Spectroscopy As a Tool for Measuring Skin Frailty: A Preliminary Review

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Spectroscopy to measure and assess skin health and skin frailty is an emerging use case for the technology. Physiological frailty in humans is a decline in the body's ability to maintain homeostasis, and this decline appears in many organs, including the skin. Skin frailty describes how this systemic frailty affects the skin. As people age or develop chronic disease, the skin loses collagen and elastin, becomes thinner, and holds less moisture. These changes matter for health, but they are usually measured with separate tests that can be invasive, time-consuming, or difficult to perform routinely. Spectroscopy is a scientific technique that uses light to probe tissue. It can potentially measure several skin biomarkers at the same time (such as collagen, elastin, hydration, and oxygenation) without breaking the skin. This review explains the concepts of skin frailty and skin aging, notes key biophysical and molecular biomarkers, and describes how current tools like ultrasound, transepidermal water loss (TEWL) meters, and corneometers are used in measuring skin health. The review will then compare how spectroscopic techniques such as near-infrared (NIR), diffuse reflectance spectroscopy (DRS), Fourier transform infrared spectroscopy (FTIR), and Raman or fluorescence methods might offer a more unified way to assess skin frailty. The review will point out major gaps in knowledge such as the lack of a clear definition of skin frailty, limited standardization of spectroscopy methods, and the need for clinical validation and regulatory approval. Further research also suggests the need to create "frailty scores," standardize protocols, and test whether these spectroscopic methods can more reliably predict clinical outcomes. However, overall, spectroscopy appears to be a promising, non-invasive approach for quantifying skin frailty.

Keywords: skin frailty, spectroscopy, near-infrared, diffuse reflectance, Fourier transform infrared spectroscopy, Raman, fluorescence methods, biophysical markers, molecular markers, skin aging

Introduction

Frailty refers to the slow decline in the body's ability to adapt, heal, and stay in balance as people age[1]. While it is typically recognized through physical signs such as weakness, slower walking speed, and unintentional weight loss, frailty also affects the skin.

The skin is the largest organ and serves as the body's main barrier against the outside world. With age, it commonly becomes thinner, less elastic, and drier. These changes are part of normal skin aging and can be driven by internal factors (such as hormonal shifts and reduced cell activity) as well as external factors (such as ultraviolet radiation, smoking, and pollution)[2,3]. However, not all aging skin is frail.

In this review, skin frailty refers to skin that is more fragile and vulnerable than expected for a person's age. Frail skin is more likely to tear, bruise, or form ulcers, and wounds may take longer to heal. The concept focuses on vulnerability and risk of complications, rather than appearance alone. Skin frailty also differs from skin fragility disorders, which are rare genetic conditions that cause severe skin fragility that typically begins in childhood[4,5]. These disorders can look similar on the surface, but they have different causes and disease courses.

Skin health is influenced by many systemic factors; poor nutrition, chronic inflammation, metabolic disease, and environmental exposures can affect the appearance and function of the skin[2,3]. With the skin being easy to see and examine, it has potential to be an indicator of overall physiological status. This makes skin frailty an interesting idea for screening and risk assessment.

Currently, there is no universally accepted "gold standard" test for skin frailty; clinicians often rely on visual inspection and their own experience[4,5]. When more detail is needed, clinicians may order skin biopsies, ultrasounds, optical coherence tomography (OCT) imaging, or use instruments like corneometers and TEWL meters[6–9]. These tools are valuable, but they can be invasive, time-intensive, or expensive, and often measure only one property at a time.

A non-invasive, efficient, and more comprehensive method to measure skin frailty would therefore be more useful. The process should be simple for both patients and health care providers, consistently measure relevant biomarkers, and provide numbers that can be tracked over time. In the field of dermatology and other medical fields, optical spectroscopy is becoming more common[7]. Spectroscopic methods measure how light is absorbed, scattered, or emitted by tissues, which can reveal information about collagen, elastin, water content, blood, and other components[7,10]. This raises a key question: can spectroscopy be developed into a practical tool to evaluate skin frailty, and in turn be used to predict overall health outcomes?

