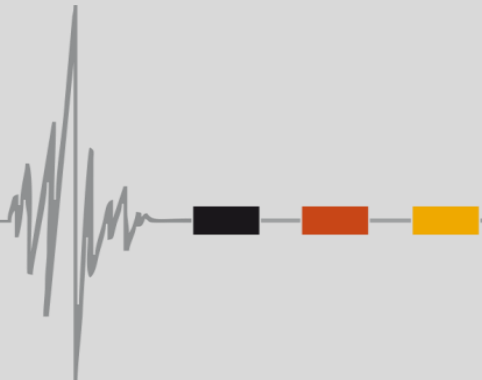


The Clinical Value of High-Frequency Ultrasound in Skin Cancer Radiotherapy

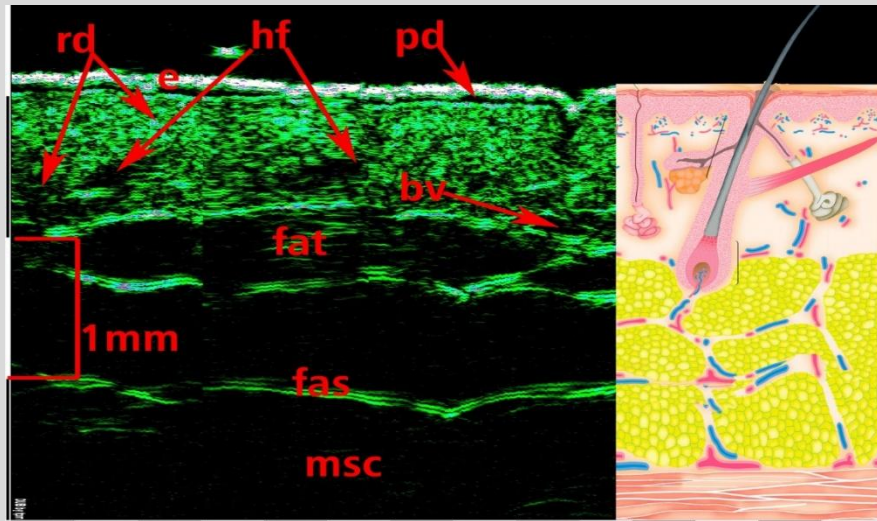
presented by: tpm taberna pro medicum GmbH



INTRODUCTION

HIGH-FREQUENCY ULTRASOUND (HFUS)

- High frequency ultrasound (HFUS) is the objective method for skin visualization and quantitative skin structure assessment.
- HFUS showing the skin micromorphology directly in the “skin vertical section” (from the epidermis to the subcutaneous fat). **Near-histological resolution up to 63-21 μm (25-75 MHz)** helps to assess skin lesions location, structure, and margins with maximum accuracy.



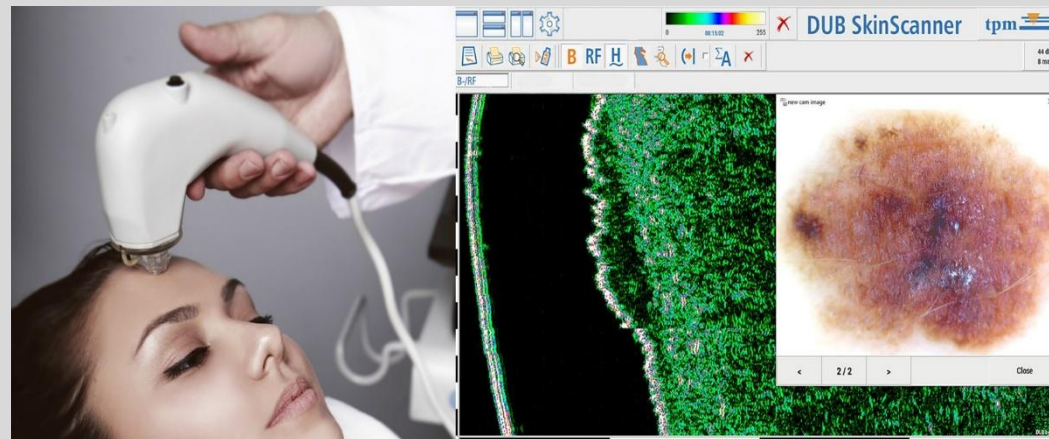
A 75 MHz scan of intact skin (left) and a diagram of the skin microanatomical structure (right). e - epidermis, pd - papillary dermis, rd - reticular dermis, hf - hair follicle, bv - deep dermal plexus blood vessel, fat - adipose tissue, fas - fascia, msc - muscle.

HFUS + VIDEODERMOSCOPY EXAMINATION

All tpm systems use combination of High-frequency ultrasound scanning and the cross-polarized video dermoscopy

This approach provides a complete tool set for complex diagnosis of the required skin area.

