The challenge of comprehensive nailfold videocapillaroscopy practice: a further contribution

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Abstract

Objective

Although classification systems and scores for capillaroscopy interpretation have been published, there is a lack of homogenisation for the procedure, especially in the way and place the images are taken, the counting of the capillaries and the measuring of their size. Our objective is to provide a deep learning-based software to obtain objective and exhaustive data for the whole nailfold without increasing the time or effort needed to do the examination, or requiring expensive equipment.

Methods

An automated software to count nailfold capillaries has been designed, through an exploratory image dataset of 2,713 images with 18,000 measurements of 3 different types. Subsequently, application rules have been created to detect the morphology of nailfold videocapillaroscopy images, through a training set of images. The software reliability has been evaluated with standard metrics used in the machine learning field for object detection tasks, comparing automatic and manual counting on the same NVC images.

Results

*A mean average precision (*mAP*) of 0.473 is achieved for detecting and classifying capillaries and haemorrhages by their shape, and a* mAP *of 0.515 is achieved for detecting and classifying capillaries by their size. A precision of 83.84% and a recall of 92.44% in the identification of capillaries was estimated.*

Conclusion

Deep learning is a useful tool in nailfold videocapillaroscopy that allows to analyse objectively and homogeneously images taken with multiple devices. It should make the assessment of the capillary morphology in nailfold video capillaroscopy easier, quicker, more complete and accessible to everyone.

Key words

nailfold capillaroscopy, deep learning, machine learning, Raynaud's syndrome, systemic sclerosis

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Introduction

Nailfold capillaroscopy is a cheap, convenient technique to study patients with Raynaud's phenomenon (RP). Its utility relies not only on its capacity to help in the diagnosis of systemic sclerosis and scleroderma-like diseases, but also on the capacity to rule out primary RP. Furthermore, nailfold capillaroscopy is increasingly used in research regarding other conditions (1).

Although classification systems and scores for capillaroscopy interpretation have been published (2, 3), there is a lack of homogenisation for the procedure, especially in the way and place the images are taken, the counting of the capillaries and the measuring of their size.

Oftentimes physicians do not gather objective data when performing their capillaroscopy reports, and rely on their intuition after observing just a few capillaries of each nailfold, and most of the time they do not take any measurement of a capillary to determine whether it is enlarged or it is a giant capillary. This can lead to bias caused by only looking at arbitrary sections of the nailfold or even only examining a few fingers of the patient. Saez *et al*. showed that the interobserver variability in the analysis of capillaroscopy images was very high (4). Boulon *et al*. (5) studied the agreement between 2 independent observers and concluded that the Maricq and Cutolo classifications have moderate reproducibility. Furthermore, it has been observed that quantitative alterations of apical diameter are an independent predictor for the development of scleroderma (6).

In the last decades there has also been an increasing number of portable microscope brands and other devices available to perform capillaroscopy and to obtain the pictures of the nail bed capillaries. This great variability of the capillaroscopic models used, with different magnifications and different approaches, obtain highly heterogeneous images that further increase the interobserver variability. Recent research points at the possibility of future systems that integrate meaningful quantitative metrics for capillaroscopy images in a partially automated way (7, 8), which closely matches our approach. Previous research about automatic location and parameters measurement of capillaries has been published using different techniques that try to improve NVC with other tools such as Doppler laser and optoacoustic imaging (9, 10).

We instead propose a deep learning and data-driven approach to nailfold capillaroscopy practice, facilitated with an interactive web-based tool. Our algorithm is able to recognise capillaries in images obtained with any microscope, generate automatic measurements of each capillary and take advantage of this information along with the physician verification resulting in an exhaustive analysis that is able to produce detailed reports of each patient. Furthermore, this platform serves as a collaborative and reporting application, where professionals can share information, discuss, validate, and boost their research efforts. It includes all necessary procedures to upload new data and organise it in separate projects, patients and examinations. We also take advantage of our own platform to prepare the training dataset and train our models on a regular basis. Thanks to the data heterogeneity, our models produce good results with images of many different origins.

Our main motivation is to help make nailfold capillaroscopy a more accessible diagnostic tool, and focus on providing a software framework for professionals to obtain objective and exhaustive data (mainly capillary count, capillary classification and measurement of capillaries apex and limbs) for the whole nailfold without increasing the time or effort needed to do the examination, or requiring expensive equipment (9, 10).