To investigate this question, this review draws on a targeted selection of peer-reviewed articles identified through literature searches in biomedical databases. The sources focus on adult human skin, age-related changes, skin fragility and frailty, relevant biophysical and molecular biomarkers (such as collagen, elasticity, and transepidermal water loss), and non-invasive or minimally invasive measurement techniques, including spectroscopic methods commonly used in dermatological research.

The sections that follow describe how skin aging develops and how skin frailty fits into that process. It then summarizes biophysical and molecular biomarkers related to skin frailty, explains how different spectroscopic methods can measure these biomarkers, and discuss current challenges and possible future directions for bringing spectroscopy into clinical practice.

Skin Aging, Frailty, and Biomarkers

Skin aging is a multifactorial process shaped by both intrinsic and extrinsic factors over an individual's life. Intrinsic aging reflects changes that occur over time due to genetic programming and internal biology such as reduced fibroblast function, altered hormone levels, and accumulation of oxidative damage. Extrinsic aging is driven by environmental exposures such as UV radiation, tobacco smoke, and air pollution. These exposures generate reactive oxygen species (ROS), which damage proteins, lipids, and DNA and speed up the breakdown of structural molecules in the skin[2,3]. Over many years, collagen and elastin fibers become fragmented, more heavily cross-linked, and less easily replaced, leading to looser, more wrinkled, and less resilient skin[2,11].

Skin frailty is closely related to these aging mechanisms but emphasizes what the mechanisms mean in practice. Frail skin tears more easily, bruises with minimal trauma, and is more likely to develop ulcers. Once damaged, it will heal more slowly or incompletely[4,5]. These issues are especially important in hospitalized patients and residents of long-term care facilities, where immobility, friction, and pressure over bony areas increase the risk of injury[4]. In such settings, thinking of a patient as "skin frail" could play a role similar to labeling someone as a "fall risk," reminding staff to take extra precautions.

In order for skin frailty to be a tool for health measurement, objective indicators must be defined. For clarity, these objective indicators are split into biophysical markers (which describes physical properties of skin) and molecular markers (which describes the skin's biochemical and cellular environment)[5,7].

Biophysical Biomarkers

Biophysical biomarkers are measurable physical characteristics of the skin and the most important ones this review will cover include elasticity, thickness and density, and hydration and barrier function.

Elasticity

Skin elasticity is the dermis's ability to stretch and rapidly recoil to its original shape[2,11]. In everyday clinical practice, elasticity is often judged informally with the skin turgor test. The clinician lifts a fold of skin, holds it briefly, and then releases it, watching how quickly the skin snaps back into place. A slow return suggests reduced elasticity or dehydration[12].

For more precise measurements, devices such as the cutometer are used. The cutometer is a non-invasive biomedical device that applies suction on the skin via negative pressure to displace the skin. It then measures the displacement of the skin from its original position and the time it takes to return to its original position. Greater displacement indicates more elastic skin, and the time indicates the ability of the skin to recover from deformation[13]. Larger deformation and slower recovery indicate less elastic, more fragile skin.

Thickness and Density

Skin thickness is the distance from the outermost layer of the epidermis to the interface between the dermis and hypodermis. Whereas skin density is the compactness and thickness of the skin layers, particularly in the concentration of collagen and elastin fibers within the dermis[2,11]. Frail or severely aged skin often appears thinner and less dense than the skin of healthier individuals of similar age[4,5].

One method for measuring these biophysical markers is the use of ultrasound. Ultrasound can be used to distinguish between the epidermis and dermis, determine density of tissues, and measure for skin thickness[6,14]. However, the results can vary depending on probe frequency, operator technique, and device settings, so consistent protocols are important when comparing results between studies[6].

OCT provides another non-invasive option. It uses near-infrared light to generate detailed cross-sectional views of the skin[7,15]. Older patients, and frail skin, tend to have reduced vasculature present. This can lead to decreased skin oxygenation, slower wound healing, and decreased delivery of nutrition[4]. However, OCT is limited by its relatively shallow penetration depth (1.5 mm) and by potential challenges with reimbursement and routine insurance coverage due to being a category III Current Procedural Terminology (CPT) code[15,16].