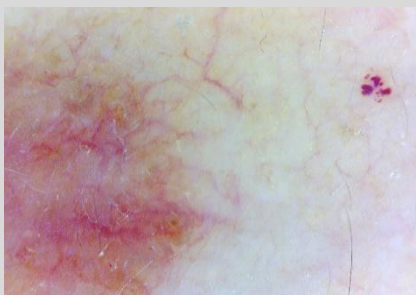
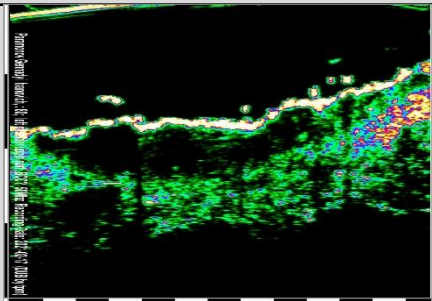
This combination allows to visualise all pathological changes beginning from the epidermal surface, and in deeper dermal and subdermal layers.



Melanocytic naevus HFU scan + videodermoscopic image

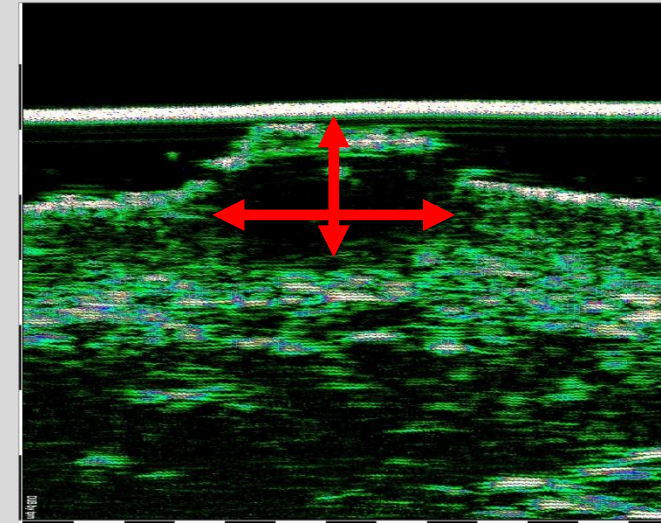
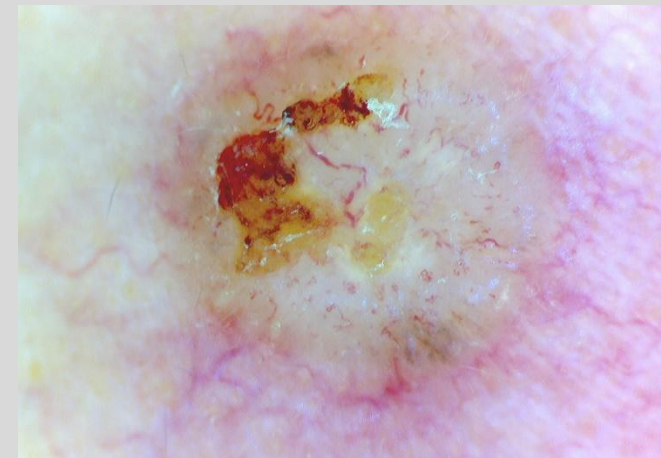
HFUS + VIDEODERMOSCOPY ADVANTAGES

METHOD	VIDEODERMOSCOPY	HFUS
DIAGNOSTIC VALUE	<p>Reading specific dermoscopic patterns for NMSC and differentiation NMSC type (BCC, SCC, Actinic keratosis, Merkel cell carcinoma, Kaposi sarcoma, Lymphomas) and Melanoma.</p> <p>Demarcation of the superficial tumor margins.</p>	<p>Evaluation of malignancy criteria (vertical growth of the tumor deep into the dermis, expansion of lateral borders, irregular edges).</p> <p>Reading HFUS patterns, typical of superficial, nodular, scleroderma-like, micronodular tumors BCCs, and SCCs.</p> <p>Measurement of the invasion depth. Melanoma Breslow and Clark indexes measurement.</p> <p>Measurement of the tumor real size inside epidermis, dermis and subcutaneous fat.</p>



SKIN CANCER IMAGING VALUE

- Early skin cancer detection
- Differential diagnosis
- Targeted biopsy
- Skin tumor is invasion depth measurement, margins assessments, tumor volume determination
- BCC morphotype differentiation at 50-75 MHz
- Adequate treatment method choice
- Treatment effects monitoring
- Relapses and complications diagnostics

