



# Correlation between 75 MHz high-frequency ultrasound and histopathology in psoriatic lesions

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## Abstract

**Background.** High-frequency ultrasound (HFUS) at frequencies >20 MHz is a valuable non-invasive tool for high-resolution skin imaging, enabling quantitative assessment of epidermal and dermal morphology with an axial resolution of 21  $\mu\text{m}$ . Such precision supports objective monitoring of dermatoses, including psoriasis.

**Objectives.** To compare epidermal and dermal measurements of psoriatic lesions using 75 MHz HFUS and histopathology.

**Methods.** Thirty psoriatic papules/plaques were imaged with 75 MHz HFUS (axial resolution: 21  $\mu\text{m}$ ) in patients who were referred for diagnostic biopsy, measuring epidermal thickness and subepidermal hypo-anechoic zone thickness. Lesions were marked for biopsy alignment, and histologic sections were evaluated along the same axis. Spearman's correlation analyzed agreement between methods.

**Results.** Mean epidermal thickness was  $220 \pm 33 \mu\text{m}$  (HFUS) vs.  $215 \pm 35 \mu\text{m}$  (histopathology;  $R = 0.82$ ,  $p < 0.01$ ). subepidermal hypo-anechoic zone thickness was  $483 \pm 97 \mu\text{m}$  (HFUS) vs.  $448 \pm 89 \mu\text{m}$  (histopathology;  $R = 0.88$ ,  $p < 0.01$ ). No significant inter-method differences were observed.

**Conclusion.** 75 MHz HFUS correlates strongly with histopathology in measuring psoriatic epidermal and dermal inflammatory changes, supporting its use as a non-invasive tool for therapeutic monitoring.

**Keywords:** high-frequency ultrasound, psoriasis, epidermal thickness, dermal thickness, non-invasive imaging.

## Introduction

Psoriasis is a chronic, immune-mediated disease driven by genetic and environmental factors, characterized by keratinocyte hyperproliferation and aberrant differentiation. Affecting 1–2% of the global population, vulgar (plaque) psoriasis accounts for 90% of cases [1–3]. Histopathologically, it manifests as epidermal acanthosis, papillomatosis, and a lymphohistiocytic infiltrate in the upper dermis, accompanied by neoangiogenesis [4,5].

Quantitative monitoring of treatment efficacy remains a clinical challenge [6]. While histopathology is the gold standard, its invasiveness limits repeated use. High-frequency

ultrasound (HFUS) offers a real-time, high-resolution (80–21  $\mu\text{m}$ ) imaging of skin layers and objective measurements of the skin structural changes [7–10]. HFUS is used for the follow-up of psoriasis, atopic dermatitis, and sclerotic skin diseases [11,16,17]. Prior studies have validated HFUS for psoriatic lesions assessments [10,12–14], but data about comparison HFUS 50 MHz and higher with histopathology are limited.

This study compares 75 MHz HFUS and histopathology in measuring epidermal thickness and subepidermal hypo-anechoic zone in psoriatic lesions, aiming to establish the correlation between HFUS and histological measurements.

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## Methods

### Study design and participants

We performed a comparative analysis of 30 psoriatic papules and plaques in patients referred for diagnostic biopsy. All participants were fully informed about the study procedures and associated risks, and written informed consent was obtained.

### High-frequency ultrasound (HFUS) imaging

Lesions were visualized using a 75 MHz probe (DUB SkinScanner; axial resolution: 21  $\mu\text{m}$ , scan width: 12.8 mm, depth: 4 mm). Epidermal thickness and subepidermal hypo-anechoic zone thickness were measured three times on each lesion. The scanning axis was marked with a sterile surgical pen for alignment with subsequent histological examination.

### Histopathological analysis

Punch biopsies or surgical excisions were performed. Specimens were fixed in formalin, paraffin-embedded, and stained with haematoxylin and eosin (H&E). Vertical sections, located along the HFUS scanning axis, were evaluated under light microscopy with magnification 100x (Nikon E20F), measuring epidermal thickness and lymphohistiocytic infiltrate depth.

### Statistical analysis

Spearman's rank correlation coefficient (R) assessed agreement between HFUS and histopathology due to non-normal data distribution. Correlation strength was interpreted using the Cheddock scale.

