

# High-frequency Ultrasound as a Quantifiable Measurement Tool in Cutaneous Chronic Graft-Versus-Host-Disease: A Review of the Literature

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Disclosures: Sonja Kobayashi serves as an educational content consultant for Neo Medical Inc



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## Introduction

- The skin is the most frequently affected organ in chronic graft-versus-host-disease (cGvHD)
- Currently, **no universally accepted practice guidelines exist** to assess disease activity or monitor treatment response in cutaneous cGvHD [1]
- High-frequency ultrasound (HFUS) is a non-invasive imaging tool** used to evaluate inflammatory and sclerosing skin diseases like lichen sclerosis, systemic sclerosis, and localized morphea [2-4]
- HFUS may serve as an objective, reproducible tool for monitoring cGvHD, yet current literature lacks a comprehensive review evaluating its utility
- Objective 1: Analyze current literature to characterize the common ultrasound features of cutaneous cGvHD using HFUS**
- Objective 2: Evaluate the prognostic value and limitations of HFUS in cutaneous cGvHD**

## Methods

- A targeted **literature search of the PubMed database** with a combination of Medical Subject Headings (MeSH) and controlled terms was performed in July 2025
- Authors reviewed 25 articles, 6 of which were included** in the current study
- Inclusion criteria:** evaluated HFUS for diagnosis, monitoring, or prognosis of HFUS
- Exclusion criteria:** Did not include patients with cutaneous cGVHD or focused on non-HFUS imaging techniques

## Results

**Table 1.** Summary of studies evaluating high-frequency ultrasound (HFUS) in cutaneous cGvHD, highlighting the study design, HFUS findings, and clinical relevance

Study	n	Aim	Findings	Clinical Utility	Time Range Patients were Evaluated	Comparison to Clinical Scoring System (NIH Consensus Scores)
<a href="#">Giavedoni et al. 2021</a>	24	Assess utility of HFUS in identifying inflammatory patterns and prognosis in scGvHD	Increased vascular flow (systolic peak $\geq 10\text{cm/s}$ , resistance index (RI) $\geq 0.70$ ) seen only in progressive/non-responsive patients (p=0.006); B-mode not predictive	Color Doppler may serve as prognostic marker of treatment response	Measured at first dermatology visit and 6-month follow-up appointment	NIH Score 1: n=2 (8.33%) NIH Score 2: n=15 (62.50%) NIH Score 3: n=7 (29.16%)
<a href="#">Gottlöber et al. 2003</a>	5	Characterize ultrasound features in scGVHD	<b>Pre-treatment:</b> 45–83% increase in dermis thickness versus healthy skin; <b>Post-treatment:</b> 18–83% reduction of skin thickness	HFUS provides quantitative, non-invasive monitoring of treatment response	Patients evaluated before and after treatment for unknown period of time	Grade 2: n=4 (80%) Grade 2-3: n-1 (20%)
<a href="#">Leiter et al. 2002</a>	6	Evaluate treatment response to PUVA in treatment-refractory cGVHD using HFUS	<b>Pre-treatment:</b> thickened, echo-rich dermis; indistinct subcutis <b>Post-treatment:</b> reduction in dermal thickness, often to levels of normal skin; clearer dermis-subcutis interface; decreased echogenicity of dermis	HFUS can confirm clinical improvement and quantify structural skin changes	Evaluated prior to initiating UV therapy, after each consecutive 10 sessions of UV therapy for a median of 25 sessions, and then every 2-months after UV therapy for a median of 10.3 months	NIH score 3: n=6 (100%)
<a href="#">Marti-Marti et al. 2022</a>	72 (22 with cGVHD)	Assess HFUS's evaluation of disease activity and its impact on clinical decisions in sclerosing dermatoses	Increased dermal thickness, loss of definition of the dermal-hypodermal junction, increased vascularity (70%), panniculitis (80%). HFUS findings were discordant with clinical evaluation in 23.6% of cases; HFUS findings altered clinical management in 19.4%	HFUS monitors disease activity and influences therapeutic decisions	Median duration of follow-up was 18 months (range 6-36 months), median frequency of follow-up was 6 months (range 2-12 month)	Not reported
<a href="#">Molinelli et al. 2022</a>	18 (10 controls)	Evaluate HFUS in assessing scGvHD	Reduced thickness of epidermis and hypodermis, increased dermal thickness observed in moderate cGvHD; HFUS changes preceded clinical signs of sclerotic disease in 3 patients	HFUS may allow early detection before clinical manifestations	One-time measurement	NIH Score Mild: n=3 (16.7%) Moderate: n=12 (66.7%) Severe: n=3 (16.7%)
<a href="#">Osmola-Mańkowsk a et al. 2013</a>	5	Assess HFUS measurements following UVA1 phototherapy	Small reductions (2-9%) in thickness seen in most patients immediately following UVA1 phototherapy; 3 out of 4 had decreased echogenicity at 3-months post-treatment, even without early change	Echogenicity may be a more sensitive long-term marker; Recommended repeat HFUS at 3-months following treatment	Before treatment, directly after discontinuation of UVA1 phototherapy (average of 27.2 sessions), and 3 months after discontinuation	Grade 2: n=3 (60%) Grade 3: n=2 (40%)

n=number of participants; scGvHD=sclerodermatous chronic graft-versus-host disease; cGvHD=chronic graft-versus-host disease

## Discussion

### Common Findings:

- Increased dermal thickness and echogenicity
  - Loss of definition of dermal-hypodermal junction
  - Isles of echo-rich spots in the hypodermis with hyperechogenic lobules and hypoechogenic septa correlating to subcutaneous fibrotic trabeculae
- ### Prognostic Role:
- Quantitative assessment of skin thickness often correlates with treatment response
  - Color Doppler flow may predict treatment non-responders [4]
  - HFUS abnormalities may precede clinical signs of cGvHD [8]
  - Monitoring treatment response with changes in skin thickness and inflammation visible on ultrasound

### Detection of Change:

- HFUS allows for serial, objective tracking of skin changes, some of which may be subclinical [4]
  - Reduction of epidermis and hypodermis thickness in cGvHD was as little as 0.037mm and 2.52mm, respectively [8]
  - Average reduction of skin thickness following therapy was as little as 0.66mm [4]

### Impact on Management:

- HFUS influenced treatment decisions in nearly 20% of patients [7]
- HFUS is particularly useful in detecting reductions in dermal thickness and fibrotic density following therapy

### Limitations:

- Small sample sizes, lack of histologic confirmation in most
- Variability in ultrasound parameters used across studies
- Need for ultrasound training and acquisition of HFUS probe

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