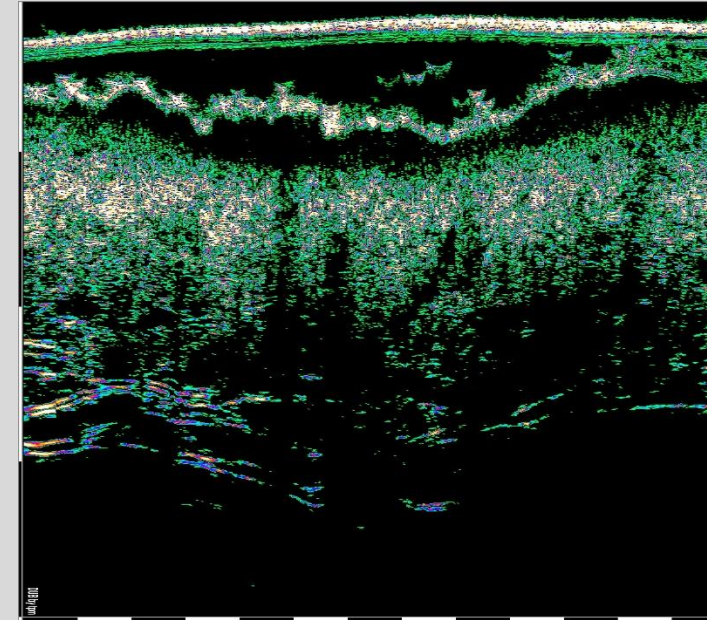
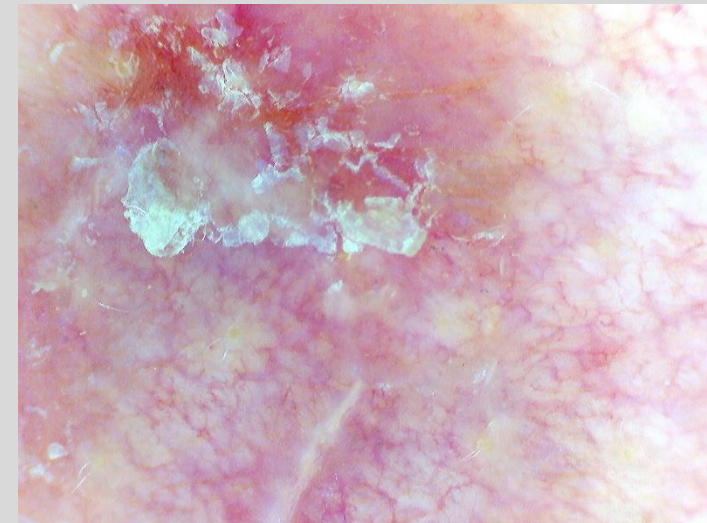


Nodular BCC, tumor thickness 2,4 mm,
tumor width 7,3 mm

HIGH-FREQUENCY ULTRASOUND AND HISTOLOGY

The HFUS skin image on the scans is visually comparable with the histological picture. HFUS scans have a high resolution and are easily interpreted by specialists. Many scientists refer to high-frequency ultrasound as in vivo biomicroscopy.

It is important that the data from high-frequency ultrasound measurements of skin micromorphology **have been repeatedly confirmed by studies** that compared the measurement results of high-frequency ultrasound and Histomorphometry.