Hydration and Barrier Function

Hydration of the skin refers to maintaining optimal water content within epidermal layers and barrier function is the stratum corneum's ability to act as a selectively permeable defense system–limiting water loss and blocking pathogens or chemicals[17]. A widely accepted tool to measure skin moisture is a corneometer. Corneometers estimate water content in the stratum corneum by measuring changes in electrical capacitance at the skin surface[8].

TEWL meters is another device to measure how well skin can retain moisture. A measured higher TEWL score indicates a weaker barrier and greater moisture loss[9]. In a study of children at risk for atopic dermatitis, 11 of the 101 children with a family history of allergic diseases developed eczema. All 11 children had higher baseline TEWL and altered skin immune biomarkers than those who did not[18]. The scale of the study warrants more research due to small sample size, but its results show that barrier-related measurements can act as early warning signs.

Molecular Biomarkers

Molecular biomarkers include proteins and other molecules that shape skin structure, repair, and immune activity. In the context of skin frailty, the most notable biomarkers this review will discuss fall into three main categories: collagen and elastin, cytokines and inflammatory mediators, and markers of glycation and oxidative stress.

Collagen and Elastin

Collagen types I, III, IV, and V provide tensile strength and structural support to the dermis, while elastin allows skin to stretch and then return to its original form[11]. As an individual ages, production of both proteins decreases, and existing fibers become fragmented, more disorganized, and heavily cross-linked. These shifts reduce the mechanical resilience of the skin and make it easier to tear or deform[2,3].

Cytokines and Inflammatory Mediators

Cytokines are signaling molecules that coordinate immune responses and wound repair. When inflammation becomes chronic, even at low levels, it can interfere with normal healing and maintain a tissue environment that is less robust[4,17]. Unfavorable cytokine patterns in the skin may therefore be a sign of greater vulnerability and slower recovery after injury[4].

Markers of Glycation and Oxidative Stress

AGEs and related oxidative markers indicate long-term metabolic and environmental stress. They are especially prevalent in people with diabetes or long-term UV exposure. AGEs bind to collagen fibers and induce further cross-linking leading to 'kinks' within the tissue matrix. AGEs also bind to immune cells and trigger the release of inflammatory mediators–mediators that generate ROS, compounding damage done to the skin[2,3].

Cost-Benefit of Biophysical and Molecular Markers

Traditionally, these molecular biomarkers are measured from skin biopsies using histology, immunohistochemistry, or biochemical assays. These approaches provide detailed information but are invasive, require laboratory processing, and are not ideal for repeated use or bedside screening[4,7].

When viewed together, biophysical and molecular biomarkers give a fairly complete picture of how sturdy or fragile the skin is. The challenge is finding ways to capture enough of this information non-invasively and in a standardized way so that "skin frailty" can be expressed as a useful number or score[5,19]. Spectroscopy offers one possible route toward that goal[7].

Spectroscopy as a Tool for Skin Frailty

Spectroscopy is based on how light interacts with tissue. Light is delivered to the skin, and the returning signal (reflected, transmitted, or emitted) is measured. By analyzing these signals, it is possible to estimate how much light has been absorbed or scattered and to infer contributions from different molecules and structures[7,20]. For skin frailty, the aim is to use spectroscopy to assess collagen and elastin, water content, barrier integrity, and blood flow or oxygen supply through one or a few quick, non-invasive measurements. By comparing spectral measurements to an established normal range, clinicians could more easily track a patient's skin health over time[7].

These capabilities mean that spectroscopic assessment of skin properties can be more than a local measurement; it can also serve as an indicator of overall physiological health status. The epidermal barrier plays a central role in protecting the body from dehydration and external threats, so barrier dysfunction can have wider physiological consequences[17]. In addition, non-invasive skin surface biomarkers and TEWL measurements have been shown to predict later development of atopic dermatitis, which is itself associated with systemic allergic diseases such as asthma and food allergy[18]. Within the broader frailty framework, such findings support the idea that skin health can act as an indicator of overall physiological vulnerability[1].