Our project is a multicentre prospective study with a follow-up of 5 years. Its main objective was to determine the agreement between the deep learning software and the consensus among several highly experienced capillaroscopists.

Materials and methods

To achieve our objectives, a complete software solution was built. It is composed of separated parts:

- A database where information is stored for the following items:
  - Capillaroscopy examinations and associated patient with their images organised by finger and nailfold sector where they were taken (or panoramic images).
  - Image collections for uploading many unrelated images, mainly for research and dataset elaboration.
  - A standard capillaroscopy form definition, and a standard capillaroscopy report template for printing results. Both of them can be customised.
  - Projects, folders and subfolders for organising examinations and collections.
- A web application for easy management and manipulation of capillaroscopy data.
- A desktop application carefully designed for capturing capillaroscopy images with almost any microscope, USB capillaroscope or any compatible camera and uploading the captured information to our database.
- Several tools and processes for dataset preparation, necessary for training and testing the different deep-learning models.

The software and its database (CAPI-DATA) have been approved by the regionals ethics committee (Aragon, Spain).

Pipeline of deep-learning models

Our current inference pipeline is composed of several models, each one with a different purpose:

1. A first-phase model that is responsible for locating and counting capillaries and haemorrhages, and classifying capillaries into normal, tortuous and ramified capillaries. This model has also been trained to detect giant capillaries as a separate category, since some of them have tortuous shape but have been labelled as giant capillaries due to their large size.
2. A second-phase model that is responsible for producing measurements of each capillary detected by the first model. Currently, this model produces measurements for the apical diameter and each capillary arterial and venous limbs' width. When a physical size calibration is available for the image, these measurements are used in order to determine whether a capillary is enlarged or giant/megacapillary.
3. An auxiliary model that is responsible for deciding, solely based on the visual aspect of the capillary, what capillaries of an image, if any, are enlarged/giant. This model is useful only when there is no physical size calibration available for an image and therefore the measurements of the second-phase model cannot be used to produce a better decision.

When apical diameter [also called capillary loop diameter (11)] and capillary limbs measurements are used, EULAR criteria described in Smith *et al*. (12) is followed, considering a capillary normal when its apical diameter length is below 20 μm, enlarged when it's between 20 μm and 50 μm and giant/megacapillary when it's over 50 μm. The same is done for arterial and venous limbs' width.

Most of the time our second-phase model produces all 3 measurements, but sometimes it will fail to produce some or all of the measurements due to bad capillary visibility or not enough model confidence. When no measurements are produced, the auxiliary model will be used for normal, enlarged or giant classification instead.

Our first-phase and auxiliary models are object detection models (13), they detect and classify all capillaries of an image in a single pass. Meanwhile, the second-phase model is a key-point detection model. It outputs the start and end points of each capillary measurement for a single capillary each time. This means that the capillaries detected on the first-phase are cropped from the original image and run through the key-point detection model.

When combined, these models produce a detailed analysis of a single nailfold capillaroscopy image (Fig. 1).

Dataset preparation

In order to make our deep learning models work with nailfold capillaroscopy images of varying origin, quality and magnification level, we commenced gathering a dataset of images provided by several collaborators and authors of this paper.

We made sure that our dataset images had been obtained with several traditional microscope models and a mounted camera, but also many devices designed for capillaroscopy examinations, mainly Dino-Lite CapillaryScope, Optilia Digital Capillaroscope, and Smart G-Scope.

The dataset is comprised mostly of images at 200x magnification level, but it also includes images at higher magnification levels (200-500x) and slightly lower magnification levels.

Based on this approach we iterated on incremental versions of the dataset until the most recent version formed by 2,713 images, all of them manually annotated and carefully validated.

This dataset is composed of several collections of capillaroscopic images of patients with Raynaud's phenomenon (primary and secondary) from nine different Spanish tertiary hospitals.

Of this dataset, we kept apart 15% of images for testing the model performance.