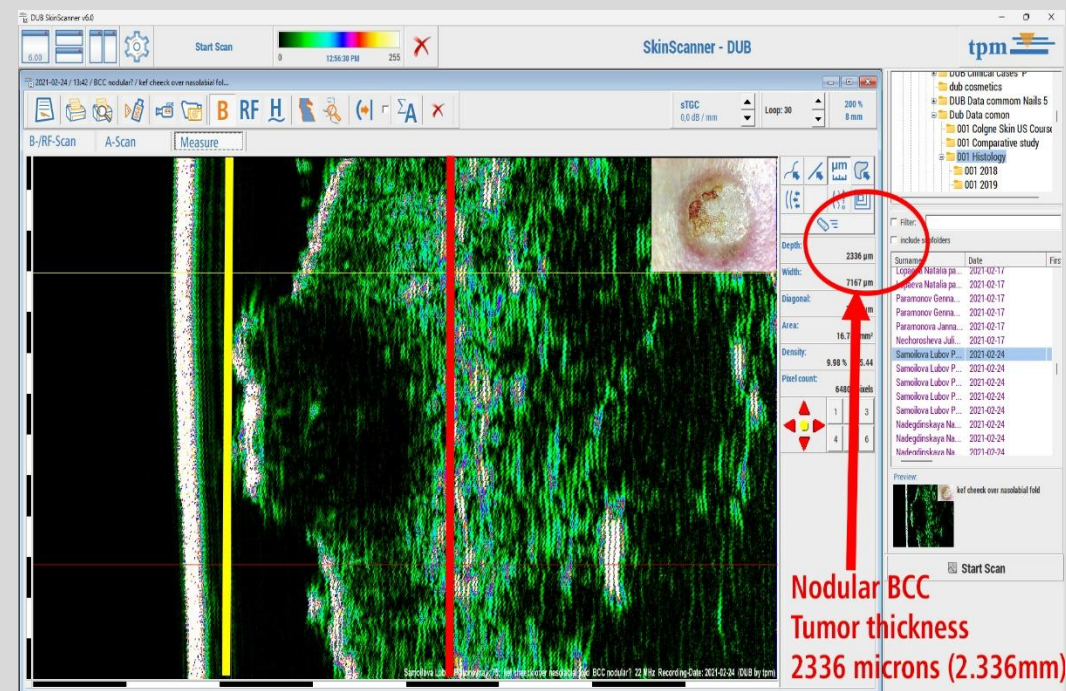
N	Frequency of ultrasound (MHz)	Type and number of investigated skin tumours	Correlation coefficient (r) or agreement	PUBLICATION SOURCE
1	16-18	Basal cell carcinoma (= 29)	Excellent correlation (ICC = 0.9) between US and histology	Bobadilla F, Wortsman X, Muñoz C, Segovia L, Espinoza M, Jemec GB. Pre-surgical high resolution ultrasound of facial basal cell carcinoma: correlation with histology. Cancer Imaging. 2008; 8(1): 163–72.
2	20	Basal cell carcinoma (= 35)	Excellent correlation (ICC = 0.9)	Jovanovic DL, Katic V, Jovanovic B. Value of preoperative determination of skin tumor thickness with 20-MHz ultrasound. Arch Dermatol. 2005; 141(2): 269–70.
3	20	Basal cell carcinoma (= 18), melanoma (= 8)	Linear correlation 98.4 %	Crisan M., Crisan D., Sannino G., Lupsor M., Badea R., Amzica F. Ultrasonographic staging of cutaneous malignant tumors: and ultrasonographic depth index. Archives of Dermatological Research, Vol. 305, 2013, p. 305-313.
4	17	Basal cell carcinoma (= 27)	Excellent correlation (ICC 0.953) for US and histology of all lesions	Song WJ, Choi HJ, Lee YM, et al. Clinical analysis of an ultrasound system in the evaluation of skin cancers: correlation with histology. Ann Plast Surg. 2014; 73(4): 427–33.
5	30 and 75	Basal cell carcinoma (= 35)	Thin BCC high correlation for 75 MHz (r = 0.870) Thick BCC: 30 MHz very high correlation (r = 0.951)	Khlebnikova A, Molochkov V, Selezneva E, et al. Basal cell carcinoma invasion depth determined with 30 and 75 MHz high-frequency ultrasound and histopathology – a comparative study. Medical Ultrasonography. 2020; 22(1): 33–8.
6	22	Basal cell carcinoma (= 117)	Excellent correlation (ICC ≥ 0.8)	Chauvel-Picard J, Tognetti L, Cinotti E, Habouguit C, Suppa M, Lenoir C, Rubegni P, Del Marmol V, Berot V, Gleizal A, Vercherin P, Dejonckheere G, Raffaelli C, Cardot-Leccia N, Azulay N, Sudaka-Bahadoran A, Perrot JL, Bahadoran P. Role of ultra-high-frequency ultrasound in the diagnosis and management of basal cell carcinoma: pilot study based on 117 cases. Clin Exp Dermatol. 2023 Apr 27;48(5):468-475. doi: 10.1093/ced/llad001. PMID: 36763772.
7	20	Melanoma (= 139)	> 0.95	Serrone L., Solivetti F. M., Thorel M. F., Eibenschutz L., Donati P., Catricalà C. High frequency ultrasound in the preoperative staging of primary melanoma: a statistical analysis. Melanoma Research, Vol. 12, 2002, p. 287-290.
8	20	Melanoma (= 40)	> 0.89	Pellacani G., Seidenari S. Preoperative melanoma thickness determination by 20-MHz sonography and digital videomicroscopy in combination. Archives of Dermatological Research, Vol. 139, 2003, p. 293-298.

N	Frequency of ultrasound (MHz)	Type and number of investigated skin tumours	Correlation coefficient (r) or agreement	PUBLICATION SOURCE
9	20	Melanocytic skin tumours (= 130)	> 0.96	Bessoud B., Lassau N., Koscielny S., Longvert C., Avril M. F., Duvillard P., Rouffiac V., Leclère J., Roche A. High-frequency sonography and color Doppler in the management of pigmented skin lesions. <i>Ultrasound in Medicine and Biology</i> , Vol. 29, 2003, p. 875-879.
10	20 and 100	Melanoma (= 13), melanocytic nevi (= 37)	> 0.99 (equal with both US frequencies)	Gambichler T., Moussa G., Bahrenberg K., Vogt M., Ermert H., Weyhe D., Altmeyer P., Hoffmann K. Preoperative ultrasonic assessment of thin melanocytic skin lesions using a 100-MHz ultrasound transducer: a comparative study. <i>Dermatologic Surgery</i> , Vol. 33, 2007, p. 818-824.
11	75	Melanoma (= 52), melanocytic nevi (= 36)	> 0.91	Guitera P., Li L. X., Crotty K., Mellenbergh R., Pellacani G., Menzies S. W. Melanoma histological Breslow thickness predicted by 75-MHz ultrasonography. <i>British Journal of Dermatology</i> , Vol. 159, 2008, p. 364-369.
12	30	Melanoma (= 68)	> 0.89	Hayashi K., Koga H., Uhara H., Saida T. High-frequency 30-MHz sonography in preoperative assessment of tumor thickness of primary melanoma: usefulness in determination of surgical margin and indication for sentinel lymph node biopsy. <i>The International Journal of Clinical Oncology</i> , Vol. 14, 2009, p. 426-430.

