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An Innovative Approach of Examining Skin Changes Associated with Scleroderma from a Mechanical Perspective, Stiffness based Novel Analysis

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Abstract: ***Fibrosing conditions represent a true dilemma in management for the clinicians. The parametric approach is used less in medicine and in many times silo thinking precludes full usage of advancements in different disciplines. For the first time, we reported a new method to measure changes associated with systemic sclerosis and correlate them to mechanical properties of the skin. Our results showed clearly how the skin is affected by this condition. These changes will continue in predetermined controlled fashion until reaching frank full blown disease. Early diagnosis simply means early management. The correlation will result in powerful evaluating tool for treatment and follow up of the disease.***

Keywords: skin, scleroderma, sclerosis, parametric approach, strain, mechanical engineering

1. Introduction / Skin, Important concepts

Every organ has a specific function, and its composition is derived by its function. Here we want to concentrate on these points:

1) Tissues, especially connective tissues, are extremely complex composite structures. Their SS curve (stress strain curve) is not uniform across all individuals. All are highly nonlinear with mixed properties of viscoelasticity and hyperelasticity. Equipped with a fascinating feedback nervous system and affected by hormonal systems. They are anisotropic with certain architecture render them orthotropic on the micro and macro scale (1)
2) Had a very important remodeling capacity. This remodeling process is very complex in its initiation propagation and regulation. Any irregularity or disorder in each step will result in some degree of change in the mechanical properties of these tissues. It is well known in composite science: the importance of different fibers combinations or the type of used fibers and their percentage and orientation in tailoring the properties of the composite. We think that the fibers are not only the present effector on the mechanical properties of the skin, but also the matrix which plays a significant role in the total mechanical properties of the connective tissues types as well as micro and macro characteristics of the tissues (2). All these are known well in histology, but it should be us well approached parametrically in case of diseases and pathological conditions.
3) Nature for tissue must be considered. Stretchable tissue such as skin is totally different in its connective tissue component (supportive components) from those supportive components in solid organs with limited capability of deforming (such as liver or spleen). In the latter situation, they are intended to retain their shape and have limited deformity capability. The plethora of conflicting mechanical properties of different tissues should be refined on a scientific basis. Many authors give different values and properties as reported in the different papers and texts (3).
4) The skin had complex 3d configurations and one of the questions that should be answered is what is happening to its different components and configurations (e.g. rete ridges) during skin mechanical loading i.e. traction? fibers of skin affected by repetitive movement results in remodeling (4). The remodeling process makes skin fibers direction predominate in certain direction (Langer lines) (5). This inherited feature of remodeling of fibers is obvious in osseous tissues. Some tissues had no remodeling capacity such as dentine or enamel (6). Non remodeling tissues already had highly organized structures even on the nanoscale.

The fibrous network of the skin is responsible mainly for its tensile properties. Many other ingredients of skin add further non-linearity features of the skin (7). The connection of skin to the deep tissues is not uniform. What we had called (skin pivoting), is due to more tethering bands of the skin. (8)

Skin had some areas where it has limited capacity to be stretched. Findings of strain deviations close to wrist joints had been demonstrated clearly in this research at the ankle joints, they explain the pivotal concept in that the tendons that pass below the skin in that area tethering skin resulting in limited mechanical properties of the skin in that particular area. (9)

2. Skin is not a single uniform cover

Skin in the flat area without pivotal attachment will deform uniformly rather than containing a sharp transition from low to high values of strain within the limited examined area. This may happen in the case of the presence of a skin tethering structure such as tendons in the close vicinity. This could be seen from the color distribution over the examined

area (10). This is gone with the concept of LOME.

It is one of the most advanced composites ever imagined. It must be clear that the skin is not pure elastic. It had viscoelasticity as well as all other tissues. Skin is not just a container of the body tissues, but also affects the dynamic status of the body and joint movements. There are static and dynamic tension lines (11)

The dermis is believed to be the main load-bearing component in the skin and is stiffer compared to the epidermis. Using the indentation method, Crichton et al. reported Young's modulus of the dermis to be 7.33–13.48MPa for 6.62- and 1.90mm-diameter spherical probes, respectively, which are higher than the reported epidermal components' stiffness in the same study. Finding the elastic modulus of the intact human skin and having the volume fraction (0.01 from Tregear99), Sanders estimated this value for the elastin fibers in the living human skin to be 2–10GPa. For the collagen fibers, an elastic modulus from 0.112 to 1 GPa52 (in the linear region) is reported in the literature.

The preservation of tissue after harvesting will dramatically affect its properties (12). In vivo analysis will give reliable results. In vivo experiments provide data on tissue in its natural state, i.e., permeated with blood, and in a typical pre-tensed pre-stressed state. In some of the in vivo experiments, the measured behavior is attributed to the dermis. However, as a result of connections between the various skin layers, it is difficult to isolate the contribution of the dermis from that of the epidermis and subcutaneous tissues, such as muscle and fat. Four classic main methods used for in vivo testing of the skin are:

- Indentation
- Torsion
- Tension
- Suction

We think that indentation and suction give very limited evaluation of the skin. Torsion is simple tension in a complex arrangement, and we think that stretching of the skin is the best test that could give the complete idea about the skin mechanical properties. Areas where skin is tethered to subcutaneous tissues will make it less displaceable than other areas.

3. Notes on Scleroderma

SSc may cause confusion as many medical specialties deal with (13). The exact etiology of SSc is unknown (14). Internists and rheumatologist vs dermatologists have different approaches to the SSc.

It needs a multidisciplinary approach. Dermatologists, Internists, Rheumatologist, Orthopedic surgeons, Rheumatologist …. Etc. can be involved in the management and treatment of this disease in one of its courses. These interventions may be in the beginning or deal with its late complications. We suggest the book (Scleroderma from Pathogenesis to Comprehensive Management) to be the first station for any researcher in this very complicated subject.

Not only would the genetic map of the diseased individual define its susceptibility being affected by SSc, but also the extrinsic factors. Although the monozygotic twins show very similar auto-antibodies profile, the clinical expression of the disease shows a different course. This must be considered as the external factors that would affect the already present risk factor for the patient. (15)

Types of scleroderma

Complete speech about SSc could be found elsewhere in many textbooks of different disciplines (rheumatology dermatology pathology……etc.)

There are two presentations of the disease: -
- Localized
- systemic

The most common classification of systemic scleroderma (also called systemic sclerosis) is diffuse and limited. The difference between them is the involvement of areas proximal to knee or elbow joints. We think that the anatomical considerations by which these parts have more movement. (16). There are two phases of the disease edematous and atrophic (7). The edematous phase precedes the atrophic. Tissues turnover is affected by many factors and the most important mechanical factors are the tear and wear. Skin turnover rates might be the clue for the distribution of fibrosis in different body regions in SSc (17).

Pathophysiology

Connective tissue found everywhere, and their autoimmune diseases could affect a single organ or multiple organs. SSc could be regarded as a manifestation of vascular injury that initiates widespread changes. (16). It had a strong underlying immunological basis (16)

Skin properties will be changed after treatment in systemic sclerosis whether to decrease the edema in the edematous stage or decrease the stiffness in the induration stage (14). This means that treatment is very important, and the changes of the disease could be regressed. Location of the lesions in systemic sclerosis and their extensions determine the type of disease (7)

As the condition progresses, the skin movement will be less. Which is resulted from an increase in fibrosis. This decrease in skin ability to be stretched or compressed with result in less remodeling of the newly deposits of collagen fibers and leading to a vicious circle that would be perpetuated. That makes skin lose elasticity even happening at a steeper curve. Up to our knowledge no grading with a wide range scale of the mechanical properties of the skin affected by scleroderma rather than the description of skin in well- established disease. It is important to mention that collagen type 1 which considered the strongest type is the most component that deposits in the case of SSc (18)

Here are some notes about the pathophysiology of the disease:

- All tissue components and arrangements if disrupted would lead to manifestations totally different from the causative factors. The tissue barriers are not as simple as many think. Immunity must be kept away from some regions and components of the body. Not only some

areas are immune privileged, but we think also some cellular components are privileged as well. An example is defective cell apoptosis had been claimed to cause SLE, as their remaining DNA will elicit their antibody response (19). Another example is that happened on the molecular basis in case of systemic sclerosis and result in in the fused organ fibrosis. Hypoxia resulting from disrupted vessels blood vessels due to autoimmunity had been claimed to be one of the causative factors of fibrosis.

- Each component of the connective tissue had certain functions. Some had a structural mechanical function and others acting as molecular messengers. The following concept is speculative, but we think that damage in certain components of the tissues will initiate a particular cellular response, as this specific component damaged configuration by itself is a molecular messenger. This signal will lead to different responses that repair or modify tissues, so that what called tissue remodeling when results when these messengers are present whether due to trauma or any other idiopathic cause. Fibrosis is one of the body's natural responses to many causes. (20)
- The study of SSc by histological studies like the study of blood coagulation by fixing blood in formalin and study it under the microscope after embedding it in Paraffin wax, as both have a molecular basis. Tissue changes are the net result of the disruption that happened on a molecular basis.
- The question remains what is the precise determination of the whole process; remodeling and the condition that initiates remodeling when there is no need for it? And is the skin manifestations across affected patients is uniform across different patients?

The pathophysiology of systemic sclerosis stands after the fact that fibrosis processes promoting and regulating mechanism is affected. Histological picture of skin in systemic sclerosis is very distinctive and the pathognomonic feature of squared-off rete pegs due to an enormous amount of collagen fibers deposition in the dermis so that its transition to deep tissue will be sharper. We think that atrophy of adnexal glands it won't affect mechanical properties of skin directly, but indirectly through stopping of the beneficial effects of these glands (16).

Histological studies reveal significant findings that contribute to the mechanical performance of the skin. These changes in systemic sclerosis had resulted in skin properties changes.

- Increase in the modulus of elasticity of dermis and epidermis. As the epidermis contributes little to the total skin mechanical performance what we have from the mechanical properties of these 2 layers come actually from the dermis. We think that what we had recorded is the behavior of the dermis. Epidermis will contribute little to the mechanical properties of the skin. So, what we had analyzed of the epidermis deformation, is what happens in the dermis (11). It is not clear to us the configuration of rete pegs of the dermis- epidermis junction under load, whether it will be flattened or remain in its complex 3D wavy configuration? and if flattening of rete pegs happens, the question is what will happen in direction perpendicular to the direction of traction, could the rete pegs be more condensed?
- Lipodystrophy could result in reduced sliding of the skin. We attribute lipodystrophy to be one of the deterrent factors on the modified Rodnan skin score.
- From a biomechanical point of view, the anisotropicity of the skin is lost due to deposing of high amount unidirectional collagen fibers, we think that they are newly formed in a rapid manner and have not taken the phase of remodeling.
- Not all areas of the skin of patients reach the same stage at the same time. Some areas may be at edematous stage while others are at indurative stage (7)

Many questions about the origin and fate of the disease are still unanswered. One of these is: why is the molecular reaction of the disease behaves so heterogeneous? Up to now, we don't know about the answers to these questions.