Detection of capillaries and haemorrhages

LabelImg (14) software was used to start manually labelling all images in a first and very limited version of our final dataset. The following bounding box annotations were marked on each image: normal capillaries, tortuous capillaries, ramifications, haemorrhages and mega- capillaries. For each normal, tortuous capillary or ramification it was also annotated whether that example was enlarged or not.

Some initial object detection models were trained with the first annotated dataset. Given that the obtained results were promising, we implemented a basic version of our image viewer software that made it possible to upload capillaroscopy images, ana-

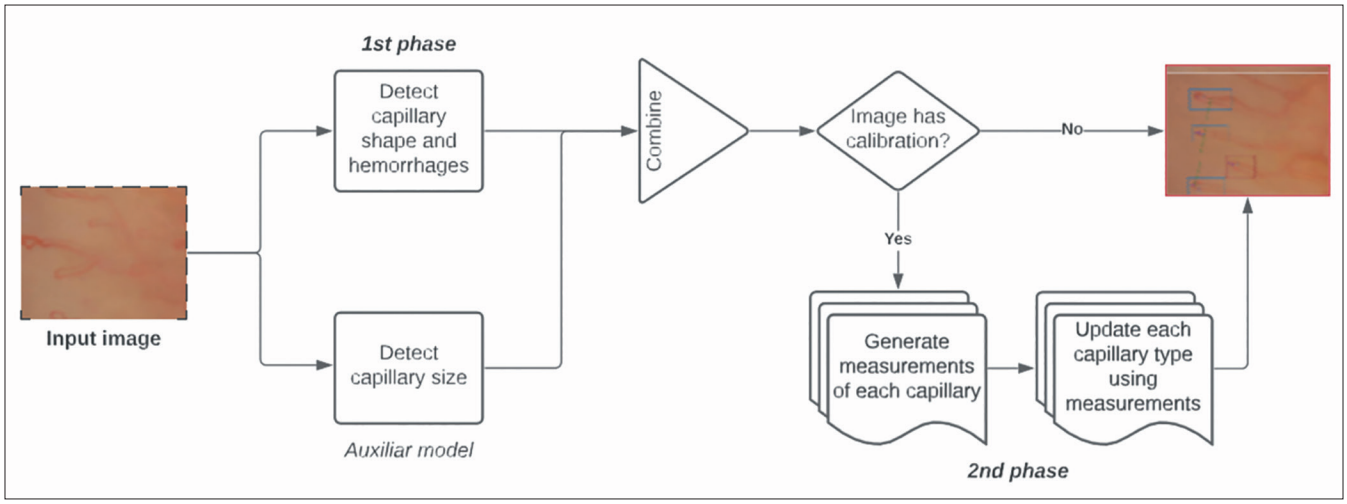

Fig. 1. Inference pipeline for one image.

lyse them and also edit the generated annotations by the software or create new annotations.

At this point we switched to using our own software as a reliable database of images for annotation and validation of capillaries, adding the possibility for each person to comment on each image and mark it as validated or not, while keeping a visual and interactive log of each action that was done with any image. This *ad hoc* user interface made it easier for us to track changes of annotations in images, track done and remaining images and collaborate on the creation of a larger dataset. It also made it very simple for our collaborators to upload their images and explore what was already uploaded.

Measurement of capillaries

Our first inference pipeline did not include the key-point detection model that we now use for measuring capillaries apical diameter and limbs width. It classified capillaries as enlarged/giant based only on their appearance. Relying only on the visual aspect of capillaries is very error-prone, so we reconsidered the image analysis strategy and decided that it was necessary to extend it by adding the automated measurements in order to improve the objectiveness of the whole system.

Using capillaries measurements makes the size-based classification of capillaries very objective and our capillaroscopy examination report more data-driven, which is a main objective in our work. But, since measuring physical distance is only possible with properly calibrated images, the existing model was kept as a secondary size-based capillary classification mechanism.

We directly used our own software for building this dataset, first adding the possibility to calibrate images, use standard calibrations for known devices and also create, modify and label measurements in all images. We stopped measuring and validating images when we had collected 18,000 measurements of each type: capillary apical diameter, arterial limb width and venous limb width.

For measuring capillaries, we trained two separate key-point detection models. The first one measured the apical diameter only, and the second one took advantage of the apical diameter measurement prior to generate measurements for the two capillary limbs. To train these models we used a basic Graving *et al*. (15) *Stacked DenseNet* configuration due to its simplicity, good performance and fast inference speed. Other keypoint detection systems [Wu *et al*. (16)] were tested but did not produce better results.