HFUS 25, 50, 75 MHz – IMPORTANT DIAGNOSTIC TOOL FOR SRT GUIDANCE

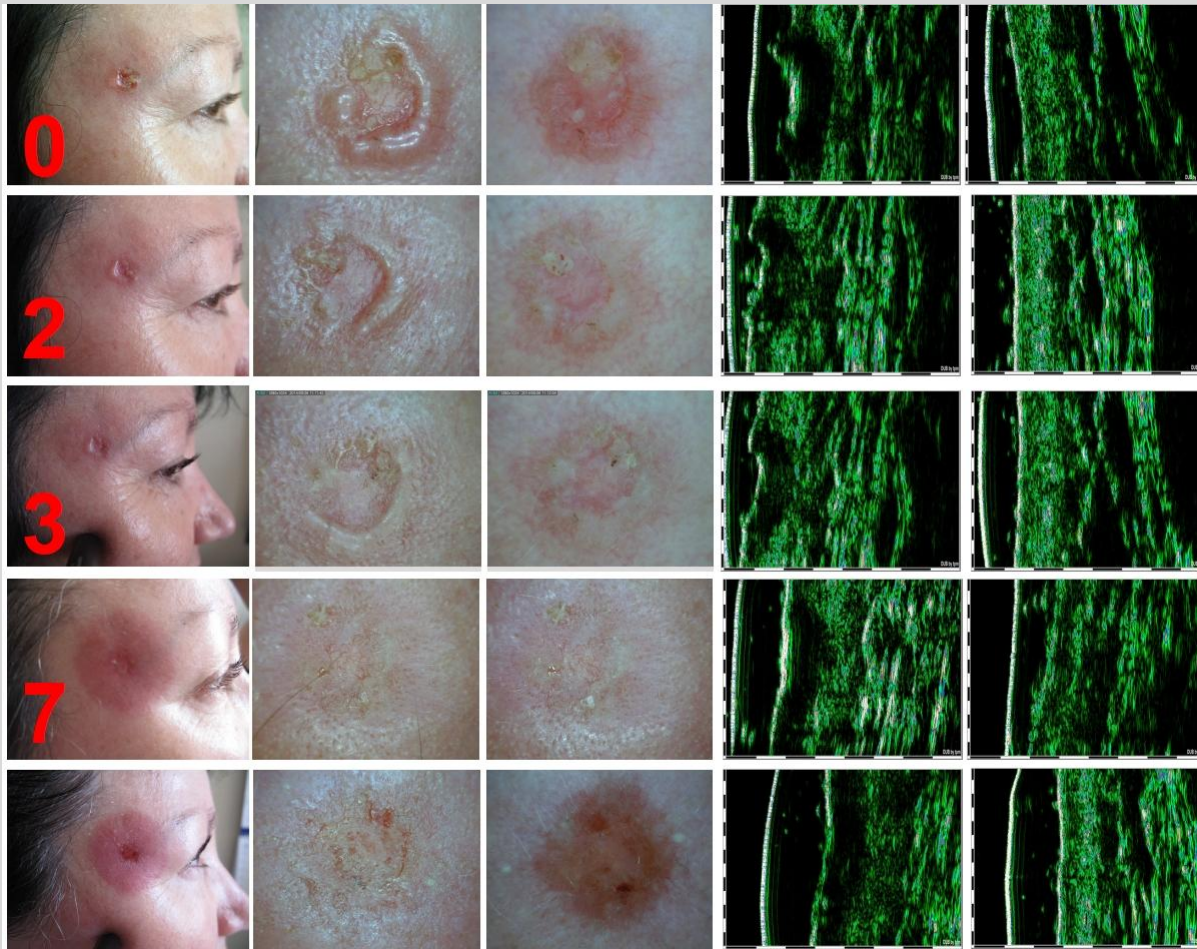
HFUS imaging provide the accurate tumor thickness/invasion depth measurement with resolution 63-21 microns prior to SRT.