## Results

### HFUS and histopathological findings

#### HFUS revealed:

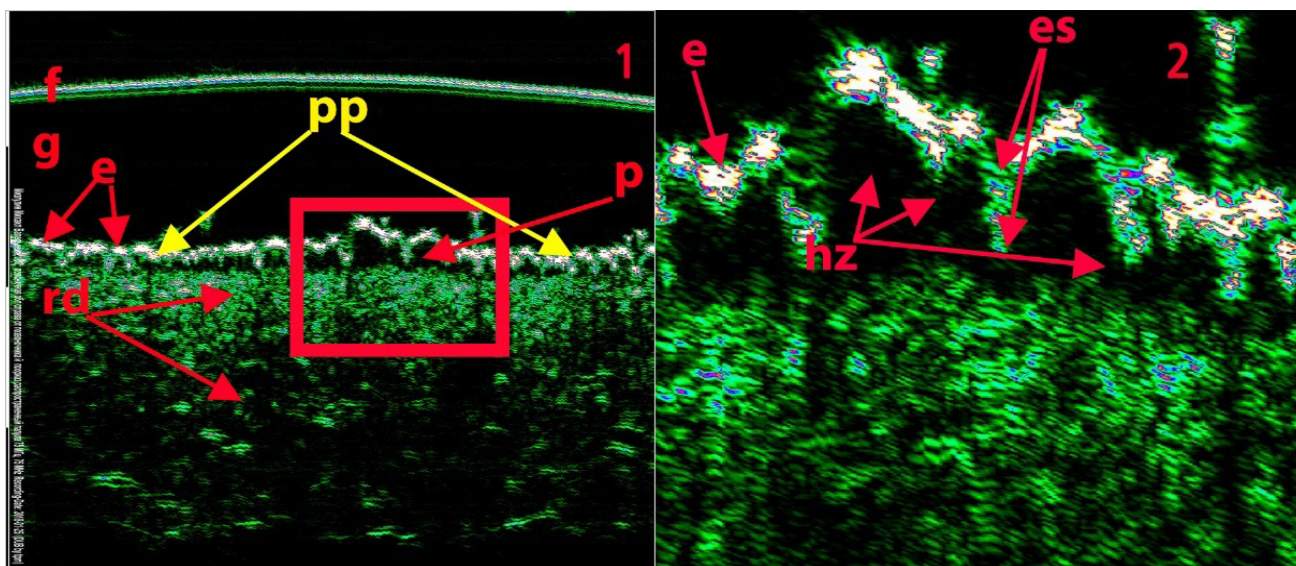
- Epidermal thickness (mean  $\pm$  SD:  $220 \pm 33 \mu\text{m}$ ) with contour waveform deformation and vertical epidermal strands penetrating in papillary dermis (Fig. 1.1, 1.2).
- A hypo-anechoic subepidermal zone ( $483 \pm 97 \mu\text{m}$ ), demarcated from the epidermis but blending with deeper dermis (Fig. 1.2, 2.1, 3.1). The upper contour of this area was wavy, hypo-anechoic sections were located between hyperechogenic vertical epidermal strands. (Fig. 1.2, 2.1, 3.1, Table I, Fig. 4).