Web application

A simple web user interface was designed to allow uploading as many images per finger as necessary. For all fingers, each uploaded image can be marked as belonging to some specific sector of the nailfold (there are four sectors called A, B, C and D, as seen in Fig. 2), unknown sector or "panoramic" (ABCD). We chose to divide the nailfold in four sectors according to methodology described in Smith *et al*. (17).

Once the images are uploaded, the application analyses them one by one and makes the results available in a built-in capillaroscopy image viewer.

Image capture application

While the web application is quick and simple enough to use (it only requires uploading a few photos, optionally indicating the sector of each one), manually placing images in their correct finger and sector category can take some time, assuming the physician was careful enough to label each photo properly while taking them with the device vendor software for image capture.

In order to facilitate the process of correctly taking photos during the nailfold capillaroscopy procedure we designed a desktop application that can function with almost any camera, is able to automatically read calibration data from some known devices and offers the possibility to manually calibrate other devices as needed.

It is also critical that each one of the taken photos includes a precise calibration. Without a proper calibration, capillary measurements still can be automated, but the physical distance

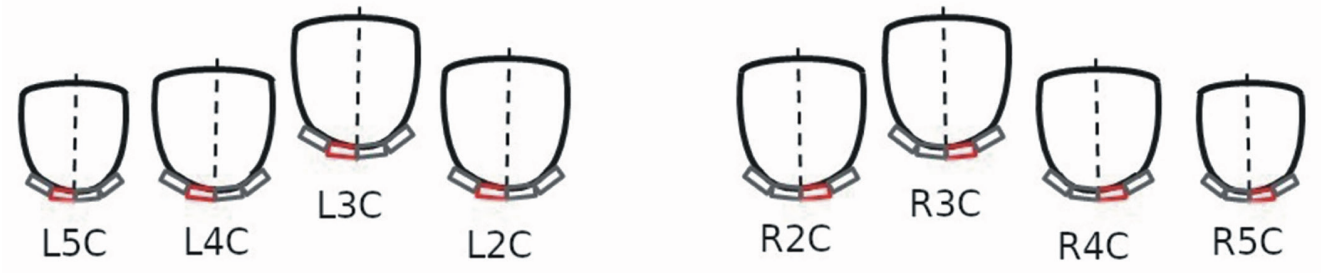

Fig. 2. Each nailfold is divided into four sectors. 'L' denotes left hand and 'R' right hand.

of each measurement remains unknown, and therefore unusable for size based capillary classification. We found that none of the image capture applications that are included with capillaroscopy devices include any useful metadata in the image files that they produce: they don't save readable information about how the photo was taken such as magnification level, physical distance reference (calibration) or even the name of the used device.

To overcome these problems and avoid any human error, all photos taken with this application are saved with the following information in its metadata, that is preserved independently of the file name:

- Finger and nailfold sector.
- Magnification level.
- Physical distance reference (manual or automatic calibration).
- Date and time the photo was captured.
- Camera model name and identifier.
- Producer software and version.

Photos at very low magnification, for example 50x, or even photos taken with a dermatoscope are not detailed enough to reliably discern capillaries, but they can be useful as a "panoramic" view of the whole nailfold, so our software makes it possible to take these images, but excludes them from the in-detail analysis and report metrics that are produced using higher magnification images, being 200x-250x the recommended magnification by the software.

Finally, to make the procedure easier, the application allows the user to upload the images directly to the web application in a single click without needing to use the web application upload form.

Statistical analysis

In order to evaluate the performance of our deep learning models, we used standardised metrics commonly used in object detection and visual information retrieval tasks in computer vision (18).

These metrics are:

- Precision: The positive predictive value. It is defined as the ratio between correctly detected objects (true positives) and the sum of true positives and false positives (detected objects that are incorrect or not actually present in the image).
- Recall: Sensitivity. It is defined as the fraction of relevant objects that are successfully detected and classified.
- IoU: Intersection over union of the real object and predicted object areas. This is used to determine whether two objects are the same object or not by evaluating the coincidence of their bounding boxes.
- AP and AR: *a*verage precision and average recall. The precision and recall metrics are evaluated at different levels of *IoU*, starting from 0.50 (good enough match) and up to 0.95 (near perfect match). This gives an averaged metric that can be used to evaluate the model performance when detecting a type of object (for example a capillary).
- mAP: Mean average precision. The mean of average precision for each type of detected object is calculated as a single summary metric to evaluate the whole model.