These data are critical for the proper choice of the energy and filter settings to achieve adequate therapeutic depth



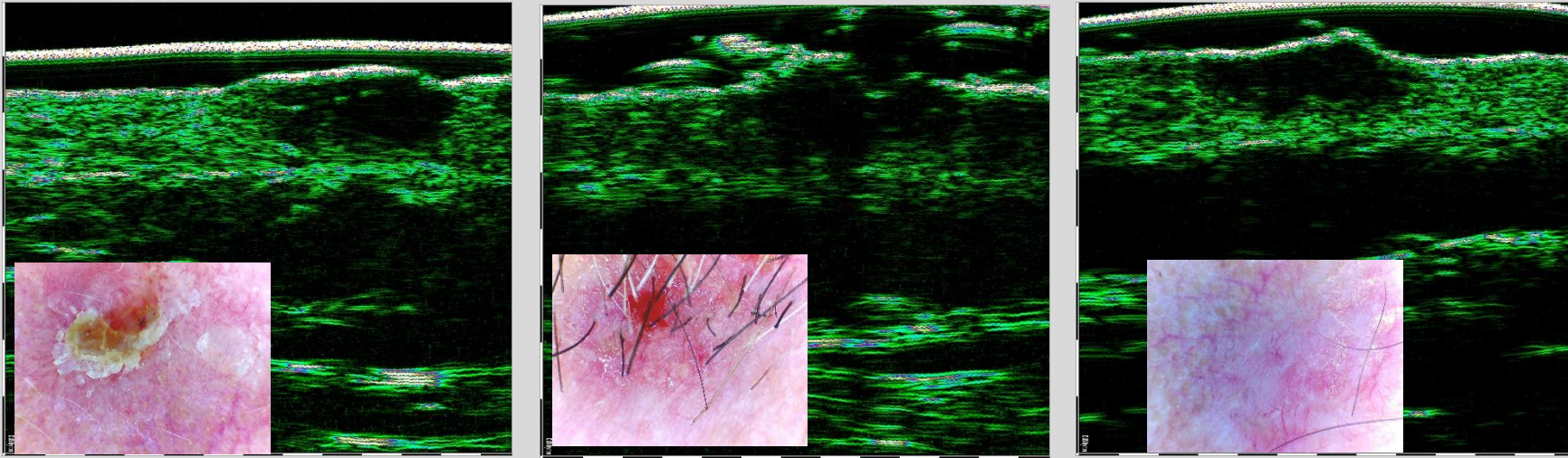
*Nodular BCC, tumor thickness 2,34 mm,
tumor width 7,2 mm*

SRT Treatment effects monitoring



Photo, Videodermoscopy in the normal and polarized light, ROI Scan 25 MHz, Control Scan contralateral
0- before treatment, 2,3,7,8- numbers of the treatment sessions.

Relapses and complications diagnostics



- 1- Hypoechoic area 6.2 x 1.7 mm, rare contour on 1350 μm from the unaffected skin surface;
- 2- Hypoechoic area 7 x 2.5 mm, rare contour on 1950 μm from the unaffected skin surface;
- 3- Hypoechoic area 7x1.7 mm, rare contour on 1250 μm from the unaffected skin surface;

HFUS DIAGNOSTIC VALUE

HFUS became the valuable diagnostic tool for the clinical-morphological BCCs forms differentiation, what is necessary for the treatment choice and patient management.

The depth of invasion and the true size of the tumor within the skin are critical data for treatment selection.

As a result of numerous studies, high-frequency ultrasound can be used to differentiate between the different clinical and morphologic types of BCCs (superficial, nodular, scleroderma-like, micronodular, etc.) and to identify signs of increased risk of recurrence.

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Performance of Ultrasound for Identifying Morphological Characteristics and Thickness of Cutaneous Basal Cell Carcinoma: A Systematic Review

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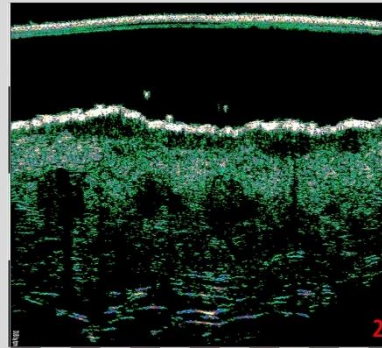
Keywords

Ultrasound · Basal cell carcinoma · High-frequency ultrasound · Imaging · Non-melanoma skin cancer

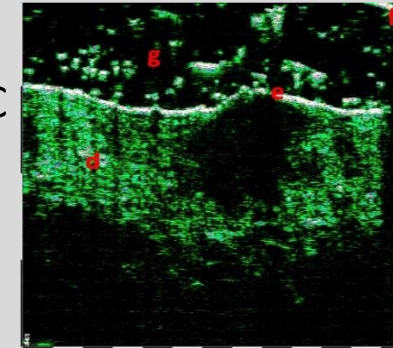
which can help in risk stratification. Performance of HFUS is significant in BCC management. Pre-surgical scans may support case selection for Mohs. HFUS can improve safety when used to plan brachytherapy treatments. help with case selec-

At Ultra-High frequencies 50-75 MHz specific ultrasound patterns for the most of BCCs morphotypes, including high-risk invasive BCCs described in the multiple studies