4. Treatment

Treatment is very important in managing SSc as the treatment could halt progression or provide regression or at least stabilize the condition of the patient at an acceptable stage (14). Current medical treatment of SSc is directed mainly toward modifying the immunity of the patient (21). Used drugs are potent and now many clinicians prescribe multiple drugs in different combinations. Most common drugs used in the treatment of SSc: Glucocorticoids.

- Cyclophosphamide.
- Azathioprine
- Methotrexate.
- Mycophenolate mofetil.
- Biologicals (Which are drugs produced by biological processes.)

Some of the biologicals used in scleroderma treatment:

- Anti-IL-6 Tocilizumab
- Anti-IL-1: Rilonacept
- Anti-TGF-ß Fresolimumab
- Antitype 1 Interferon

The treatment in the early stages of the disease is better than in the more advanced stages, as no such physical changes and resolution of fibrosis in advanced stage is much harder than the resolution of edema at the beginning of the disease. In addition to the previous two dilemmas, the vascular changes may be irreversible (22)

We suggest following up on the effect of any therapy by measurable criteria with a wider scale that gives consistent results rather than limited highly subjective methods such as modified Rodnan skin score. We have good advances in the provision of experimental animal models, which are immunologically based, each model should be characterized not just histologically, but also mechanically. The use of animal models could not be applied directly in humans but provide good insights on the molecular designation of scleroderma causative factors. (16)

Systemic sclerosis is a heterogeneous disorder and careful categorization of the disease by putting the patient in a

correct category is essential in obtaining a good cohort. Cohort enrichment gives a better evaluation of trials` results (16). With current tools, we might still be unable to recognize individuals in different stages of disease and the effects of different treatments on the results of the disease.

Current method used in diagnosis of cutaneous involvement in SSc.

Skin in SSc could be measured by:

- MRI
- MRSS (modified Rodnan skin scoring)
- Elastography and ultrasonography
- Plain x-ray radiography.

There's no rationale to do a biopsy of SSc patients for research purposes (16). This is also applied for clinical diagnosis as this disease has a pathognomonic appearance in its established form. The benefit of systemic sclerosis classification is differentiation between diseased and not diseased person and classification of disease into classes or stage so that the treatment could be facilitated (16) Inconsistency of the current diagnosis tools of SSc in the initial presentation of the disease signs is clear (23). An example when we are talking about systemic sclerosis sine scleroderma, they say that even half of the patients in the study excluded from having cutaneous involvement and diagnosed with SSc Sine Scleroderma, latter they have developed cutaneous manifestation after a period of time (24). The explanation of this is that those patients originally may have had cutaneous involvement, but it was not measurable. In the American rheumatologist Association (American college of rheumatology) original classification criteria of SSc, skin remain the cornerstone in the diagnosis. Even with their revised criteria skin also has the lions share. (16)

The initial diagnosis of systemic sclerosis is proven to be highly subjective in many instances and many cases went undiagnosed, as well as treatment outcome could not be easily evaluated (25). Many tests and measurements developed to qualify skin involvement in systemic sclerosis (25), but they depend upon clinical examination and sometimes on photography. Photography could have many types of distortion that affect results or readings, which affect the evaluation of the disease when reviewed (26).

Problems associated with the current tools

One of the reasons that make the reliability of the clinical tests related to mechanical properties of skin questionable is that the mechanical properties are already lacking or poorly defined (10). To explore the properties of a material, it should be subjected to changes and analyze its changes (27). Every testing to a certain mechanical property includes some sort of energy application. Most tests include physical forces (putting the material under tension, torsion, flexion, shear, or compression). (27). The direction of force application is important when dealing with material that is not isotropic. Applying forces horizontally parallel with the skin surface will demonstrate most of the picture of skin mechanical properties, while vertical force may be limited in the context of SSc evaluation (2)

Clinical manual examination could not demonstrate the effects of disease on many examined areas, as it lacks specificity and sensitivity. Other investigations, like ultrasound, could demonstrate involvement (28). Even when this involvement is mild or in the internal organs (29). When manual methods constitute one of the diagnosis criteria, many cases could be missed if the signs of the disease are not fully developed. When the American Rheumatism Association/ American College of Rheumatology want to make classification criteria with a large multicenter database, many patients had not been diagnosed and missed, even they were the start of the disease in that time (16)

We could use skin to differentiate between different stages of the disease. Some skin areas may appear normal, even in well-established SSc cases. Many features of SSc couldn't be identified by clinical examination. The clinician could not be aware of the stage of SSC whether it is in the edematous or at the start of the atrophic phase. (7)

Manual palpation of the patient's skin may not yield accurate data. The grade of manual palpation is dependent upon just the examiner and what's she/he feels. Hence the conveying of the results to other clinicians, when discussing the condition, may be suboptimal in comparison to automated processes, where results are told in numbers (7). Also, biopsy doesn't always give an idea about the case, because the properties of the biological materials will be changed after preservation, processing and during lab preparation of the samples (30). Our work is to determine objective criteria that could be used easily in SSc (7)

As the natural change of the skin is happening over a long period of time, it is more difficult to be followed by other classical methods (31), we need an accurate precise tool to capture the skin conditions every time we test it.

Modified Rodnan Skin Scoring (MRSS) breakdown

Skin must be represented by numbers rather than vague words or general words, that in many circumstances are poorly conveyed or understood (10). We think that detection of skin involvement in case of SSc must not dependent upon MRSS solely as it may miss many diseased individuals (2)

Both modified Rodnan skin score and presence of palpable tendon friction rub could be considered as highly subjective and depend upon the examiner. Implementation of measuring tape when deforming skin during a clinical examination to test the amount of skin displacement during stretching is helpless as there is no reference to return to the same point every time and we must have results with at least sub-millimeter specificity and sensitivity (16).

MRSS is one of the most commonly used manual examination methods to evaluate the cutaneous involvement of systemic sclerosis patients (32). It has 3 grades (33):

- 0=normal skin
- 1=mild thickness
- 2=moderate thickness
- 3=severe thickness with inability to pinch the skin into a fold

Skin deformity, when performing MRSS, is complex. It involves and includes multiple components which impart its inconsistency. Here we want to show the different deformations that the skin will take so that the examiner could pinch the skin, which is the core criterion of this skin test:

1) The score depends on the friction between the skin of the examiner's finger and the patient`s skin.
2) There are two regions of bending in the skin. We suggest that this type of skin deformity world make a slight effect on the total skin resistance to deformity. The difference between them is where the compression and tension will occur during deformation. Even though this difference had no significant effect up to our estimation, we think that it is important to be mentioned.

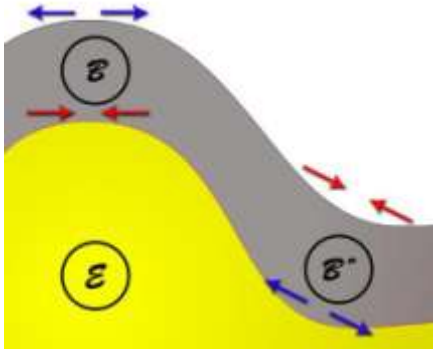

Figure 1: Difference in bending of different skin regions when pinching the skin. Blue arrows indicate expansion, while red arrows indicate compression.

3) There will be expansion of tissue in the bulk of the pinched tissue. We think that resistance of the skin in case of systemic sclerosis to be pinched is due to defect in this component of skin deformity during pinching as the ligaments between dermis deep fascia would be fibrosed. Histological studies show the characteristic feature of squared-off appearance at the reticular dermis and extend the deeper subcutaneous tissue while in healthy tissues (34). We can regard these ligaments had higher stiffness than those in the normal skin.
4) In the area beneath the site of examiner finger placement, there will be more compression. If the subcutaneous fat layer remains unchanged by the disease, they may be atrophied, they will remain and provide some source of skin sliding properties of the skin.

From our analysis of the movement of the skin through the ultrasound and the structure we have examined, we believe that some of the movement is happening between the deep fascia and the deepest structure. The ultrasound examination was done for a healthy person. In the case of a diseased individual, we think that it will be to a lesser extent which results in a higher grade of MRSS.

1) The areas of tension on both sides of pinching prevent the advancing of each side toward each other. We regard this area as the second detrimental factor for the pinchability of the skin.
2) Area of shear in between the skin surface and the Deep structure. Whenever the subcutaneous fat tissues remain, it would keep the skin from having the ability to slide over the deep tissues. Although the capability to show this feature in the sclerodermic patient would be attenuated due to the possibility of lipodystrophy.

Individuals have variable skin thicknesses (35), so we think that would affect the MRSS and depend on the chosen anatomical position. Even in the same position, there are many different changes or big differences if the orientation of skin pinching is different from orientation to other (36) Modern instruments (like ultrasound) unlike manual estimation, make the diagnosis easily with high confidentiality, even in the clinically asymptomatic in the early stage of the disease and it provides wide range scale instead of narrow scale like in manual tests (2)

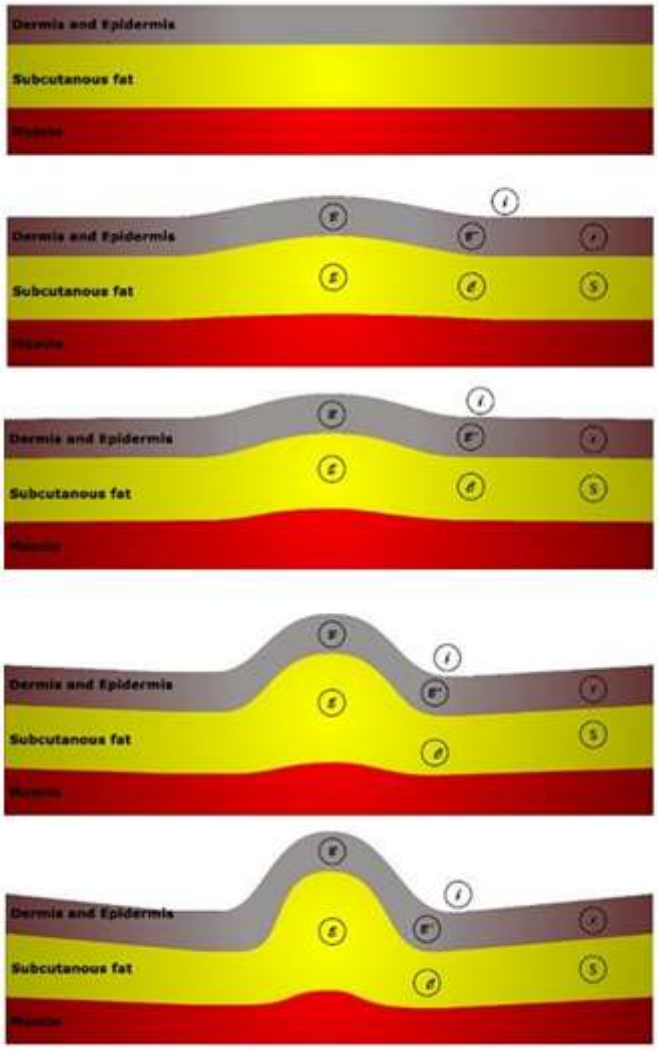

Figure 2: Explanation of the different regions of different deformations when the MRSS test is done. B bending area, B" bending in opposite direction, E expansion area, C compression area, t tension area, S sliding area, f friction area.