For all of these metrics possible values range from 0 (worst) to 1 (best).

Results

For the two object detection models, we prepared a dataset of 2,713 images of patients with RP, which contain annotations for each type of element to be detected (see amount of annotations in Table I).

Table I. Amounts of annotations for each type of object, total and enlarged.

Type	Total	Enlarged
Capillary	23,753	9,415
Tortuosity	4,426	2,351
Ramification	640	388
Giant capillary	1,081	—
Haemorrhage	2,100	—

Table II. Metrics for detection of capillaries and haemorrhages.

Metric	Score
All label types	
Average precision (AP) @ IoU=0.50:0.95	0.471
AP @ IoU=0.50	0.758
AP @ IoU=0.75	0.504
Average recall (AR) @IoU=0.50:0.95	0.625
By label types - AP @ IoU=0.50:0.95	
Haemorrhage	0.463
Giant capillary	0.524
Ramification	0.279
Tortuosity	0.491
Capillary	0.600

Detection of capillaries and haemorrhages

For this model we used the total number of annotations, merging normal and enlarged samples, with the objective to have the model learn about the "shape" of capillaries and haemorrhages.

We used a *Retinanet* (19) configuration of *MMDetection* machine learning framework (20) with some basic data augmentation. Using newer and more powerful models did not lead to better results, probably due to the low number of classes in our dataset.

Haemorrhages are difficult to clas-

Table III. Metrics for detection of capillary size (normal/enlarged/giant).

Metric	Score
All label types	
Average precision (AP) @ IoU=0.50:0.95	0.515
AP @ IoU=0.50:0.95	0.811
AP @ IoU=0.75	0.563
Average recall (AR) @ IoU=0.50:0.95	0.663
By label types - AP @ IoU=0.50:0.95	
Enlarged capillary	0.567
Normal capillary	0.453
Giant capillary	0.525

Table IV. Precision and recall with model output confidence of 0.40 or more and *IoU* of 0.50 or more.

Type	Precision (%)	Recall (%)
Capillary	83.84	92.44
Normal capillary	75.94	87.52
Enlarged capillary	75.96	91.59
Megacapillary	74.52	91.4
Tortuosity	74.41	89.46
Ramification	50.70	57.14

sify with great precision because the bounding boxes of images with many adjacent haemorrhages can be labelled and counted by humans in very different ways. But since the goal is to detect the presence of haemorrhages, and they don't need to be measured or counted very precisely, we can say that the model is able to successfully indicate the presence of haemorrhages in capillaroscopy images.

Categories with a high number of examples (capillaries in all different shapes) can be detected with a high recall without great loss in precision. See Table II for evaluation metrics of this model.

Detection of normal, enlarged and giant capillaries

For this model we used all annotations except for haemorrhages (detected by the first model), with the objective to have the model learn about the "size" of capillaries and classify them as normal, enlarged or giant. See Table III for evaluation metrics of this model.

Precision and recall

When we test the model on the testing set, requiring a minimum output confidence of 0.40 and a minimum *IoU* of 0.50 we obtain a precision of 83.84%. The system was able to recognise 92.44% of the total number of capillaries (Table IV). With the exception of the ramifications that present a recall and precision slightly above 50%, in the rest of the findings the precision percentages are in all cases above 74% with a recall greater than 85%.

Measurement of capillaries

Our training set was formed by 15,352 manually annotated and validated capillaries with all three measurements. The test set is formed by 1,690 capillaries with all three measurements.

In non-blurred capillaries with good visibility, where the apex can be observed, our system produced the correct apex measurement most of the time: in 88 % of the test set data when model confidence is at least 0.50. Limb measurements were also placed in a reasonable spot of each limb, given that limbs measurements could be potentially placed in very different sections of the limb. In this case, results are obtained in 84% of the test set examples. Example measurements can be observed in Figure 3.