Diffuse Reflectance and Near-Infrared Spectroscopy

Diffuse reflectance spectroscopy (DRS) measures light scattered in all directions after interacting with pigments and microstructures. The shape of the reflected spectrum depends on absorbers such as hemoglobin and melanin and on scattering from collagen and other structures[7,20]. In one study, DRS measurements at 980 nm showed a 93% correlation with skin capacitance, suggesting that DRS could act as a non-invasive marker of barrier integrity[21].

Near-infrared spectroscopy (NIR) uses longer wavelengths that penetrate more deeply into tissue and are particularly sensitive to hemoglobin and water. In dermatology and related fields, NIR has been used to monitor changes in tissue oxygenation over time. The depth of sampling can be adjusted by changing the spacing between light sources and detectors placed on the skin[7,22]. A study by Mizukoshi found age was a significant factor that affected NIR spectroscopy readings of oxygenation levels[23]. This suggests that NIR may be useful for assessing microvascular blood flow and oxygen delivery in aging or frail skin.

Both DRS and NIR can be performed relatively quickly and have the potential to be built into portable devices. However, measurements are sensitive to factors such as probe pressure, skin curvature, and pigmentation. Standardized measurement protocols and good calibration procedures are therefore important if these techniques are to produce reliable and comparable data[7].

FTIR, Raman, and Fluorescence Approaches

Other spectroscopic methods look more directly at chemical composition. FTIR measures characteristic vibrational absorption bands from molecules like proteins, lipids, and water[7]. Small differences in amino acid sequence and structure give each collagen type a slightly different FTIR signature. This allows FTIR to distinguish collagen subtypes and separate collagen from elastin in tissue samples[10]. Because of this, FTIR can serve as a powerful tool in indirectly measuring skin elasticity.

Confocal Raman spectroscopy (CRS) measures inelastic scattering of light and provides information about specific molecular bonds. CRS can generate depth-resolved profiles showing how water, lipids, and other molecules are distributed through the outer skin layers[7]. Skin thinness can also be measured using CRS. In 2012, A Böhling conducted a study where the thickness of the outermost layer of the skin was measured using CRS and compared it to the more traditional method of laser microscopy. Böhling measured the outermost layer at multiple locations across the body and found that both methods gave similar readings for skin thickness[24].

Fluorescence spectroscopy detects light that is emitted by molecules after they have absorbed energy. Several naturally occurring skin molecules, including some AGEs and structural proteins, are fluorescent[2]. Changes in fluorescence intensity or shape can reveal cumulative photodamage, metabolic stress, or shifts in matrix composition, all of which are relevant to the development of frail-like features.

Compared with DRS and NIR, FTIR, Raman, and fluorescence approaches usually provide more detailed biochemical information but require more complex equipment and longer data collection times. As of current use cases, they are mainly utilized in research settings and early validation rather than in routine clinical screening[7].

How Spectroscopy Compares to Other Tools

Current non-invasive skin assessment tools generally focus on single aspects of skin health[6,8,9]. High-frequency ultrasound and OCT emphasize structure, such as layer thickness and density[6,15,16]. Corneometers and TEWL meters target hydration and barrier function[8,9]. Physical examination focuses on what can be seen and felt (such as color, texture, scars, and wounds)[4]. Each method offers useful information, but most give a fairly narrow view.

Spectroscopy does not replace these techniques, but its strength lies in how much information can be packed into one measurement. A single spectrum can, in principle, reflect contributions from several biomarkers at the same time: collagen and elastin, water, hemoglobin, and scattering from microstructures[7,10]. This opens the door to building a composite spectroscopic index of skin frailty. In theory, such an index could combine features related to collagen–elastin structure, hydration and barrier function, and NIR-based oxygenation into one score. That score could then be compared with clinical outcomes such as skin tears, pressure injuries, or delayed wound healing[4,23].

However, before a composite index like this could be implemented clinically, spectroscopic measurements would need to be standardized and carefully compared with existing reference methods in real-world clinical settings[7].

Challenges and Future Directions

Although spectroscopy shows promise, several important challenges must be solved before it can be used routinely to measure skin frailty.

One major challenge is that there is still no clear, widely agreed definition of skin frailty. Different clinicians and researchers use the term in different ways, and there is no standard list of clinical signs or thresholds[1,4,5]. Progress will likely require consensus on which visible signs (such as recurrent tears, frequent bruising, or chronic ulcers) and which quantitative measures (such as reduced elasticity, thin dermis, or high TEWL) should define a “skin frailty” state.