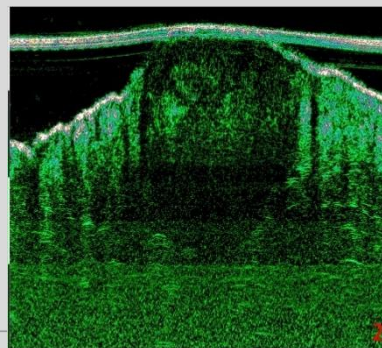
Superficial BCC



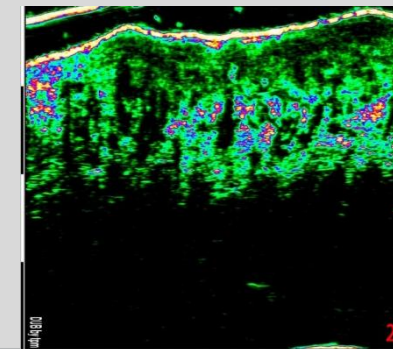
Sclerodermiform BCC



Nodular BCC



Micronodular BCC



HFUS BCCs Clinical-morphological forms differentiation

The histologic subtypes encompassed by the term “aggressive growth pattern,” including micronodular, infiltrative, sclerosing, and morpheaform patterns, are more likely to recur than the nodular and superficial BCC

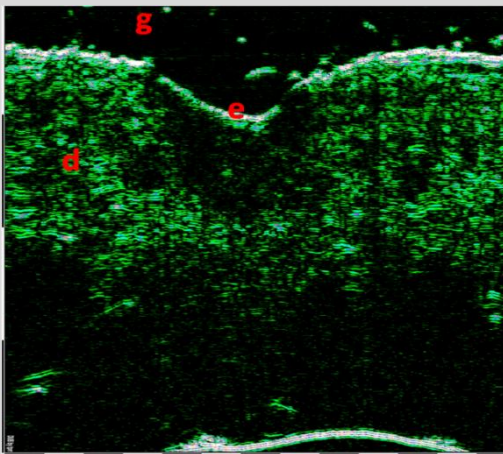
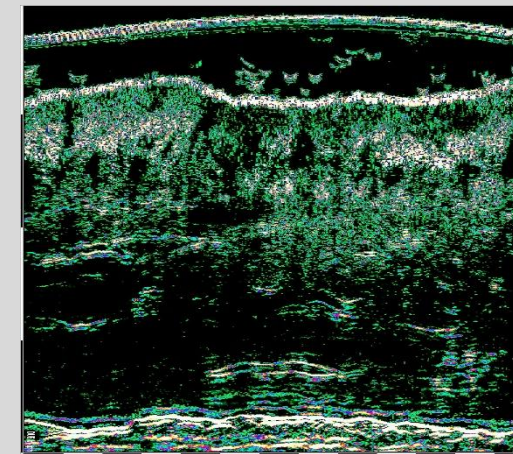
Before SRT extremely important to define tumor subclinical extensions far beyond the clinically visible borders

Clinical guideline recommends 7.0 to 10.0 mm (5.0 mm near critical structures) margins for invasive BCCs when using SRT

The use of high-resolution dermal ultrasound (HRDUS) is emphasized for confirming tumor depth and morphology.

A large retrospective study (analyzing 7,994 BCC lesions) found that with image-guided SRT, high-risk subtypes achieved up to 99% local control at two and five years, comparable to low-risk types.

McClure EM, Sedor G, Jin Y, Kattan MW. Image-guided superficial radiation therapy has superior 2-year recurrence probability to Mohs micrographic surgery. Clin Transl Radiat Oncol. 2023 Sep 17;43:100678. doi: 10.1016/j.ctro.2023.100678.



CLINICAL SIGNIFICANCE OF HIGH-FREQUENCY SKIN IMAGING IN RADIOTHERAPY

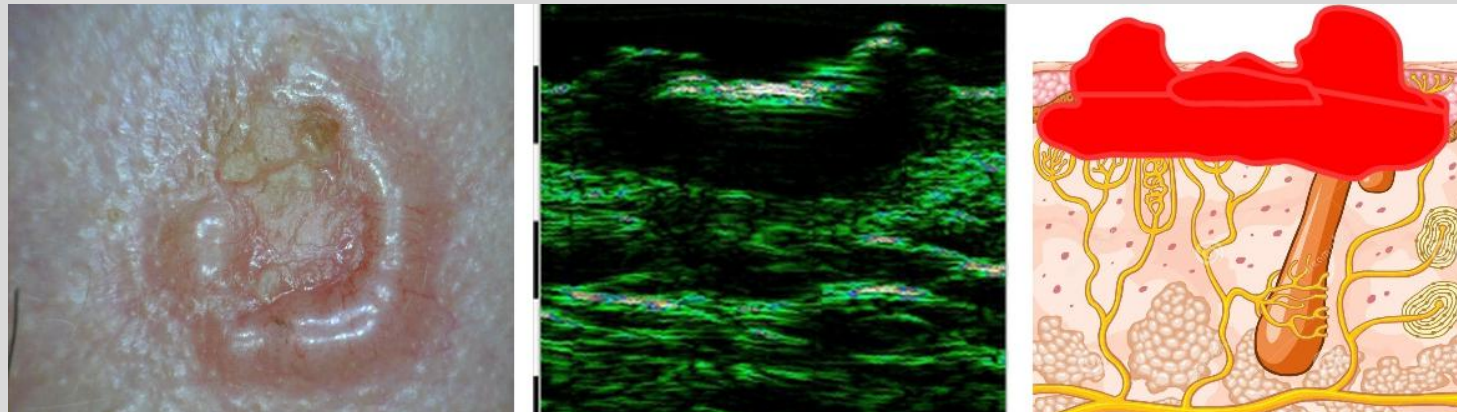
Objective and Precise Tumor Visualization and Measurements: HFUS provides high-resolution imaging of skin layers, enabling precise tumor measurement beyond clinical inspection and improving targeted treatment while preserving healthy tissue.