Durometer

The Durometer had been suggested to be a simple non-invasive valid reliable device to be used for examining the cutaneous changes in SSc patent (37) (38) (39).

These points must be considered when judging durometer in skin evaluation:

- With skin testing with a durometer, the compression effect will be the greatest feature to be faced. Some displacement of tissue escaping from all directions

around compressed layers of skin.

- It is intended for isotopic continuous solid materials and sometimes gives different results according to the site of examination. While we want a method to give a picture of all points in the examined field over the horizontal scale whatever the nature of the material is.
- There are many types of durometers, each would yield different results.
- Most times it is compared to highly subjective classical methods, and by this comparison, the contrast is clear. It absolutely reduces the rate of inter-rater variations, but it also had limited reading for compression only.
- To map a certain area, we need many measurements in order to designate that area.
- The durometer couldn't be used in some anatomical areas from a practical point of view, while our method reveals the properties of the skin whatever structures below are. When examining skin or testing it by conventional methods, it could imply deformity of skin the favor of another and may not give sufficient data. Skin test by suction (usage of cutometer), which had only small diameter, could induce changes only in the superficial part skin. We think that most of the expansion area will happen in the epidermis and dermis and less involvement from deeper parts of the skin.

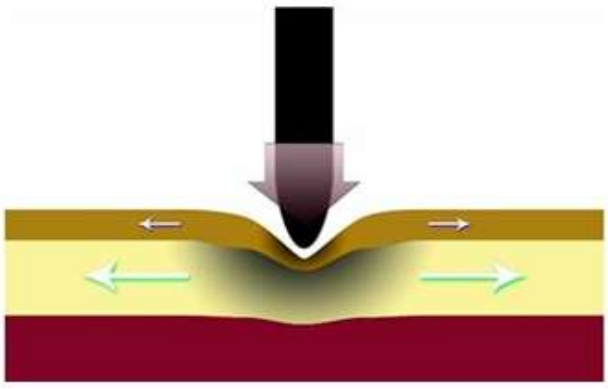

Figure 3: When the skin is indented, there will be a displacement of tissues out of the pressed area

When testing skin with the suction test (like in case of cutometer) the reverse will happen, and we think that suction is better in evaluating these skin properties as it will depend upon expansion in skin component more than the compression

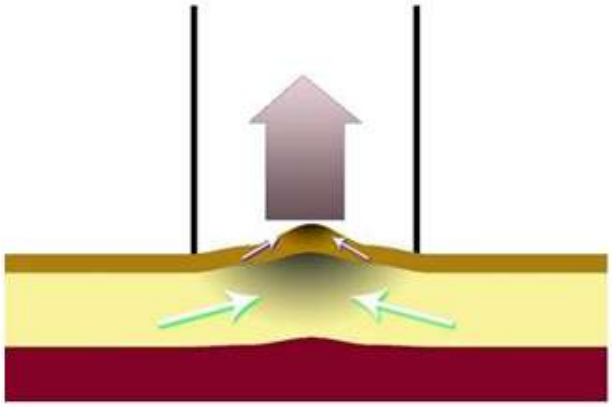

Figure 4: In contrast to indentation, suction of the skin will induce different expansion of different skin regions.

5. Notes on our methods used in case of Scleroderma

In our current approach, large regions of the skin could be tested simultaneously without any invasive intervention as well as not touching of the skin or placing any sensor on the skin rendering it very useful, where these sensors could affect the mechanical response of the skin and the total stiffness of the skin will be changed.

While studies for the molecular basis of SSc and the types of autoantibodies may predict the course of disease (40), our work is targeted toward the recording of final events through recording the deformity pattern of the skin. When studying the strain of the skin, anatomical consideration must be regarded in the context data analysis as the results would be different from different body sites.

What we make us choose stretching of the skin is that this will show up skin displacement for a large area of the skin. In addition to the tension, the compression on the other side of tension will be readily recorded. In the case of the torsion skin testing, we will have limited areas and we think its complex results will render the result more difficult to analyze. Also, the component of the torsion test is the same as the stretching, but in a different configuration (basic components are tension, compression, and shear)

Every surface point in the skin had two mechanical interactions to the points it is attached:

1) Interaction with the adjacent points on a horizontal scale.
2) Interaction with underlining on a vertical scale.

These 2 points will define the different aspects of the mechanical properties of the skin.

Regions of skin traction or stretching could be explained through the knowledge of different SS (stress strain) curves. Some regions reach ultimate deformation and stop further deformation. It must be clear to know that the question remain need answer is:

1) What will stop the skin from further stretching?
2) Which component of these components would stop the local area from additional deformation or displacement?
3) Is it the underlying tissues or is it the surrounding tissues? We suppose the areas of the skin deformation are four:
   - Rigid skin: due to the effect of attached scale tape, it has no deformity.
   - Deforming skin is the area adjacent to the rigid skin where the most severe deformation is happening at.
   - Stretching skin is adjacent to the deforming skin and it will bridge the deforming skin and surrounding skin.
   - Global skin which lies beyond the stretching skin.

There are intermediate areas between these areas, and they represent the transitional zones between the preceding areas. A wider transitional zone simply means higher skin elasticity.

The question here is: what is the correlation of these regions

of movement to the movement that happened across the vertical layers of skin and subcutaneous tissues?

Plots of the skin displacements and strains must be summarized to evaluate skin properties across different systems and studies. The aim of electrocardiography is to get the electrocardiogram in which the physician could interpret the condition of a patient's heart (41), and we want in our approach to put standards for skin analysis so that it could be investigated in the future through these plots like exactly how we investigate the heart conditions through ECG. The analysis was retrieved from the deformation ion of the skin utilizing mathematical calculation of the points already drawn on the skin surface. LED lighting equipment is very efficient in providing the lightening of the sample (42), unfortunately, the lid during transport had been damaged as it stopped from working during the experiment. We depend on sunlight and generic light during data capturing.

Introduction to our results, how is the best way to interrupt them.

These are concepts that should be respected when analyzing the results:

1) Arrangement of the displacement components

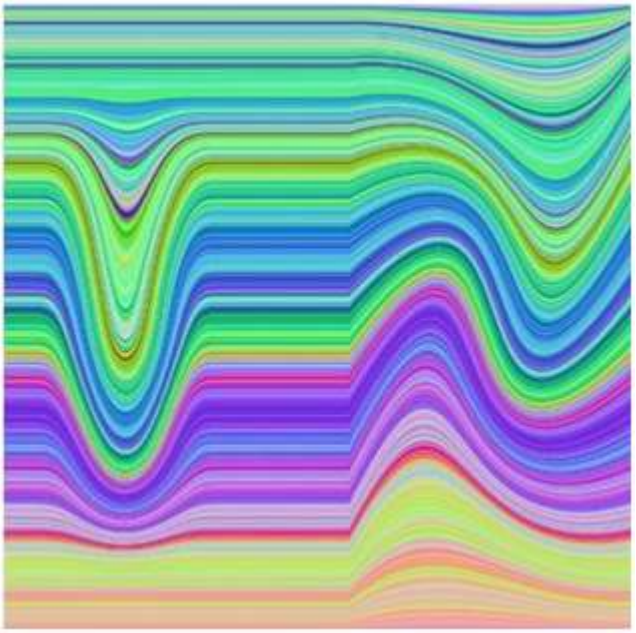

Figure 5: Simple representation of the stretching test versus twisting test

We supposed the twisting test is done by two components that attached to the skin and rotated at the center point between them. Twisting could be considered as at least two rotating stretching components in opposite directions. So, the calculation of results in case of twisting would be more complex and might distract the researcher. In every trial to solve uncertainty, simple configurations must be assumed at the beginning followed by more complex variations. We must start to define variables in a serial manner until all variables are solved. In mathematics when you get a polynomial function, you can't solve it in a single step. According to this concept we had chosen to stretch the skin and analyze the deformation. Also, we consider indentation and suction well as the torsion test need testing equipment that would obscure the displacement field, although we want to test these methods in the next time in addition to our method.

2) Growing of regions of the pattern

As it is clear that the first and final pattern are identical at the start and end. The steps that are intermediate between them to reach the final status clearly show that the pattern on the left side is different from that on the left. The difference in the growing of the region with time is apparent. In the case of the pattern on the left side, all regions are growing by the same ratio until reaching the end.

The figures on the right show that the central region precedes all regions and reaches its full size in the first steps and then the other region in sequence what we called sequential growing. In this growing, no region will begin to grow until the preceding region reaches its ultimate shape.

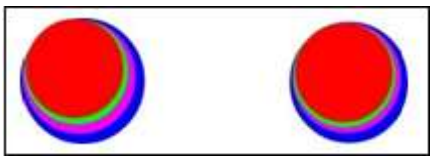

Figure 6: at the start, both have the same size.

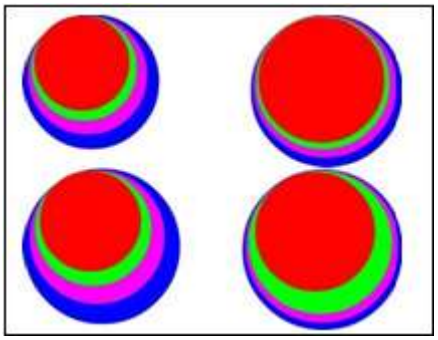

Figure 7: in the intermediatory stage the difference is apparent.

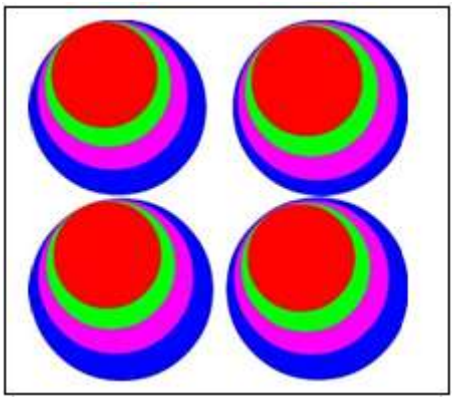

Figure 8: growing of different pattern regions could be more important than the major and minor values themselves. In the figures on the right, the reverse might happen when the outer regions might begin to enlarge at the first steps of the growth instead of the inner regions.

