

Evolving Methods in Fibrosis Quantification

A Scoping Review of Modalities Across Organ Systems

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Background

Fibrosis, defined as the pathologic accumulation of extracellular matrix secondary to dysregulated wound healing, is driven by sustained myofibroblast activation and aberrant tissue remodeling that supplants physiologic reparative mechanisms.^{1,2} The mediators implicated in hypertrophic scarring and keloid formation, including TGF- β , PDGF, and matrix metalloproteinases, are conserved across hepatic, cardiovascular, pulmonary, and renal fibrogenesis.^{3,4}

The clinical consequences of fibrotic progression are organ-dependent and include, but are not limited to, pathologic cutaneous scarring, hepatic cirrhosis, myocardial dysfunction, pulmonary insufficiency, and renal failure. Accurate fibrosis quantification is essential for disease staging, therapeutic monitoring, surgical planning, and prognostic stratification; however, no unified framework currently exists for systematic cross-organ comparison of quantification methodologies.

In wound healing, fibrosis quantification informs clinical decision-making, ranging from surgical timing, determination of candidacy for anti-fibrotic therapies, and response monitoring following corticosteroid injections, laser treatments, or radiation therapy for keloid prophylaxis. Current clinical tools remain limited by inter-observer variability and poor cross-institutional reproducibility.^{6,7}

Histopathologic biopsy remains the reference standard for fibrosis assessment but is constrained by invasiveness, sampling heterogeneity, and inter-observer variability.⁵ Non-invasive imaging, circulating biomarkers, and AI/deep learning algorithms have emerged as complementary quantification strategies, however, these methodologies remain fragmented across organ-specific disciplines with limited cross-system synthesis. Systematic evaluation is warranted to identify approaches translationally applicable to wound healing and surgical care.

Objectives

To systematically identify, evaluate, and synthesize peer-reviewed literature on fibrosis quantification methodologies across five organ systems: hepatic, cardiovascular, pulmonary, renal, and integumentary.

To delineate comparative utility, organ-specific applicability, and translational potential of histopathologic, imaging-based, molecular, computational, and clinical scoring techniques.

To characterize organ-specific methodological considerations, map temporal trends in modality adoption with emphasis on AI integration and identify domains where quantification tools remain underdeveloped.

To evaluate the translational applicability of cross-organ quantification methodologies to fibrosis assessment and wound healing outcomes.

Methods

A systematic scoping review was conducted in accordance with PRISMA-ScR guidelines. PubMed, Embase, and the Cochrane Library were searched from January 2014 through September 2025 using structured queries combining fibrosis quantification terms with organ-specific and modality-specific descriptors. Inclusion criteria required peer-reviewed original research reporting quantitative fibrosis assessment in at least one of five organ systems.

Each article was classified using a dual-counting framework designed to quantify the distribution of fibrosis quantification methodologies across organ systems and modality groups.

- A primary assignment algorithm assigned each article to exactly one best-fit modality group using a hierarchical decision rule, producing mutually exclusive counts that sum to the total cohort (N = 563).
- A complementary multi-count analysis tallied all modalities and organ systems addressed within each article, capturing the full extent of cross-modal and cross-organ overlap.

Classification dimensions included modality group (imaging, histopathology, AI/technology, clinical tools, molecular/biomarker), organ system (hepatic, cardiovascular, pulmonary, renal, integumentary), imaging subcategory, disease context, and study design.

Results

A total of 563 articles satisfied the inclusion criteria: 405 clinical/human studies (71.9%), 106 phantom/validation (18.8%), 64 animal models, 32 protocol papers, 14 ex vivo, and 8 in vitro.