Treatment planning on the basis of these measurements and subsequent changes can be made in energy, dosing and time dose fractionation (TDF), and radiation field size.

Dynamic Treatment Adaptation: Daily HFUS assessments during Radiotherapy facilitate real-time adjustments to radiation planning, optimizing accuracy.

High Treatment Efficacy: Recent studies shows excellent recurrence-free survival (99.68% at 2 years; 99.54% at 4–6 years), with outcomes unaffected by high-risk locations, highlighting HFUS-guided precision.

Superior Outcomes: Compared to non-image-guided methods, Radiotherapy under HFUS control achieves higher treatment efficacy (99.3%), demonstrating its clinical advantage.



CLINICAL SIGNIFICANCE OF HIGH-FREQUENCY SKIN IMAGING IN RADIOTHERAPY

Objective and Precise Tumor Visualization and Measurements	<p>Crisan M., Crisan D., Sannino G., Lupsor M., Badea R., Amzica F. Ultrasonographic staging of cutaneous malignant tumors: and ultrasonographic depth index. Archives of Dermatological Research, Vol. 305, 2013, p. 305-313.</p> <p>Khlebnikova A, Molochkov V, Selezneva E, Belova L, Bezugly A, Sedova T, Molochkov A. Basal cell carcinoma invasion depth determined with 30 and 75 MHz high-frequency ultrasound and histopathology - a comparative study. Med Ultrason. 2020 Mar 1;22(1):31-36. doi: 10.11152/mu-2233. PMID: 32096785.</p> <p>Laverde-Saad A, Simard A, Nassim D, Jfri A, Alajmi A, O'Brien E, Wortsman X. Performance of Ultrasound for Identifying Morphological Characteristics and Thickness of Cutaneous Basal Cell Carcinoma: A Systematic Review. Dermatology. 2022;238(4):692-710.</p>
Differential Diagnosis BCCs subtypes and BCC vs SCC	<p>Siskou S, Pasquali P, Trakatelli M. High Frequency Ultrasound of Basal Cell Carcinomas: Ultrasonographic Features and Histological Subtypes, a Retrospective Study of 100 Tumors. J Clin Med. 2023 Jun 7;12(12):3893. doi: 10.3390/jcm12123893.</p> <p>Chen ZT, Yan JN, Zhu AQ, Wang LF, Wang Q, Li L, Guo LH, Li XL, Xu HX. High-frequency ultrasound for differentiation between high-risk basal cell carcinoma and cutaneous squamous cell carcinoma. Skin Res Technol. 2022 May;28(3):410-418.</p>
Treatment planning: energy, dosing and time dose fractionation (TDF), and radiation field size.	<p>Yu L, Moloney M, Zheng S, Rogers J. High resolution dermal ultrasound (US) combined with superficial radiation therapy (SRT) versus non-image guided SRT or external beam radiotherapy (XRT) in early-stage epithelial cancer: a comparison of studies. BMC Cancer. 2023 Jan 28;23(1):98.</p>
Dynamic Treatment Control	<p>Raszewska-Famielec M, Borzêcki A, Krasowska D, Chodorowska G. Clinical usefulness of high-frequency ultrasonography in the monitoring of basal cell carcinoma treatment effects. Postepy Dermatol Alergol. 2020 Jun;37(3):364-370.</p>
Treatment Efficacy Increase	<p>Harris PM, Farberg AS, Hopkins J, Ma L, Serure D, Robbins B, Osborne C, Bravo L, Lausser P, Boatner A. The State of the Art of Image Guided Superficial Radiation Therapy Treatment of Non-melanoma Skin Cancer in Outpatient Dermatology Clinics in the United States and Review of the Literature. Oncol Ther. 2025 Mar;13(1):31-48.</p>

CLINICAL SIGNIFICANCE OF HIGH-FREQUENCY SKIN IMAGING IN SRT

Conclusion:
HFUS significantly improves
precision, adaptability, and efficacy
in skin cancer radiotherapy,
supported by strong long-term
outcomes.



25 MHz



25 & 35 MHz
50 & 75 MHz