In all of the previous figures the highest value is represented by the red color and the lowest values represented by the blue color. In both of the figures on the left and those on the right, the first and final result has the same value with the same distributions, but the growing of the region is totally

different from that on the right.

3) How the values of the parameters are shifted from region to another

Strain distribution had equal importance in the analysis of the highest values of just the highest values, and each pattern had three features (43):

- Values
- Distribution
- gradient

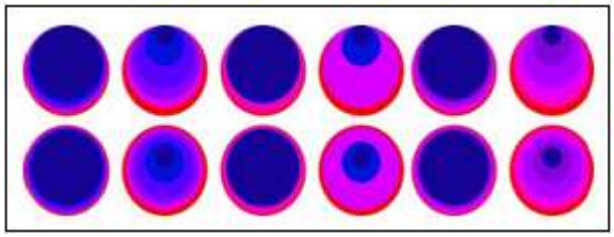

Figure 9: The gradient between the highest and lowest values gives great clues to explain the differences between what seems to be the same pattern. Different gradient location necessarily means different pattern

The plotted displacement vs time will clearly show this concept when we show the results. Pattern of distribution of the values is more representative and important than the highest values only, as the pattern will give the correct idea about the condition.

Every point in the skin when tracted is prone to the following tethering components:

- underlying tissue layers (shear effect)
- points behind it on the traction line have the highest effect (tension effect)
- from points against it on the traction line intermediate resistance (compression effect)
- effects of the adjacent points have the least effect (shear effect)

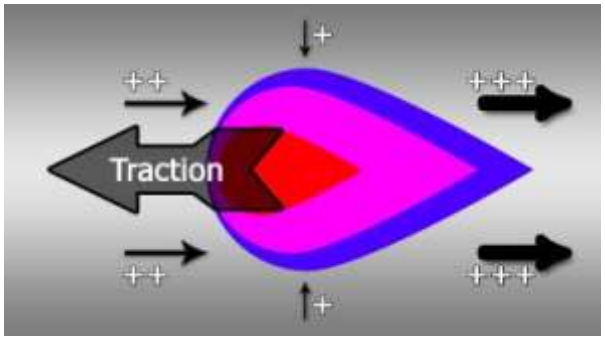

Figure 10: When the skin is stretched, different site adjacent to the traction site would resist the deformity. No. of + sign indicates the amount of resistance of each region as we think.

As the point becomes more away from the fraction site, the relative amount of the force that comes from underlying tissues will grow higher relative to that pull it. The traction force will be dissipated progressively as the point becomes further away from the traction site.

Our method vs. other methods

MRSS is highly subjective with a limited scale and many variables that affect the final decision of the examiner to give the grade for an examined area. A fundamental concept in scaling in engineering is that the narrow scale of measurement may put similar values in the same grade or level. While if we had extended scale, differentiation between measurable units could be achieved more precisely. Let's suppose the unit of measurement is half a meter. People's length grades will have the highest value no more than 6 grades, as the longest man hadn't passed 3 meters. It will be senseless measure as a person with Achondroplasia well had the same grade as a kid.

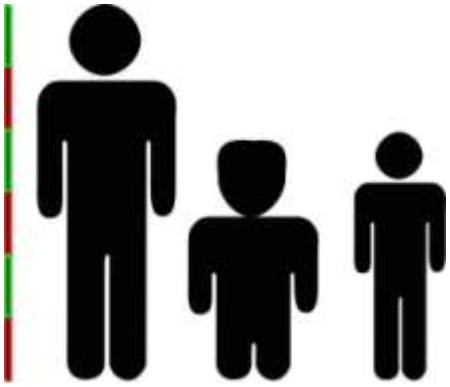

Figure 11: Achondroplastic individual may be shorter than another person with less Chronological age. With such a scale on the left with minimum units, length description might be limited.

In the previous example, follow-up could not be beneficial unless significant change reached that could be perceived by most people. In the previous example, we have no gray value, either white or black. Human senses could be adapted easily and subtle gradual change in the long term might be passed without being noticed. This is about one value, but in a case when evaluating something with multiple values the process will be more prone to errors.

Many ultrasonic machines are equipped with codes that enable the operator to evaluate the dynamic response of the tissues, as in the case of elastography, but at the same time these are limited measurement. Surface measurement could provide better insights to the clinicians.

Conversion of numbers into figures and colored plots will facilitate the process of diagnosis. It would enable doctors also from fellow up to the conditions and understand it easily (2). As would be shown in our results, the different plots with endless combinations between different variables, many conditions could be easily analyzed and explained. It is better to determine the anatomical site of examination and the traction site. So examined parts have the same site across all individuals. Our methos like ultrasound, both are non-invasive and capable of real time demonstration.

In the inflammatory stage, we think that the modulus of elasticity of skin could be lower than the healthy person as the tissue's layers had more space for movement over each other (14). The changes occurring deep in the skin could be characterized on the surface by our method. Skin changes reflect the changes in the internal organs. It could be a feature used to determine the prognosis of the disease. Skin features such as thickness and tightness are the only major diagnostic criterion (7). Displacement field and strain distribution and other features that analyzed from material

behavior under different loading conditions will define materials' properties.

Many engineering concepts applied in the medical fields must be understood with the context of its original use. The major and minor strain is an indication of the formability of the metal sheet that could be used in evaluating skin, but it must be understood in the context of its use (44)

In our method different analysis could be done according to the sensor used (i.e. UV photography). In addition to this samples of measurement are stay in hand as it could be analyzed at any time or future analysis. In our study, we used relatively slow speed cameras, and thus some parameters could not be retrieved, nevertheless we carefully arranged what we thought was enough to capture skin strain and deformations. Unfortunately, it was not enough, and some data (such as acceleration and acceleration changes) couldn't be captured.

Why we had chosen the forearm.
Skin remains the most determinant of systemic sclerosis diagnosis. The skin had elasticity with multiple additional features such as viscoelasticity. The viscoelastic properties of whatever the sample of material could be measured using our method depend on mechanical parameters such as displacement and strains. Choice of the forearm is for many reasons. First of all, is easy to be exposed by the patient in contrast to other areas (such as the abdomen, back, thigh…. etc.) especially in conservative communities such as our community. Ease of pattern application and good movement of the skin over the deep tissues are available in the forearm. What makes us analyze the whole anterior or volar surface of the forearm is that local strains and displacements may be missed if we chose the other side which is need rotation the forearm and placing it in more uncomfortable position. Interpretation of the whole skin of this region is important to see if any presence of effect from adjacent anatomical structures, such as what we found in there is joint and in the oblique strain. The forearm is a very important area and many hand flexors pass over the radius and ulna beneath the skin.

Our examinations of the forearm had been done where the forearm flexed 90 degrees and hand is in the anatomical position. Other anatomical conditions when the hand is rotated or the forearm at anatomical position needed it to be studied. This may show the effect of the muscle positions on skin deformation. We had put a point with reproducible location. In addition to this, standardized skin sticker is recommended to offer consistent results across all the study in the same patient and other patients (2)

Forearm examination would yield consistent results as it has good skin with good soft tissue (muscle and fat). It has a good range of movement across any local coordination for any chosen point, especially at the middle of the volar surface (2). In the case of fingers' skin, due to limited space that is crowded with many different anatomical structures and scarce subcutaneous fat with local tethering of skin and presence of multiple joints, render this area more difficult to be measured and for the result to be interpreted (2). Male and female age between 15 and 70 had no significant difference in the properties of their skin (7). We suggest that mechanical properties are also similar even though we hadn't done an analysis to approve this. We think that in case of systemic sclerosis the fibrosed skin will have the same mechanical features also if they are at the same stage of disease progression.

In this research (10), authors had gotten sufficient sensitive data from each patient that had been used to divide them into groups, we think because they take small elliptical area (about 5.6* 6 cm), each person from one group could have the same pattern of a person in another group if the location of the examined area was changed. Volar aspect of forearm had multiple regions of skin elasticity and also it depends upon the direction of applied force (10)

A line drawn from the point where biceps brachii cross the greatest skins crease of the elbow joint on the anterior side of the forearm, to the highest distant point in the middle of the greatest crease of the wrist joint. At half of this line, a medical-grade sticker has adhered to. A scale already stuck to the medical sticker which is then utilized for traction.

5. Results

In order to understand the properties of a material, at least two criteria should be implemented to explore more of the hidden aspects of material properties. Not just the total displacement should be calculated, but also their displacement in Y and X direction, as this would give a clearer idea of skin when lying in the line of traction and when it is in a position away from it on its sides. There is displacement with the direction of the traction scale and displacement vertical to it.

We had seen full features as the two regions at the distal area of the forearm:

- The ulnar angle is nearly fixed.
- The radial angle is more mobile.

There is a well-demarcated elliptical zone of strain had long axis run out from the proximal end of the ulna to the distal end of the radius we correlated this to the joint and the underlying muscle and in harmony with the context of rotation of the forearm at the ulnar axes. In study (10) close to our work, we observe the inclined pattern of the skin at the distal area of the forearm close to our findings.

We think that there are not only just skeletal joints, but also there are cutaneous joints, which represent the areas where more extension +/- friction or wear between them and most of the deformity happens there. We think that the architecture of the collagen fibers in these areas is totally different from the collagen fibers in other areas. This feature of the skin must be addressed globally, for all skin regions. It may have strong effects on the skin flaps of that specific region. Surgical flaps must not be designed on the basis of the blood supply only, but on the properties of the skin in that area. The elliptical region should be characterized globally across different ages because it may give additional insights into the mechanical properties of the skin. (45) When different variables are plotted against time in the 2D plot, the resultant curve will have a certain degree of zigzag.

The degree of smoothness of curves regarding these values (displacement, strain, velocity, acceleration) was in the current sequence.

1) Displacement and strain have the clearest smooth curve that could be recognized.
2) Velocity and Acceleration are the least clear and most messy. We suggest motorized tractor to attain constant deformation and constant effect and better comparable results.

We consider using motorized traction in the next research to suppress this wavy variation in the curves of analysis. The application of the motorized tractor will also omit the unintended deviation of tractor due to manual traction. Manual traction may deviate to the right or left. It will also provide:

- constant speed and acceleration
- constant direction of movement
- constant amount of applied force

What made us choose to select the point and the long axis of movement and in the central axis to use it as traction site, is what we strongly think that they are freer of tissues that tether them than those near the joints. This tethering causes them to have lateral movement. We think that tethering is less here, and the displacement would be most affected by the traction force.

We chose 12 points on the line that we chose for the placement of the traction site and compare some of the values associated with them. These principles and results of these points have given us the idea about the SCLERODERMOMETER. The diagram of plotted values of displacement of these 12 points against time of the sclerodermic person and healthy person clearly show the non-uniform displacement pattern for the former and uniform displacement pattern for the latter of skin. In the case of healthy skin, the final displacement clearly shows uniformly distributed over all the points while in the diseased skin the nearest point to the skin attached scale shares most of the greatest displacement.