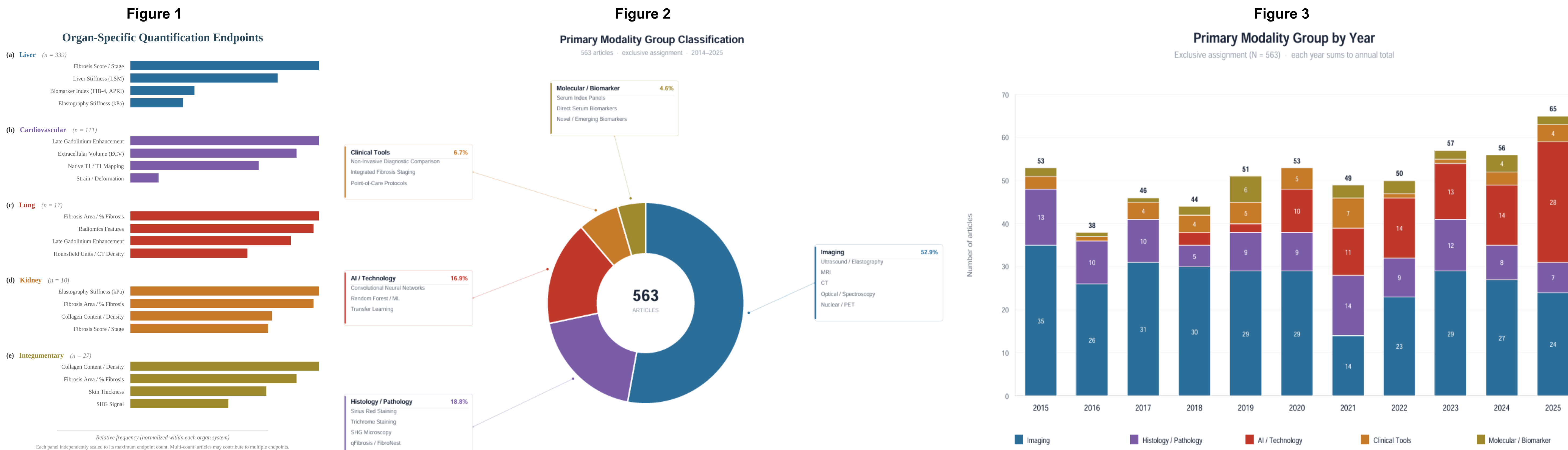


Figure 1. Top quantification endpoints by organ system, independently normalized to illustrate organ-specific measurement paradigms. Integumentary endpoints include collagen content, fibrosis area, and SHG signal.

Figure 2. Primary modality classification of 563 articles by exclusive best-fit assignment, with imaging subcategory breakdown.

Figure 3. Temporal trends in primary modality group distribution, 2015-2025, showing emergence and sustained growth of AI/technology-focused publications.

Discussion

Surgical Planning Applications: Fibrosis quantification has direct implications for preoperative planning and intraoperative decision-making. In plastic and reconstructive surgery, objective assessment of dermal fibrosis informs surgical timing in burn scar revision, evaluation of tissue flap viability in irradiated fields, and longitudinal therapeutic response monitoring in hypertrophic and keloid scarring. High-frequency ultrasound, OCT, and SHG microscopy enable non-invasive measurement of scar thickness, dermal architecture, and collagen organization analogous to established quantification frameworks in hepatic and cardiovascular domains.

Organ-Dependent Modality Selection: Optimal modality selection is dictated by organ-specific anatomical and pathophysiological considerations: elastography predominates in hepatic assessment due to validated diagnostic thresholds; cardiac MRI affords superior myocardial tissue characterization; HRCT remains the standard for pulmonary fibrosis quantification. These organ-dependent paradigms have potential applicability to integumentary fibrosis quantification, where hepatic elastography threshold models may inform standardization of cutaneous stiffness measurement and cardiac tissue characterization principles may guide dermal composition analysis.

AI as Quantification Augmentation: Prior to 2018, AI/technology publications were absent from the dataset and subsequently increased to constitute the second-largest primary category by 2025. Convolutional neural networks applied to digitized histopathology enable automated fibrosis staging with reduced inter-observer variability relative to manual scoring. Platforms such as qFibrosis demonstrate capacity for standardized cross-institutional quantification and may be extensible to objective cutaneous scar assessment.

Enduring Role of Histopathology: Histopathologic techniques, including trichrome staining, picrosirius red, and SHG microscopy, retain reference standard status across all organ systems examined in this review. The integration of AI with digital pathology constitutes an emerging hybrid paradigm that combines the cellular-level spatial resolution of tissue-based assessment with the objectivity and throughput of computational analysis.

Translational Implications

Integumentary Fibrosis Assessment: Integumentary fibrosis constituted 7.8% (44/563) of the quantification literature, indicating a relative paucity of validated assessment tools despite substantial clinical relevance. Methodological frameworks established in more extensively studied organ systems, including hepatic elastography threshold models, cardiac MRI-based tissue characterization, and AI-augmented digital pathology, warrant further investigation for adaptation to cutaneous fibrosis quantification. Such approaches may complement existing clinical assessment instruments including the Vancouver Scar Scale and POSAS.

Clinical Care Delivery: The organ-specific modality signatures identified in this review have translational relevance to the delivery of wound care and healing. Non-invasive fibrosis quantification enables longitudinal monitoring of therapeutic response without repeated biopsy, a consideration of particular importance in burn and trauma populations where serial tissue sampling carries additional morbidity. In hepatology, validated elastography thresholds already inform clinical decision-making regarding disease surveillance and transplant candidacy; while analogous threshold development for cutaneous stiffness and collagen density metrics could similarly standardize wound healing assessment and facilitate evidence-based timing protocols for implementation of interventions.

Limitations and Future Directions: Within this review, renal and integumentary fibrosis quantification methodologies remain comparatively underrepresented relative to hepatic and cardiovascular domains. Cross-modality validation studies enabling direct comparison of diagnostic performance metrics are limited within the current literature. While endpoint standardization across institutions and organ systems remains an unresolved challenge that constrains multi-center collaborative research and meta-analytic synthesis. The predominance of liver-centric study populations within the dataset may further limit generalizability of modality performance findings to other organ systems. Development of cross-organ harmonized fibrosis quantification endpoints, with particular attention to integumentary applications, represents a priority area for future investigation.

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