#### Histopathology:

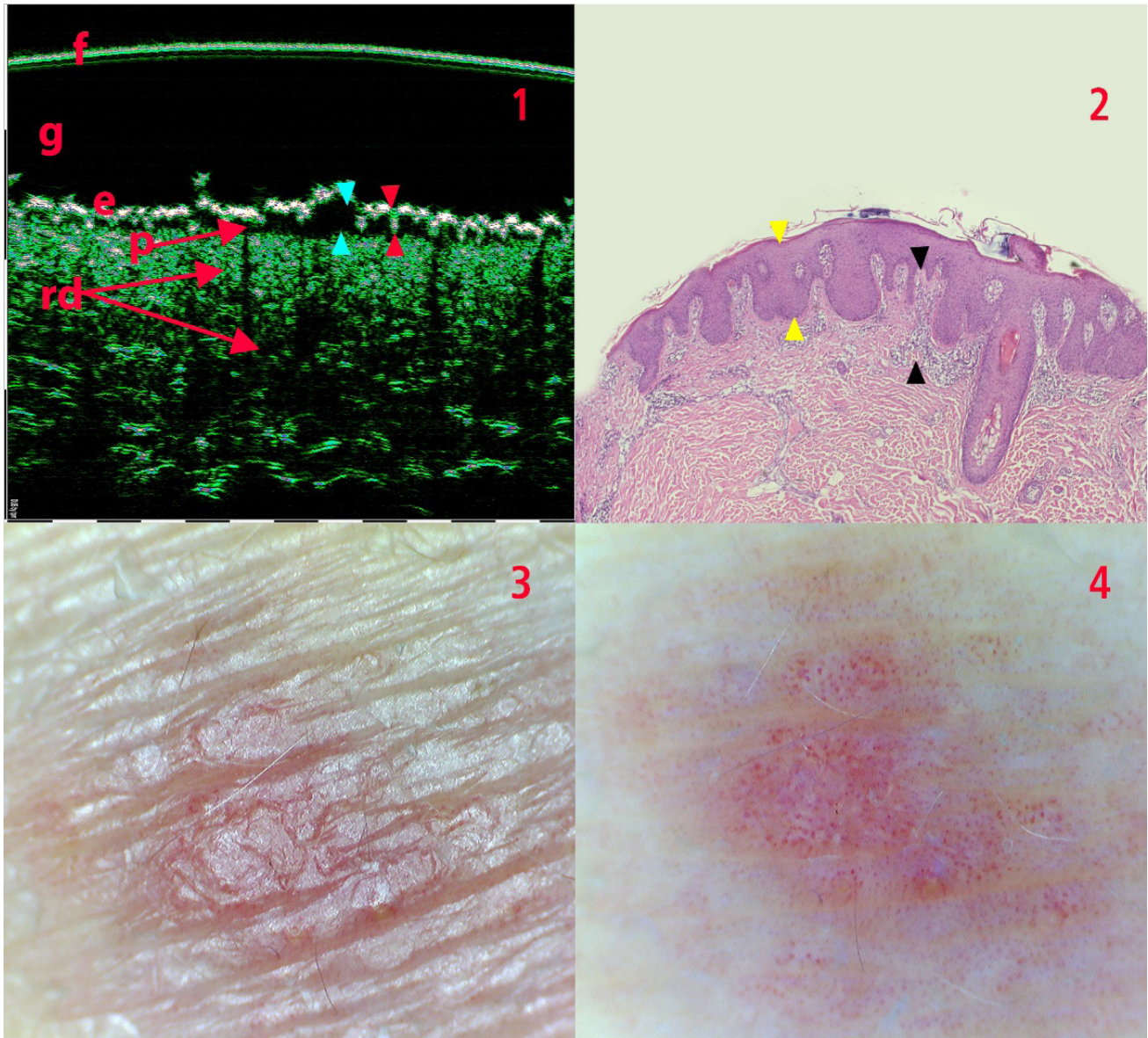
- Acanthosis, hyperkeratosis, and thinning of the Malpighian layer over dermal papillae.
- Papillary dermal edema, increased papillae length, capillary proliferation, and lymphohistiocytic infiltrate ( $448 \pm 89 \mu\text{m}$ ; Figures 2.2, 3.2, Table II, Fig. 5).