Another issue is the lack of standardization among spectroscopic studies. Different groups use different wavelength ranges, probe designs, measurement times, and data-analysis approaches[7,22]. As a result, it is hard to compare or combine data results across studies. Community guidelines on basic topics like calibration, probe placement, contact pressure, measurement timing, and minimum reporting standards would make the field more consistent and easier to interpret[7].

Validation is also crucial. Spectroscopic signals need to be compared directly with established methods such as histology, ultrasound, OCT, corneometry, and TEWL across different patient groups[6,7,9]. Longitudinal studies would be particularly useful. As an example, a spectroscopic frailty score measured at baseline could be tested to see whether it predicts later development of pressure ulcers or recurrent skin tears. Without this type of evidence, spectroscopic markers will remain mostly theoretical[4].

There is also no widely accepted spectroscopic frailty score yet. Building one would involve choosing a normalized set of spectral features, deciding how to weight each feature, and then testing how well the combined score matches real-world outcomes in large cohorts[7,19]. Statistical modeling and machine-learning tools can help identify which features are most informative, but any resulting models would still need to be transparent, checked for overfitting, and examined carefully for bias.

Finally, there are practical and ethical questions. These include how to navigate regulatory approval, how to keep devices reasonably priced and portable, and how to train clinicians and technicians to use them correctly[7]. Because spectroscopic data can be detailed and may be combined with other medical information, issues such as data security, patient privacy, and fairness in algorithm design also need careful attention[21].

Even with these challenges, the overall direction for future work is fairly clear: clarify what is meant by skin frailty, standardize spectroscopic methods, perform strong validation studies, and plan carefully for how such tools would fit into everyday clinical workflows.

Conclusion

Skin frailty provides a useful way to think about how aging and disease affect the skin's ability to tolerate stress and heal after injury. Rather than focusing only on appearance, the concept draws attention to serious complications such as tears, ulcers, infections, and slow healing[4,5]. Better measurement of skin frailty could help identify high-risk patients earlier and guide preventive care in hospitals, outpatient clinics, and long-term care facilities[1].

This review has described how aging changes skin structure and function, summarized key biophysical and molecular biomarkers, and outlined how both traditional tools and newer spectroscopic methods measure these features[2,6,11]. Spectroscopic techniques–including DRS, NIR, FTIR, Raman, and fluorescence–are especially interesting because they may capture several relevant biomarkers at once in a non-invasive way[7,10,23]. However, spectroscopy is not yet ready to act as a complete "skin frailty panel" in the way a blood panel would offer a large amount of information with blood draws. Clearer definitions, more consistent protocols, stronger validation studies, and practical strategies for clinical use are still needed[4,7].

In an aging society, simple and non-invasive methods that can detect declining resilience early are becoming increasingly important. With further refinement and testing, spectroscopy has the potential to turn the skin–an organ that is easily visible and accessible–into a sensitive indicator of overall health and vulnerability[1,7].

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Table 1 Comparative features of spectroscopic modalities for skin frailty

