrasonography. In a preoperative study, it can reveal significant information in great detail such as examination of the various skin layers and their corresponding thicknesses, indicating the tumor nature (cystic or solid), morphology, extent, thickness, and precise location; detecting subclinical non-palpable satellite lesions (hidden lesions) close to the main one; detecting loco-regional lymph nodes; infiltration of pertinent anatomic structures; and differentiating between cancer recurrence and fibrosis of previous surgery before surgical intervention in addition to be a valuable non radiating tool for postoperative follow up for NMSC after

surgical excisions, to determine the presences or absence of early recurrence before skin ulceration.

Preoperative data from HFUS is crucial for assisting surgeons in making decisions, minimizing the extent of surgical defects, and enhancing surgical planning. This can shorten the length of the procedure, determine the site and extent of the excision, and determine the best method for surgical closure.

The presence of lymph-vascular or perineural invasion, as well as the histologic type, conformation of the free safety margin circumferentially and in depth, are subsequently determined by a histological analysis of the skin lesions.

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Conflict of interest:

The authors declare that they have no conflict of interest.

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