#### Correlation analysis:

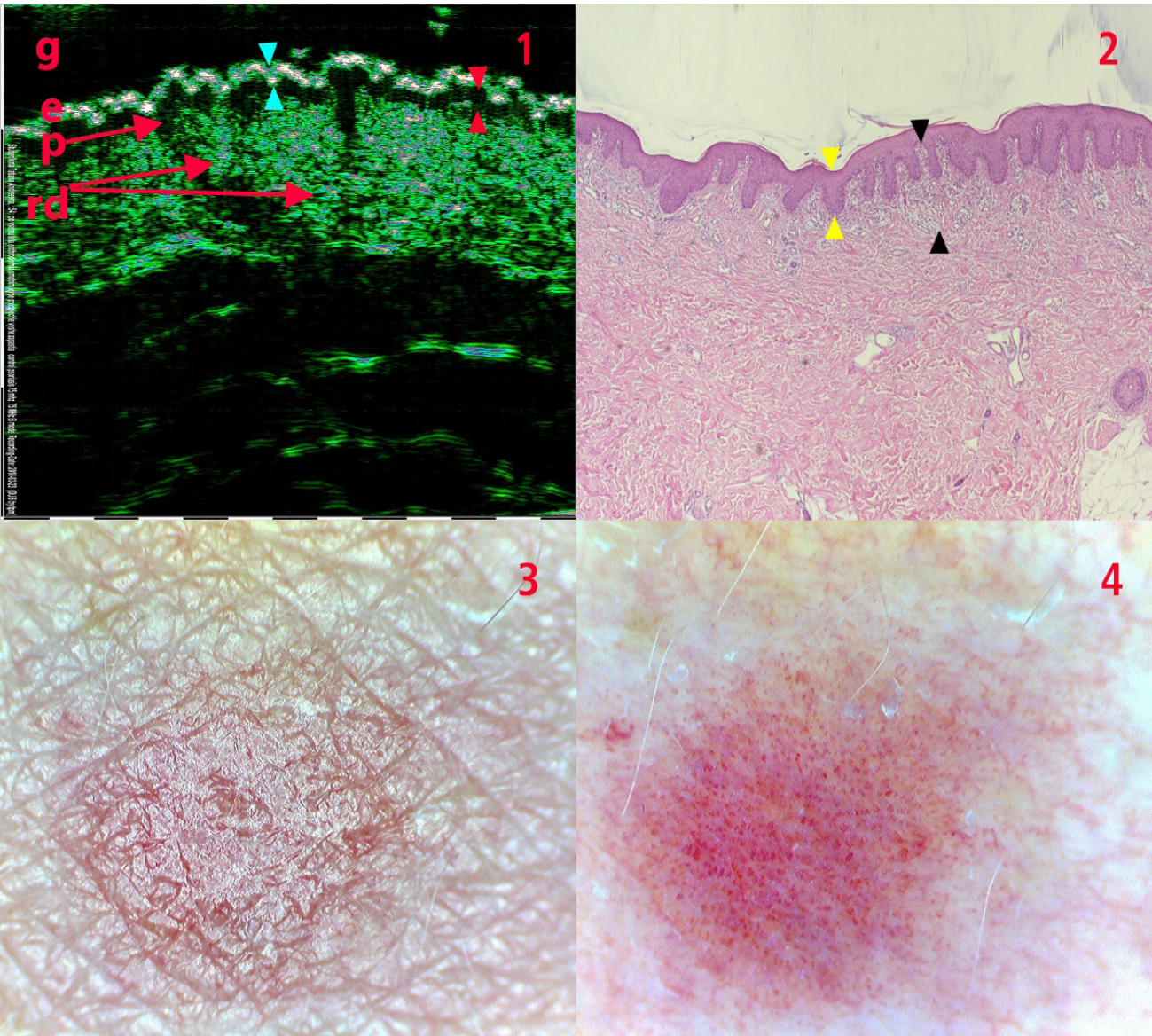
- Epidermal thickness:  $R = 0.82$  ( $p < 0.01$ ).
- Subepidermal hypo-anechoic zone thickness:  $R = 0.88$  ( $p < 0.01$ ).
- There were no statistically significant differences between the epidermal thickness and subepidermal hypo-anechoic zone by high-frequency ultrasound and histological method.



**Figure 1. 1.1** – 75 MHz image of the psoriatic papule; **1.2** – same image in the zoom mode magnification 5X, magnified area is highlighted with a red square at figure 1.1. (f – foil on the probe tip, g – ultrasound gel, e-epidermis with waveform deformation, p- papillary dermis, rd- reticular dermis, pp- psoriatic papule, lateral papule borders shown with yellow arrows, es- vertical epidermal strands, hz- hypo-anechoic subepidermal zone).



**Figure 2. 2.1** - 75 MHz psoriatic papule image (f – foil on the probe tip, g – ultrasound gel, e – epidermis with waveform deformation, p – papillary dermis with hypo-anechoic subepidermal zone, rd – reticular dermis, blue arrows – vertical epidermal strands, red arrows – subepidermal hypoanechoic zone); **2.2** - histological image x100, yellow arrows – epidermis with epidermal ridges, black arrows papillary dermis with elongated papillas and lymphohistiocytic infiltrate; **2.3** - non-polarized videodermoscopic image; **2.4** - polarized videodermoscopic image