Also, the strain pattern shows that the strain in the case of diseased skin will reach larger values after that next point strain would raise, but in a healthy person, the strains in the successive points will raise gradually and more evenly in all points and the difference between final values of the strains of these points had an approximate value. Gowing of the strain and displacement pattern should be scrutinized very carefully. While in the diseased skin the difference between the first and second in the final reached value is larger than the second and third and so on

1) Maximum displacement pattern 2- Relative displacement speed.

These 2 criteria could be the keys in the identification of the skin mechanical properties. We suggest putting them to be tested criteria for the scleroderma or any skin evaluation. Even in the study on the skin stretching (10), when the stretching force-directed proximally the same inclined deformation pattern had been seen (as apparent in the figure of the study). The stretching skin strain in the case of the patient with scleroderma has a well-defined pattern periphery than that in healthy person.

The strain is first the maximum displacement second the pattern of displacement in each quarter of the maximum displacement.

When analyzing a condition such as systemic sclerosis, the pattern and the evolution of this pattern during traction should be analyzed rather than just comparing the highest value of variables between two to samples of the examined population. When scleroderma affects the skin, it will have an apparent different pattern of skin displacement when stretched and growing of the deformity throughout the applying of the traction force is non-uniform sequential and areas nearer to the traction site reach the maximum deformation area early, so in the next steps they will not deform more.

While in the healthy skin the growing of each area will not achieve its maximum until the final stage of the deformity and the expansion will occur more uniform pattern in all regions of skin surrounding the traction site. Each deformity of a point on the surface represents the local deformity of that area including both dermis and epidermis, which had many affecters (10)

- Attachment to the surrounding tissues on the horizontal level
- Attachment with underlying the tissues on the vertical scale

From the primary evaluation of the analysis results, we conclude that the radio angle for the forearm has the highest strain and the ulnar angle has the lowest strain.

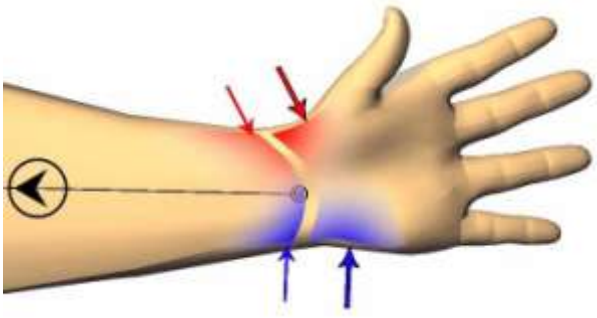

Figure 12: The hypothenar areas share close feature to the distal radial angle of the forearm as well as the thenar area with the ulnar angle.

The skin of the palm of the hand when stretched could displace the skin of the forearm, but the reverse hadn't happened. We haven't done a full analysis of this finding, and we will include it in the future works. The skin at the thenar area is more moveable than that of the hypothenar area and when the hand is fully abducted. Slight creases appear and strain will be distributed over the area proximal to the wrist joint over the distal part of the forearm. While in the case of medial side that also continues distally with the skin of the hand, strain, where the hand is objected, will suffer from obvious creasing.

Sclerodermic patient's results

As this work is a comparison of a single sclerodermic case to a single healthy case, we want to put the basis of future work

where more cases will be included. The patient we examined her forearm skin was diagnosed previously with SSc and she is on methotrexate with folic acid. She recently received cyclophosphamide as hospital-based administration. Consent was received from the patient with an explanation of the impact of the results of our work on the diagnosis of SSc before the commencement of the examination.

Figure 14 shows clearly the pattern applied to the whole volar aspect of the forearm. A point on the sticker had been chosen as an extensometer. It had been used as a guide to examine the different deformities and results during movement, as it is correlated to the movement of the scale tape. The scale tap is made from elastic material reinforced with glass fibers embedded within it, imparting on it a very high stiffness. The sticker region could be regarded as a non-deformable traction region.

Figure 13: Three points are our reference. proximal where the tendon of biceps brachii crosses the largest skin crease. The middleone is between the proximal and the distal point on the most distal point in the middle of the greatest skin crease at the wrist joint.

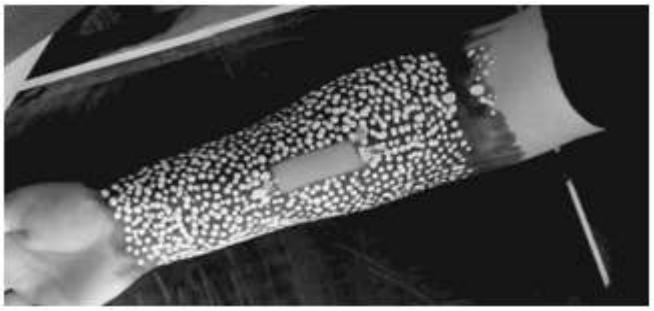

Figure 14: The dotted pattern applied over the whole volar surface of the forearm. Only the region of sticker is void from the pattern.

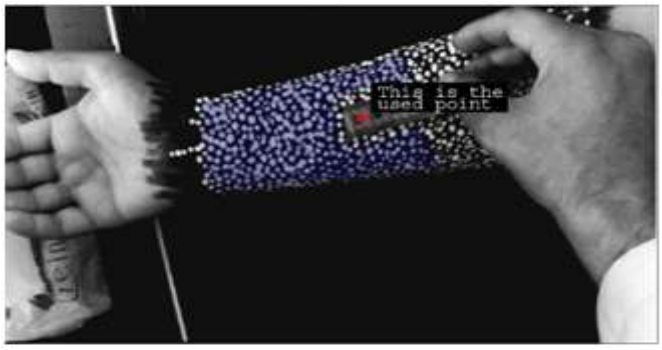

Figure 15: dotted pattern had been applied over all the volar aspect of the forearm. The stretching is done by traction of simple scale tape attached firmly to a medical-grade skin sticker. Red point had been regarded as a reference. The blue area indicates the area of the skin that had been analyzed.

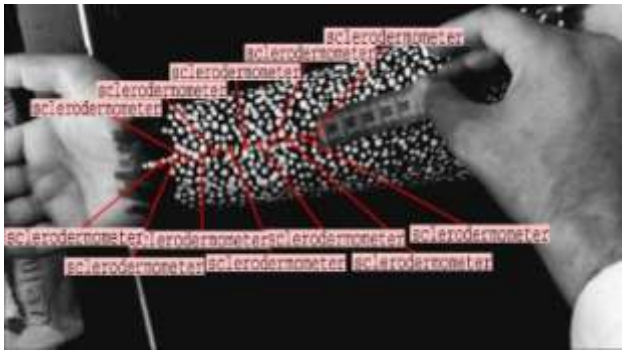

Figure 16: Twelve points (which had been defined as sclerodermometer) from the sticker place to the most distal point in the greatest skin crease at the wrist joint were regarded as parameter of deformation changes. They are located on the same line that the sticker attached to its midpoint.

Previous figure clearly shows 12 points in a straight line that extends from the traction site to a point in the middle of the greatest crease at the wrist joint. They had been distributed with the distance between them nearly the same. The results of the analysis of these 12 points displacements are behind the idea of sclerodermometer.

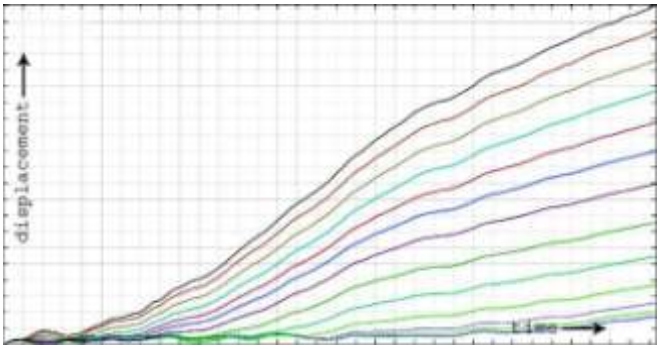

Figure 17: Curves of the displacements of the sclerodermometers. The lowest curve represents the displacement of the farthest sclerodermometer from the traction site which has the lowest values (sclerodermometer no.1). That on the top represents the sticker displacement of the sticker. The curve just below the top one represents the sclerodermometer closest to sticker site on to the sticker and has the highest values ((sclerodermometer 12)

The distant points had very limited displacement in comparison to those in the normal person

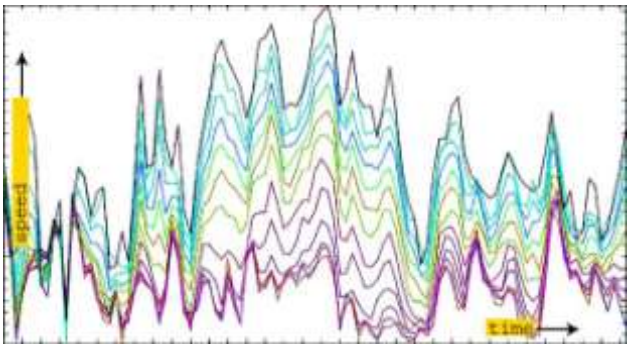

Figure 18: 2D plot of sclerodermometer speeds against time.

The speed of the proximal sclerodermometer is clearly shown to be close to that of the sticker in contrast to what had been results in a healthy person. The gapping is located in the middle of the time equally distributed over all the sclerodermometer.

We divide the displacement of the sticker into sex steps and analyze strains and displacements of the skin of the forearm. We depend upon the total displacement of the sticker to know where the start of each step is.

As the total displacement of the scleroderma sticker was about 10mm, that means we evaluate the strains and displacements of the forearm skin every 1.5mm of the sticker movement. The displacement plot had been regionalized into segments and each distal segment has value less than the neighbor segment proximal to it by 1 mm. it has value higher than the distal neighbor by 1mm.

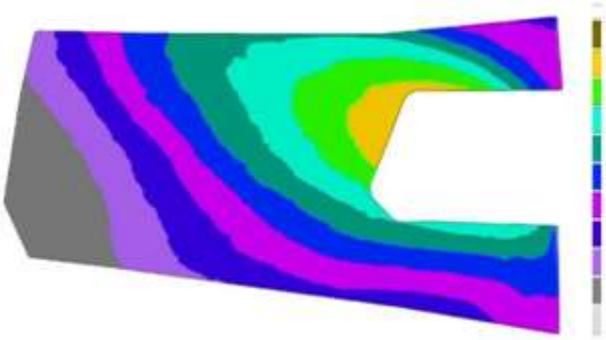

Figure 19: Displacement in step 6. We think that the histogram could represent the summary of the changes, which should be read thoroughly.

