

APPLICATION FOR WORLD SCLERODERMA FOUNDATION SPECIAL WORKING GROUPS - Project proposal

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Project title: “Skin Ultrasound Working Group”

Background

Over the last three decades, increasing evidence has accumulated to support the application of ultrasound (US) for skin assessment as a diagnostic and monitoring tool for systemic sclerosis (SSc) in clinical practice and research settings¹. This has been possible through technological improvements, including higher frequency transducers and new imaging and measurement techniques.^{2, 3} Advantages of US over the mRSS (actual gold standard), include, in particular, its objectivity, higher intra- and inter-reproducibility and sensibility to detect minimal changes, which can definitely contribute to improve the management of patients with SSc.^{4, 5}

In addition, a large number of recent trials of early have failed to demonstrate statistically significant improvements in their primary endpoint using mRSS despite encouraging pre-clinical data and apparent improvement in composite clinical endpoints.⁶⁻⁹

However, there is a lack of sound evidence concerning standardization of skin ultrasound examination in SSc (including standard scans, technical equipment and settings, skin sites examined), hampering its appropriate use in clinical practice and research.¹ As skin US is evolving, its role in patient diagnosis and monitoring needs to become clear and defined.

The aims of the working group will be:

- 1 to promote network and share of knowledge and expertise in skin US research among clinicians with an interest/expertise in SSc
2. to design and facilitate collaborative research initiatives
3. to establish for the first time general points to consider/recommendation for skin US assessment in SSc for clinical practice and research
4. to explore further research, in particular validation work needed to consider skin US a valid surrogate in future SSc clinical trials.

Methods: The project will consist of the following steps:

- (1) First task force on-line meeting to formulate key clinical questions related to standardization of skin ultrasound scanning procedures in SSc
- (2) Performing the SRL on the use of US of skin involvement in SSc.
- (3) Second task force on-line meeting to review the results of the SLR and formulate first draft of points to consider/recommendations on the scanning procedures summarised from the literature review.
- (4) Developing consensus on the points to consider/recommendations including open discussions of the document followed by a Delphi exercise

- (5) Developing a research agenda with the most important topics to be covered in this field.
- (6) Submission of manuscripts to world scleroderma congress/journals.

Milestones of the project

M1: 1st to 4rd month - First task force on-line meeting

M2: 5th to 9th month - Second task force on-line meeting

M3: 10th to 16th month - SLR draft and developing consensus

M5: 20th to 24th month – Recommendations and research agenda paper (preparation and submission)

Significance for the patients

Skin involvement is of major clinical and prognostic relevance in SSc and often the primary outcome in clinical trials. Also, the importance of the body image, from the patient's perspective, has significant impact in several domains of the disease. In particular, the disfigurement in visible skin areas and physical changes often leads to difficulty in social interactions, social anxiety and avoidance of social situations, as well as impaired sexual function and depression.

In addition, a number of recent trials of promising anti-fibrotic interventions have failed to demonstrate statistically significant improvements in mRSS despite encouraging pre-clinical data and apparent improvement in composite clinical endpoints. This supports the need for an objective, reproducible and sensitive measure of skin involvement for clinical assessment and particularly to support the development of much-needed new pharmacological interventions.

Participants

This task force will include a research fellow, a methodologist, a health professional, one research engineer, and 10-12 rheumatologists/internal medicine experts or with a special interest in skin ultrasound in SSc, representing six countries (Portugal, Italy, UK, France, Sweden, Japan). Please see below the composition of the proposal task force.

Budget

Funding from WSF will be used to cover the work of one research fellow and one methodologist in charge of performing the systematic review and recommendations.

Task Force: Tânia Santiago (Portugal), Eduardo Santos (Methodologist, Portugal), Barbara Ruaro (Italy), Gemma Lepri (Italia), Alain Lescoat (France), Roger Hesselstrand (Sweden), Marie Wildt (Research engineer, Sweden), Lorraine Green (UK), Shinji Watanabe, (Japan), Francesco Del Galdo (UK), John D. Pauling (UK), Annamaria Iagnocco (Italy), José AP Da Silva (Portugal).



Coimbra 5th January 2021.

On behalf of all authors,

Tânia Santiago, Proponent (Rheumatologist and PhD Student)

Jose AP da Silva, Convenor (Full Professor of Rheumatology)

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