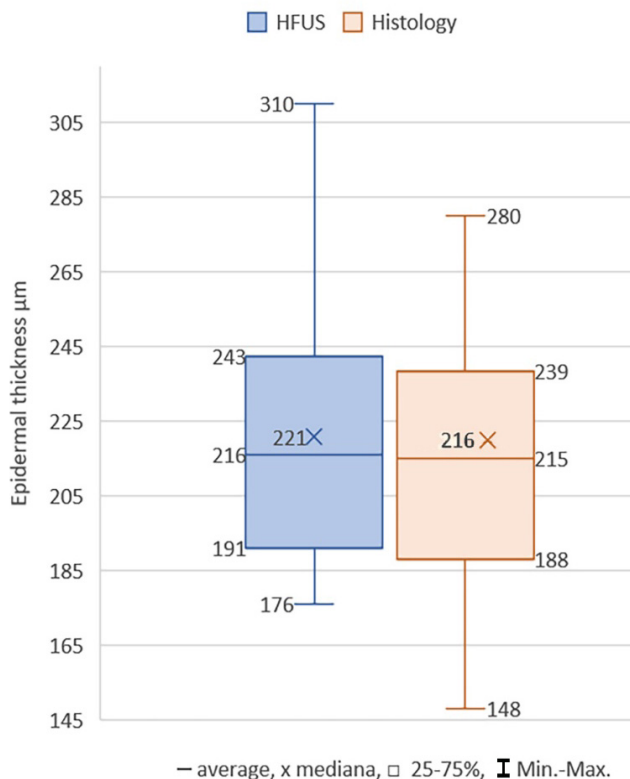
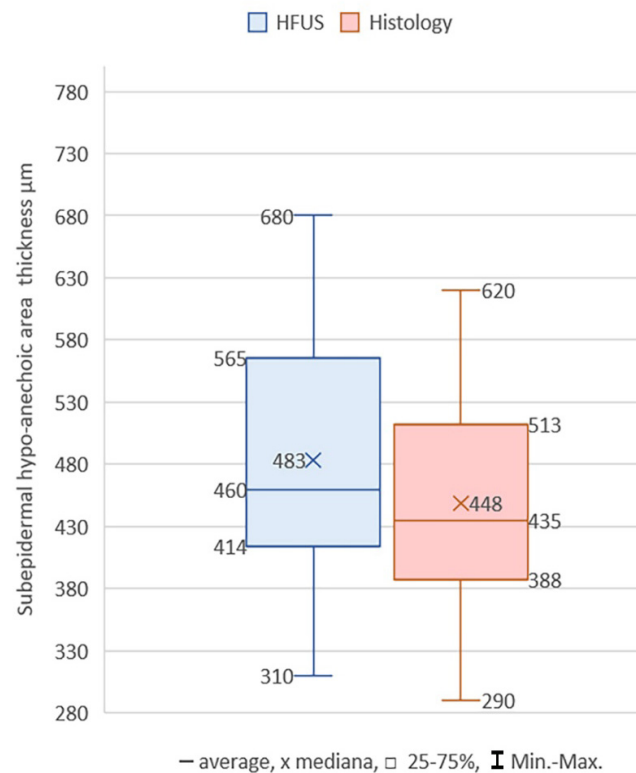
**Figure 3.3.1 - 75 MHz psoriatic papule image** (g – ultrasound gel, e-epidermis with waveform deformation, p- papillary dermis with hypo-anechoic subepidermal zone, rd- reticular dermis, blue arrows – vertical epidermal strands, red arrows - subepidermal hypoanechoic zone); **3.2** - histological image x100, yellow arrows – epidermis with epidermal ridges, black arrows papillary dermis with elongated papillas and lymphohistiocytic infiltrate; **3.3** - non-polarized videodermoscopic image; **3.4** - polarized videodermoscopic image.

**Table I.** Values of epidermal thickness in psoriasis according HFUS imaging and histologic study.

| Epidermal thickness $\mu\text{m}$ |         |    |        |        |                |            |        |        |        |
|-----------------------------------|---------|----|--------|--------|----------------|------------|--------|--------|--------|
| Method                            | Average | N  | Min.   | Max.   | Std. deviation | Std. error | 25%    | Median | 75%    |
| HFUS 75 MHz                       | 220.93  | 30 | 176.00 | 310.00 | 33.67          | 6.15       | 191.00 | 216.00 | 242.00 |
| Histology                         | 215.70  | 30 | 148.00 | 280.00 | 35.29          | 6.44       | 188.00 | 215.00 | 236.00 |
| Total                             | 217.27  | 60 | 148.00 | 310.00 | 34.33          | 4.43       | 188.50 | 215.50 | 239.00 |