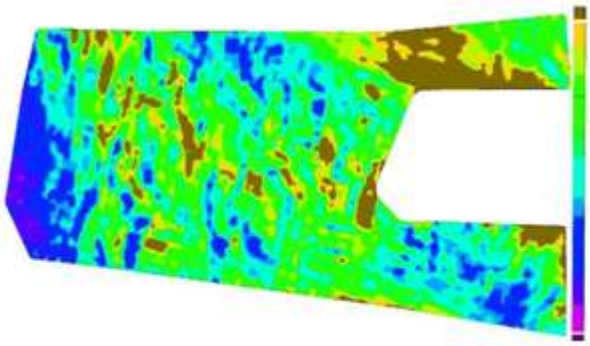

Figure 20: Equivalent mises strain. The red areas indicate where most inter parts displacement is happening at. Interestingly there are marked strains at both sides, lateral and medial of the sticker. While in the healthy person had been occurred on a single side only which could be due to rotation of the scale tape when it was stretched

The displacement plot of systemic sclerosis patients suggests that skin has higher stiffness. We can conclude that the disease increases the tethering of skin to the underlying tissues, as the peripheral area near the wrist joint had displacement less than 1 mm clearly more than that in the healthy patient. And the region of displacement just distal to taction site, while in healthy person it occurs also proximal to the traction site.

In systemic sclerosis, the dermis will be stiffer, and its stretching capability would be lesser than the normal skin due to the excessive amount of newly deposited collagen fibers. Before conducting the study in the beginning, we thought that increase the stiffness would be reflected by an increase of the displacement in the periphery and less in the center with less ranged pattern. But the histogram of the legend, values plotted the distributions of these values…etc. show different results.

In the sclerodermic skin, the strain area will have a well-demarcated region that moves with the direction of the traction giving it the appearance of a moving island. We attribute this islandly movement pattern due to the effect of reduced elasticity.
This is going with a strain plot in sclerodermic patients. The strain (equivalent mises strain) clearly shows most of the strain in the area between the sticker and rest joint and least in the periphery in comparison to the healthy patient. In the healthy patient, the strain in the periphery is more.

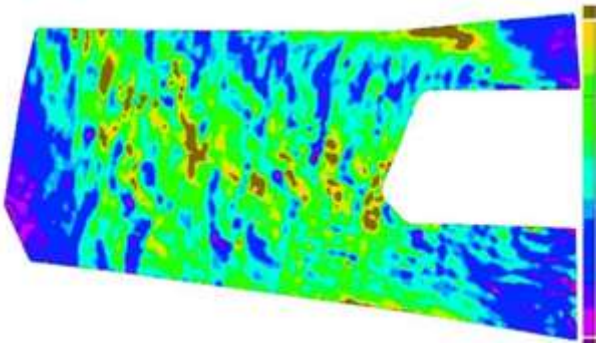

Figure 21: Major strain of the sclerodermic patient. It defines the strain only in major diameter direction. Which is not necessarily in the Y direction. It must be clear that in these figures, we establish the concept that could be used in the future for better evaluation of scleroderma.

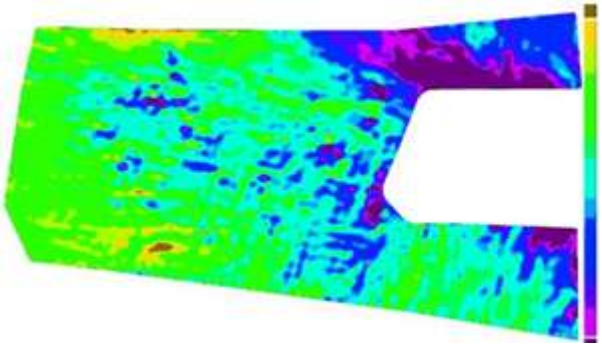

Figure 22: Minor strain of the sclerodermic patient. It defines the strain only in minor diameter, which is not necessarily in the X direction.

We had chosen three criteria to Measure strain:

- von Mises equivalent strain
- Hencky equivalent strain (both components on semi major and minor axes of the strain ellipse)

The first is more capable of capturing shear strain increments in comparison to the later (44), especially we have shear areas lateral and medial to the sticker region where strain should be captured. Although we hadn't included their graphs here. Dynamic growth of the strain was not informative like what occurred in the case of displacement, this could be due to manual traction and the motorized could

give better data.

In both healthy and sclerodermic individuals, the SS curve is highly nonlinear. The regions close to the traction site would enter the steeper curve and will behave differently from more distant regions which impart more complexity to such job of skin analysis. Such supposed idea goes with the histological theory of the role of crimpled collagen and elastin fibers in defining the SS curve of the skin. In addition to the previous results, we want to extract the movement of the skin in each axis in isolation of another axis.

Any displacement had 2 components.

- X component
- Y component

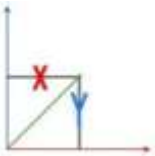

Figure 23: Any points have calculatable X and Y coordinate.

We start to represent the displacement in the X axis. We customized the legend of the X displacement to have the highest value of 1mm and the lowest value of -1mm. Every region of incremental increase by 0.1 from zero has a specific color. We would also segmentalize the region of legend that extends from 0 down to -1 in the future work, as we had not done it here in this time. The legend of the Y displacement is the same as the total displacement plot. The results of the X displacement was:

Figure 24: X Displacement in final step

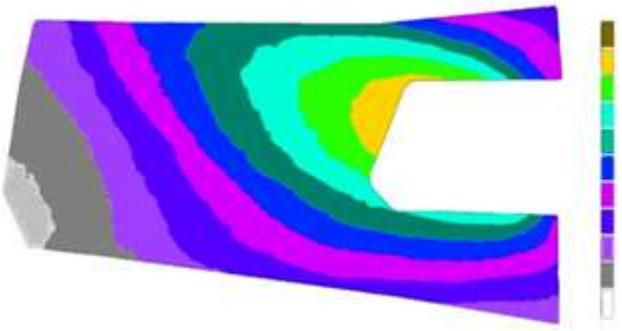

Figure 25: Y Displacement in final step

Normal patient result

Exact arrangement and analysis we did for the sclerodermic patient had been done for the healthy person.

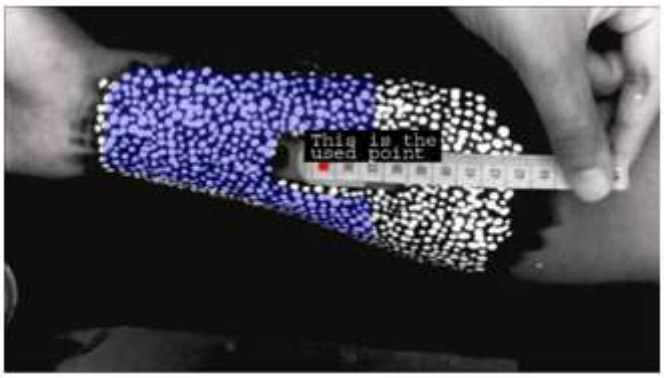

Figure 26: dotted pattern had been applied over all the volar aspect of the forearm. The tractor is a simple scale tape attached firmly to a medical-grade skin sticker. Green had been regarded as extensometer.

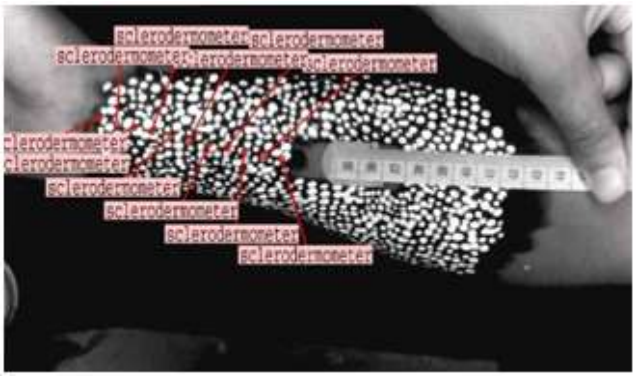

Figure 27: Sclerodermometers of the healthy subject.

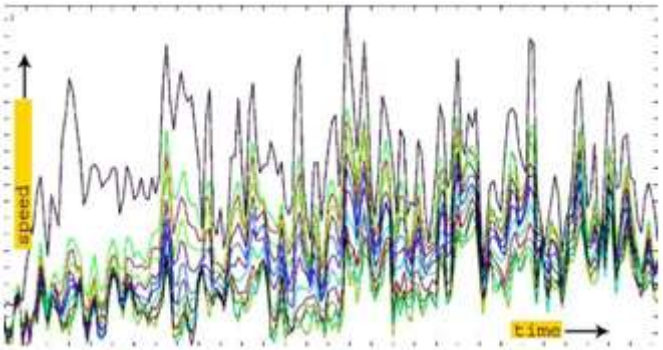

Figure 28: 2D plot of sclerodermometer speeds against time. The speed of the proximal sclerodermometer are clearly shown to be close to that of the bottom in contrast to what had been results in the healthy person. Gapping happens at the beginning of the traction, and it occurs mainly between the traction site and the other sclerodermometer. This is related to the fibrous content of the skin. Ratio of collagen to elastic is very compromised in case of scleroderma and this is an example of the impact of the histological features on the mechanical properties of the biological materials.

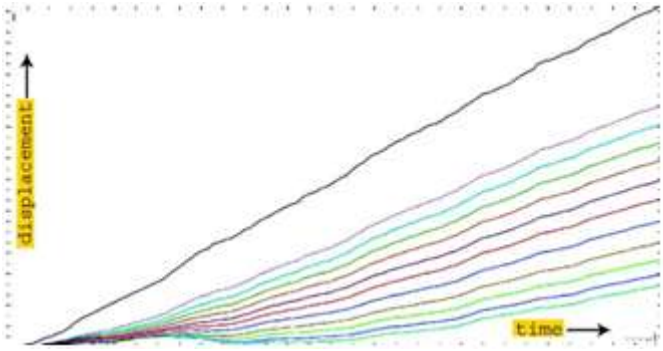

Figure 29: Curves of the displacements of the sclerodermometer. Even distal sclerodermometer had a good amount of displacement. The difference between the traction site and other sclerodermometer is obvious. The distance between all sclerodermometer are nearly equally distributed

We do for the healthy subject results analysis the same as what we do previously to those of the sclerodermic subject. By dividing the displacement of the sticker into sex steps and analyze strains and displacements of the skin of the forearm. We depend upon the total displacement of the sticker to give equal displacements.

Before analyzing the displacement plot of displacement and compare it to the other sample (healthy versus diseased), we strongly suggest not to pay more attention to the highest and lowest values than to the pattern and the patterns growth, as we discussed earlier.