Modality	Main Signal	Sensitivity/Specificity	In-vivo Penetration	Technical Complexity	Portability	Validation	Key Pros	Key Cons
Diffuse Reflectance Spectroscopy (DRS)	Backscattered light influenced by hemoglobin, melanin, and collagen-related scattering; can reflect barrier integrity through associations with TEWL	Good sensitivity to vascular and pigmentation changes; moderate specificity because signals from multiple chromophores overlap	Superficial to mid-dermis, with depth dependent on wavelength and probe geometry	Requires spectral calibration and control of probe pressure, angle, and ambient light to ensure consistent measurements	Generally compatible with handheld or fiber-optic probes; fast acquisition makes it suitable for portable systems	Shows promising correlations with barrier function, but no validated spectroscopic frailty metric yet; limited longitudinal testing in frail cohorts	Non-invasive, rapid measurements; captures both vascular and structural information in a single spectrum; potential surrogate for barrier status	Sensitive to pressure, skin curvature, and pigmentation; requires protocol standardization; difficult to isolate contributions from overlapping chromophores
Near-Infrared Spectroscopy (NIR)	Absorption signatures from oxygenated and deoxygenated hemoglobin and water, allowing assessment of microvascular oxygenation and tissue hydration	High sensitivity to changes in oxygenation and water content; moderate specificity due to broad, overlapping absorption bands	Reaches deeper layers than visible-range DRS–typically several millimeters into dermis or subcutaneous tissue, adjustable via source-detector spacing	Requires wavelength-dependent calibration and attention to detector spacing; oxygenation indices rely on computational modeling	Well-established hardware; supports continuous or bedside monitoring; feasible for point-of-care use	Used clinically for perfusion studies; age-related differences reported, but no standardized NIR frailty index or regulatory-approved device for this purpose	Probes deeper microvasculature; highly relevant for evaluating perfusion and oxygen delivery in frail skin; adaptable to wearable or bedside systems	Limited biochemical specificity; susceptible to melanin levels, motion, and placement variability; requires modeling to separate skin and deeper tissue signals
Fourier Transform Infrared Spectroscopy (FTIR)	Mid-infrared vibrational absorption from proteins, lipids, and water; capable of distinguishing collagen subtypes and elastin	Very high biochemical specificity with strong sensitivity to subtle structural alterations	Restricted to very superficial layers due to strong water absorption; often focused on the stratum corneum or ex-vivo samples	Requires precise optical alignment, reference spectra, and computational analysis; in-vivo measurements are technically demanding	Mostly benchtop systems; in-vivo probes exist but are used mainly in research environments	Clear research evidence for detecting matrix changes, but limited validation in aging or frailty-specific populations; no standardized clinical protocols	Provides detailed biochemical information on collagen, elastin, and lipids; directly linked to structural markers of elasticity and matrix integrity	Limited penetration depth; longer acquisition and analytical requirements; less practical for rapid or bedside screening

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Modality	**Main Signal**	**Sensitivity/Specificity**	**In-vivo Penetration**	**Technical Complexity**	**Portability**	**Validation**	**Key Pros**	**Key Cons**
Confocal Raman Spectroscopy (CRS)	Inelastic scattering signatures that identify specific molecular bonds, enabling depth-resolved profiles of water, lipids, and selected biomolecules in the epidermis and superficial dermis	High molecular specificity and sensitivity to gradients in hydration and lipid content; capable of detecting subtle compositional shifts	Depth-resolved within the epidermis and superficial dermis, depending on system configuration and focusing precision	Requires accurate optical focusing, spectral calibration, and advanced data processing; acquisition times are longer than DRS or NIR	Mainly research-grade systems; point-wise measurements require stable positioning and trained operators; limited availability of portable units	Validated measuring of stratum corneum thickness/hydration against reference imaging methods, but not yet applied to frailty-specific metrics or large clinical studies	Provides detailed, layer-by-layer biochemical information; can quantify hydration and lipid distributions and verify epidermal thickness; strong chemical specificity	Small sampling area, longer acquisition times, and higher technical demands; limited penetration depth; currently unsuitable for routine clinical screening
Fluorescence Spectroscopy	Emission from intrinsic fluorophores such as AGEs and structural proteins; reflects cumulative photodamage, metabolic stress, and glycation-related changes	High sensitivity to AGEs and photodamage-related fluorophores; moderate specificity due to overlapping emission from multiple contributors	Primarily superficial to upper dermis (limited by absorption and scattering), typically within a few hundred micrometers	Requires controlled excitation-emission calibration and correction for scattering and absorption effects; may require spectral unmixing for accurate interpretation	Compact probes and handheld fluorescence systems are feasible; however, measurement protocols and clinical interpretation are still under development	Used to assess AGEs and photodamage, with suggested ties to chronic disease burden; however, frailty-specific validation and prospective clinical studies remain limited	Directly reflects long-term metabolic and UV-related stress; rapidly captures biochemical signals linked to aging and cumulative skin damage	Composite signals from multiple fluorophores reduce specificity; sensitive to skin tone and recent UV exposure; interpretive thresholds not standardized for frailty assessments