**Table II.** Values of subepidermal hypo-anechoic area obtained by HFUS imaging, and inflammatory lymphohistiocytic infiltrate thickness measured by histological method.

| Method      | Thickness `µm |    |        |        |                |            |        |        |        |
|-------------|---------------|----|--------|--------|----------------|------------|--------|--------|--------|
|             | Average       | N  | Min.   | Max.   | Std. deviation | Std. error | 25%    | Median | 75%    |
| HFUS 75 MHz | 483.37        | 30 | 310.00 | 680.00 | 97.07          | 18.03      | 416.00 | 470.00 | 548.00 |
| Histology   | 448.03        | 30 | 290.00 | 620.00 | 89.58          | 16.63      | 390.05 | 440.00 | 500.00 |
| Total       | 465.87        | 60 | 290.00 | 785.00 | 94.25          | 12.27      | 392.00 | 450.00 | 533.25 |

**Figure 4.** Epidermal thickness value diagram (µm) Diagram of average, minimum and maximum values of epidermal thickness according to 75 MHz HFUS and histology measurement.**Figure 5.** Subepidermal hypo-anechoic zone thickness value, and inflammatory lymphohistiocytic infiltrate thickness measured by histological method (µm). Diagram of average, minimum and maximum values of subepidermal hypo-anechoic zone thickness, and inflammatory lymphohistiocytic infiltrate thickness measured by histological method.

## Discussion

HFUS was reported to be a valuable instrument for the clinical examination, psoriasis severity objective assessment, and treatment efficacy monitoring [7,8,10,12-14].

The main HFUS features for the psoriatic lesions include a thickening of the epidermis and dermis, and hypo-anechoic band corresponding to the papillary dermis [7,10]. Also, some authors use the terms hyperechoic band, corresponding to the psoriasiform hyperplasia in

the epidermis and the hypoechoic band or subepidermal low echogenicity band (SLEB), corresponding to the inflammatory changes in the superficial dermis [10,12-14].

Dini et al. provided HFUS 70 MHz psoriatic lesions examination and observed an undulated superficial hyperechoic band and the SLEB. The average thickness of the superficial hyperechoic band was 0.2157 mm, the SLEB thickness was 0.7535 mm [12], which is close to the values obtained in our study. Negrutiu et al. measured the thickness of the epidermis and the dermis at psoriatic

plaques with 20 MHz, median value for epidermis was 0.95 mm, for dermis 2.447 mm [10]. The epidermal thickness in our study was much less, which can be explained by the significant difference in the frequency of the probes. The epidermal reflection at frequencies in the 18-20 MHz range is much stronger than at frequencies 70-100 MHz. The resolution in the range 70-100 MHz is much higher than at 20 MHz and could be used for the epidermal thickness measurement with better accuracy [21].

Comparisons between the results of high-frequency and histological measurements of skin morphological parameters have been performed in many studies: superficial basal cell carcinoma (BCC) thickness ( $r=0.87$ ), nodular BCC thickness ( $r=0.95$ ) [19,20], melanoma ( $r=0.908$ ) [22], scleroderma ( $r=0.69$ ) [18], atopic dermatitis ( $r=0.63$ ) [15].

However, based on the available literature, we did not find published studies that compare high-frequency ultrasound >50 MHz and histological measurements of psoriatic papules/papules.

To the best of our knowledge, this is one of the first studies demonstrating a correlation between 75 MHz HFUS and histopathology in quantifying psoriatic epidermal and inflammatory changes. High-frequency images of the epidermis and histological sections revealed that vertical epidermal strands which penetrate the papillary dermis match to acanthotic epidermal ridges. Hypo-anechoic wave-like areas located between these strands correspond to enlarged and deformed dermal papillae. The shape and thickness of the hypo-anechoic subepidermal area (SLEB) correspond to the location and thickness of the lymphohistiocytic infiltrate in the papillae and upper layers of the dermis.

This study has certain limitations: small sample size ( $n = 30$ ); larger cohorts could validate generalizability. Depth limitation (4 mm) precluded adipose tissue assessment. Hyperkeratosis-induced acoustic shadowing may require keratolytic pretreatment [12]. Future studies could explore higher frequencies or combined imaging modalities.

## Conclusion

75 MHz HFUS correlates strongly with histopathology in measuring psoriatic epidermal and dermal changes. Its non-invasive nature and quantitative output make it a promising tool for objective psoriatic lesions monitoring.

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