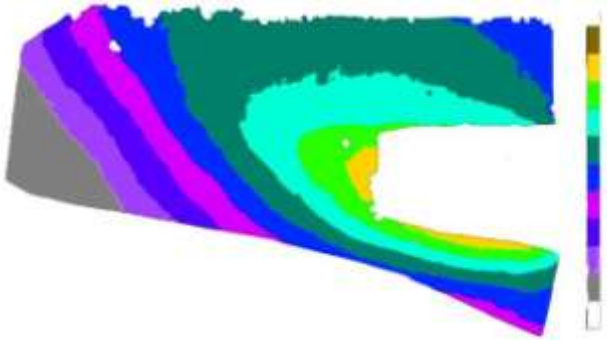

Figure 30: Displacement in step 6. The edges between the different regions in healthy individual is more irregular than in the sclerodermic, which indicate a smoother transition between each adjacent 2 regions.

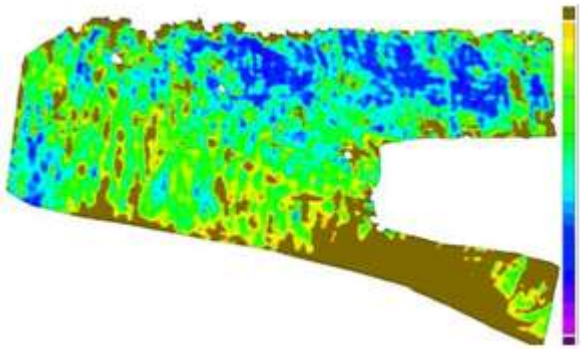

Figure 31: Equivalent mises strain. The red areas indicate where most inter parts displacement is happening at. Interestingly there are marked strain in the furthest regions of the forearm, wherein case of sclerodermic skin the strain occurred mostly in the vicinity of the sticker region and in the tension line distal to the sticker.

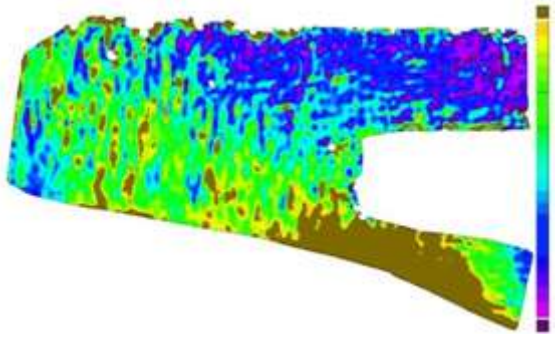

Figure 32: Major strain of the sclerodermic patient. It defines the strain only in major diameter direction. Which is not necessarily in the Y direction. It must be clear that in these figures, we establish the concept that could be used in the futures for better evaluation of scleroderma.

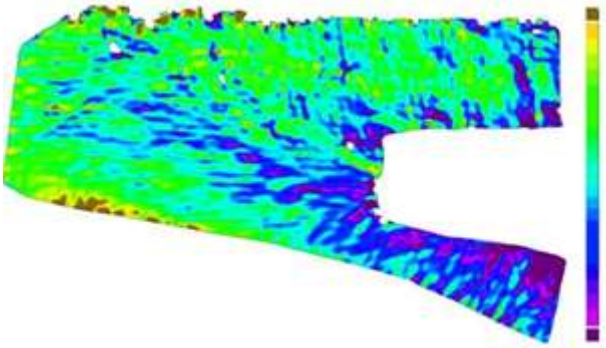

Figure 33: Minor strain of the sclerodermic patient. It defines the strain only in minor diameter. Which is not necessarily in the X direction

In addition to the previous results, we want to extract the movement of the skin in each axis in isolation of another axis. We start to represent the displacement in the X axis. Surprisingly as the start of the movement instantly whole of the skin shifted medially (negative value in the X direction), and only small region of the skin begin to raise up (laterally in the positive X direction). We customized the legend of the X displacement to have the highest value of 1mm and the lowest value of -1mm.

The displacement X had its longest axis in the sclerodermic patient, which was different from the healthy individual. Every region of incremental increase by 0.1 from zero has a specific color. We would also segmentalize the region of legend that extends from 0 down to -1 in the future work, as we had not done it here in this time.

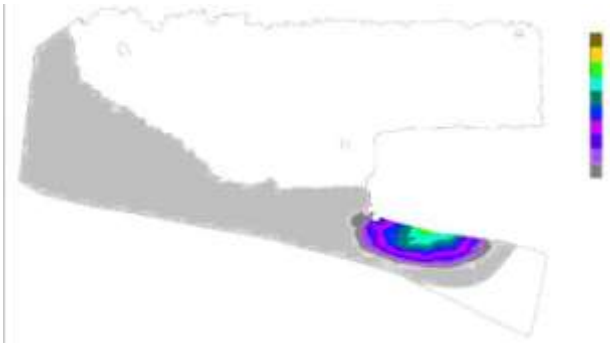

Figure 34: X Displacement in final step

The analysis in the Y axis along the line of traction was.

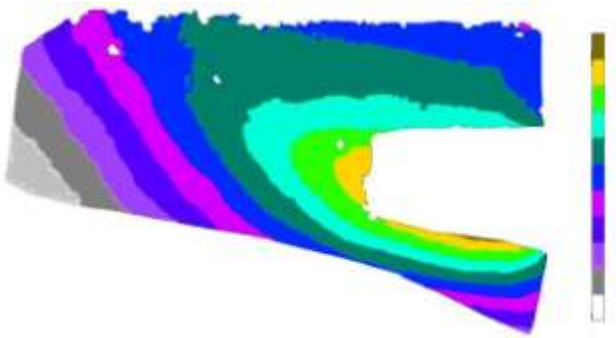

Figure 35: Y Displacement in final step

We think that all the analyses pf skin must include both the dynamic and static status of the strains and displacements. We haven't done a thorough analysis of the strains steps because they are less regular than the displacement and we wait for large no. of samples for the establishment of analysis guidelines. We shall do it in the next editions of this work.

6. Horizons of our work

We can demarcate the boundary of diseased areas using modern tools that facilitate the administration of local treatment such as intralesional injection. Tissues adjacent to the affected areas in case of the limited form of SSc could be marked with high sensitivity and specificity. (14)

Results of analysis of different well established and diagnosed rare conditions could be kept as references to compare them with future results from the new patients. This may dispense the need for high-cost laboratory analyses, which had been done diagnosed with the old cases. Most of the investigations of the autoantibodies in case of scleroderma are highly expensive and not always available (42)

We could couple our work with ultrasonography to yield a better understanding of the results (42). Rapid skin relaxation through rapid release after full traction had been tried in our work, but we think the results were suboptimal as our gear had a limited frame rate, yet it is higher than those used by many other authors. It needs cameras with a higher frequency than what we had arranged. This could exploit the full feature of skin including creep and viscoelasticity by embracing the state of art analysis equipment (14)

Viscoelasticity of the skin could be calculated through skin stretching, especially the release of the skin or when the skin is stretched at different speeds. We hadn't done this procedure due to limited hardware as it needs a camera with higher frequency, but we think it must be done as it will reveal the full picture of skin properties.

Mechanical properties of the skin if well-characterized, current flaps classifications could be further reclassified. The current excision and incision lines concept could be further refined. We could follow the course or progress or regression of the disease by ultrasound or our method (7)

In order to parameterize our approach to evaluate skin, the area of the strain could be further calculated to establish the effect of the size of the forearm on the resultant strain. This is done thought 3d scanning of the forearm. 3d scanning of the forearm will give the best results because application of measurement tape would apply some forces which may distort the shape of the forearm, while in case of 3d scanning the forearm will be imaged in undistorted condition.

Ultrasonic evaluation of the thickness of different skin layers will make the approach even more optimal. We had not exploited this powerful technique to explore the effect of the skin deformity speed on the results and their rapid relaxation after fast skin traction. Creep properties could be further demonstrated. As when the fluid content of skin increased in the edematous phase of SSC, echogenicity will be decreased (7), we think that skin would be more elastic. We must admit that our method provides features extracted from surfaces deformation, but features such as thickness could be evaluated by ultrasound (14)

The behavior of skin under such deformity or such movement explained for us the natural behavior of the skin. Current surgical incisions could be further customized to the new concepts from the new observations that could be obtained from these techniques. We examined the area of stretching distal to the sticker, not the areas of compression medial to the sticker. This could be done by using thread instead of measurement tape. Because the tape obscures the deformation below it and prevents analysis from being done to that area.

Even when we try to apply constant speed when stretching the skin during, the application of a motorized tractor is advisable to attain more constant acceleration and velocity. In the case of motorized traction, the amount of the applied force could also be uniform across all studies. When skin is moving during normal activities there will be creases that occur at the angles of movements due to muscle contractions. We can exploit the analysis to categorize the degrees for the grades of skin creases without traction or external effects.

This work could be expanded to involve the evaluation of structures other than skin such as cornea. Corneal damage in autoimmune disease. The cornea of a patient could be investigated or examined using this technique in which we should apply a good pattern (42). Analysis of the normal deformity and strains of the skin near joint during different anatomical movements, such as flexion, extension, abduction, and adduction could be done. It will provide an insight into the different lines of the skin without the application of external force rather than the force from the adjacent and underlying tissues.

Although we use our work on loading conditions by tracking the skin in one direction. Stretching in other directions +/- changing the traction site position could be used to demonstrate or explore their effects on the resultant deformities and strains.

7. Digital model of durometer

The model of Cinema4D had been utilized to simulate a

durometer of skin. The head of the durometer was a sphere with a radius of 1mm and the indentation depth up to the full radius.

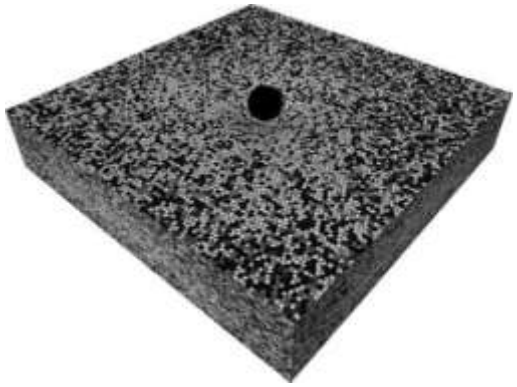

Figure 36: Skin model and the indenter that represent the durometer, after moving indenter down by 1mm

We render video footage of the indentation and the material that is used to represent the indentation was given customized setting to be totally translucent. The resulting deformity was then analyzed by using our method.

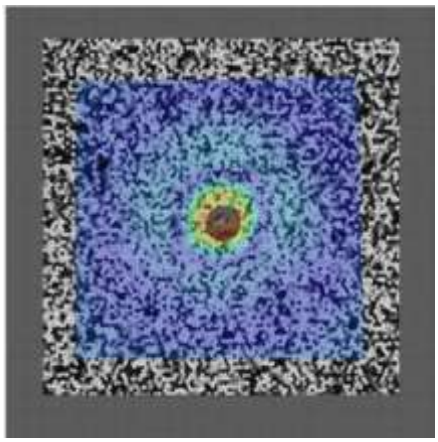

Figure 37: The displacement map overlaid on the model after engagement of the indenter with the skin by depth of 1mm.

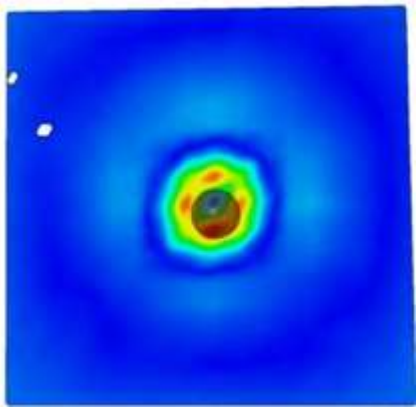

Figure 38: Displacement map with a partially transparent black colored circle represents the displacement in the XY plane, which had very limited capability to represent the extensibility of the skin. The extensibility of the skin best revealed by stretching it in the horizontal or XY plane.

The result of the indenter model showed that the displacement of the virtual skin model exceeds 100 microns in such a homogenous isotropic model (the model dimensions were 20mm*20mm*4mm). In addition to this, when the skin is compressed, the softer layer would be deformed at the beginning followed by the stiffer. The question that could arise from the previous assumption is which layer of different skin layers would take most of the deformation when the skin is indented.

To simulate the interaction of fingers of the examiner and the skin of an examined patient, we simulate the sphere of 3mm radius and the skin model like the same previous model (the model dimensions was 20mm*20mm*4mm). The sphere intruded in a straight line into the skin by about 1.3mm in its first part of the movement. After that continue to the indentation and complete depth of 2mm with concomitant slide to the right side by 5mm. We think that is one of two components resemble what is exactly happening when performing MRSS.
The model was:

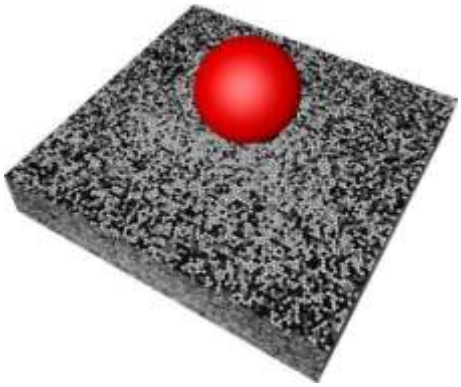

Figure 39: Sphere of 3mm radius above the model by 0.5m. The dimensions model of skin is 20mm*20mm*4mm

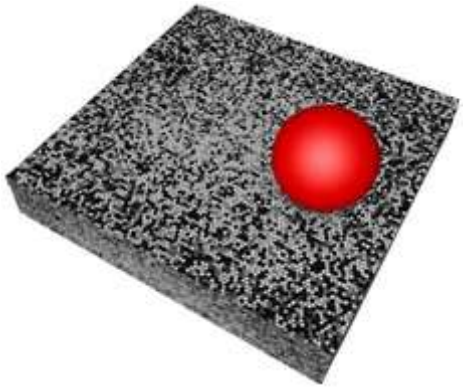

Figure 40: Sphere had completed its movement. Slight packing of the skin model material against the ball, while on the other side there is more space between the sphere and the model

The movement of the model was evident in the next lateral views

Figure 41: Sphere at the start of the animation. The grid contains sets of squares, with dimensions of 1mm for each square.

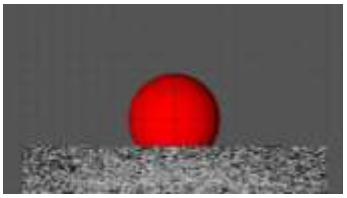

Figure 42: Sphere position after the first step of movement competed. The movement was only on the axis Z by about 1.3mm into the skin

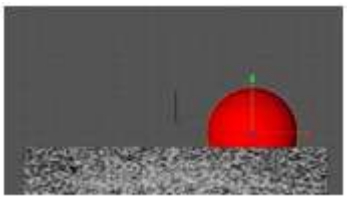

Figure 43: Sphere movement is completed. The track of movement indicates the whole treatment.

The results of the analysis of the data exported from Cinema4D were clear in the following figures. We give the sphere transparent material to see the deformation below it. This is not applicable in reality, as the sphere will cut the light from passing through it, or even if it made from transparent it will distort the light while passing through it. In both assumptions, no valid pattern of the areas below the sphere could be gained. In such physical experiment if done the displacement of the adjacent regions beyond the skin in contact with the sphere could be captured.

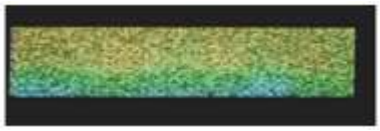

Figure 44: Displacement field of the lateral wall overlaid over the skin model.

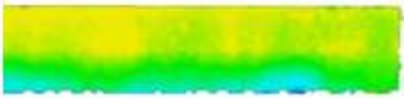

Figure 45: Displacement field of the lateral wall of skin material indicates clearly the displacement had significant value even when it was distant from the indentation site by about 10mm.

There are 3 regions clearly defined.

The analyses of the lateral wall, by no way, dispense the need for analysis of the region directly below the indenter, both for the physical and digital models. Ultrasonography provides invaluable real-time data grabber of deep tissues changes and deformations.

And top view displacements analysis reveal

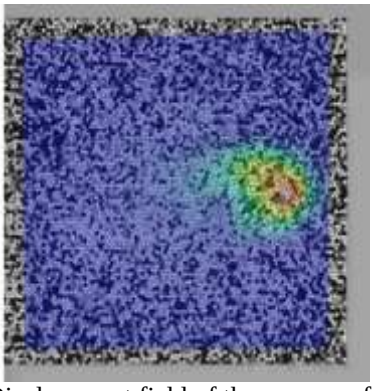

Figure 46: Displacement field of the upper surface overlaid over the skin model.

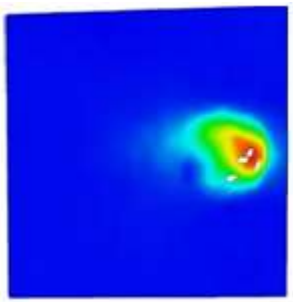

Figure 47: Displacement field of the upper surface skin material indicates clearly the displacement had significant value even when it was distant from the indentation site by about 10mm. The regions are clearly defined. Although we moved the sphere by 5mm some of the areas displaced more than this value indicating compression and it had been dragged by the sphere. This goes with the analysis of the latter wall.

8. Zainab`s Law

Nothing in biology is not governed by stiffness.

Biological systems had the least possible stiffness and highest possibleprestrain on nano, micro and macro scale.

Stiffness is the capacity of a mechanical system to sustain loads without excessive changes of its geometry (deformations) (Rivin 1999, #). Biofeedback is avery complex process.

Stiffness could be defined in another way as the ability to resist deformation, where this particular deformation could be mechanical, electrical, chemical, optical, aerodynamic, auditory …. etc. All biological processes are governed by stiffness. It is imperative for biology researchers to understand engineering systems to collaborate with engineering researchers to build a parametric scalable biological model.

Stiffness plays a significant role in developing regulation of body metabolism and continues to control bodies postmortem. (Saadoon, n.d., #)

It is not only controlling the body in its healthy status, but all pathological changes are also governed by stiffness. In all stiffnesses tissues had ability to transduct all loads (mechanical, chemical, auditory, …. etc.) into chemical

messaging and vice versa. Our aim here is neither to give comprehensive details about them nor enumerate all the aspects that they involve. The Biomechanical engineering discipline is the most intensively studied area because it is palatable subject for researchers from biological background with touchable elements and easy to memorize terms with familiar perception. The simplest scale for measuring stiffness in mechanical engineering discipline is displacement. Analogue to this criterion in other bioengineering disciplines needed to be well defined. This scale is the easiest to obtain and follow, but it is not meant to be used by the body. The second criterion that could be used is strain. We suggest reviewing this value whenever reviewing displacement because gradient of stiffness could not be clear unless relativity of the changes.

We could say that mechanical stiffness specifically and other stiffnessesalso tend to be least in the biological system.

It is applicable on from cellular level up to macroanatomicalstructure.

These are example of processes where mechanical stiffness clearly control them:

- Embryogenesis, where it involves all steps.
- Oncology, where tumors will modulate tissues, microenvironment causing increased stiffness that precedemetastasis and local invasion as well as other processes.
- Cellular
- Bone
- Implant interaction and biocompatibility are greatly affected by this criterion.
- Postmortem changes are designed well.
- Fluid flow where blood rheological properties had a variable stiffness across the circulation.

In growth subject, we need stiffer tissue element with less stiffness element that mostly had capacity to proliferate. The deformation in the element with least stiffness affects the cells resulting in transduction the govern the cellular response. This is best seen in the endochondral ossification route.

In the case of mechanosensation related organs, whether in skin or in auditory function, the first organ that receives the mechanical loadsare the stiffest, while the end element in the sensory cycle will have the least stiffness. Both have well calibrated prestraininng.

In the dentition, we see this in the arrangement of dental structures. Enamel is the stiffestand hardest organ in the body. Dentine hade a very complex organization that enable mechanical sensing possible for secondary and tertiary dentine deposition as well as excellent trauma response where nonlinear stiffness had a pivotal role in lessening the damage to the craniofacial structures. Cementum and PDL complex provide the required stiffness to facilitate proprioception and normal response that affect the fatigue life of dental structures.

The large joints with high load bearing capacity had the same previous arrangement. This could be called the gradient of stiffness. In the living tissues it is very intricate. Hardware, which mostly deranges this gradient by changing the stiffness via the fibrosis associated with the surgery or the placed hardware itself, will affect the tissues drastically. Stress shielding and cortical hypertrophy.

9. Noor ruler

Any ruler could be Noor'sruler.

In all the 3 papers that we had studied different aspects of the skin we had demonstrated the capability of tracking the mechanical properties of the skin and correlating them with measurable criteria. The simplest criterion is displacement.

The relative changes in position or displacement of sequential points, in the paper of scleroderma we had called them sclerodermometer, will give an insight into the mechanical properties. We here suggest a clinical tool depending on points with inter-distance of 5 mm between them.

10 points could be marked on the skin of the patient. Aruler could be glued to the skin and exposed to a force that causes displacement of the skin. The new position of these points after their pulling will give an insight into the mechanical properties of the skin.

It will give an instantaneous result and it could be assigned in many directions. It is ideal to monitor skin properties in the case of global changes such as in case of scleroderma or postmortem changes.It is simple way with need of tools that available anywhere. It could be done in almost any cynical setting. The changes could be recorded using any modern smart phone.

Modern smart phones have cameras thatare capable of capturing decent photos. These photos could be used in the initial presentation or the follow up visit of the patient. We had assumed different configuration using measuring tape or rigid ruler that could be used in any clinical setting.

Acknowledgement

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