Discussion

Although other classification and scoring systems have been published for the interpretation of capillaroscopy (5, 21), we propose a different approach based on deep learning that can be easily used in any situation or with any device.

The metrics in our results not only are promising, they prove the system already useful for capillaroscopy practice. The system is able to detect and count most of the capillaries in any NVC. Our object detection models achieve a *mAP* of 0.471 and 0.515. Given that state of the art *mAP* for object detection models on very large datasets such as *COCO* (22) (the cur-

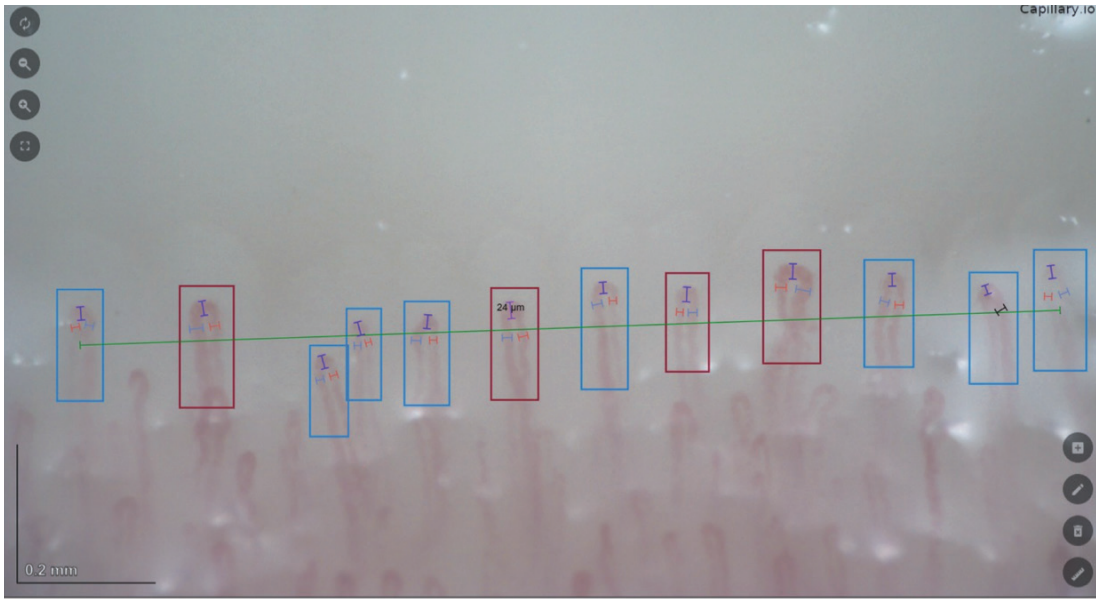

Fig. 3. Detected and measured capillaries example.
The buttons on the right are used to modify the annotations.

rent reference challenge in object detection research) is 0.557 (23), the overall system can be already considered to be in an advanced state.

All types of detected capillaries in images had a high precision and recall, with worse results for ramifications, probably due to the smaller number of ramification examples in the dataset in comparison with the other types of capillaries. Nevertheless, mean precision was 72% and mean recall was 85%, across all classes.

Also, by having capillary measurements, the effective accuracy of the system improves as long as a well-calibrated capillaroscope is available (several devices on the market have automatic calibration), by being able to take advantage of the measurement information to correct possible capillary size classification mistakes made by the object detection model.

Our software is able to automatically count and recognise capillaries in images obtained with any microscope, generate automatic measurements of each capillary and take advantage of this information resulting in an exhaustive analysis that is able to produce detailed and objective reports of each patient that allows the physician to perform an objective analysis. Although other internal and external validation studies are necessary, this high level of precision and recall allows positioning the tool as a potential automatic capillary analysis system.

These automatic quantitative statistics reported by capillary counting and measurements will facilitate the detection and suggestion of well-known patterns such as sclerodermiform patterns classified into early, active or late patterns according to Smith *et al*. (3).

In conclusion, a simple, easy to use web-based system to manage and analyse nailfold capillaroscopy images has been created using current methods in deep learning. It may be a very useful tool to standardise the collection and interpretation of capillaroscopy pictures and could provide great research in that field.

Acknowledgments

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They are all part of the Group of Systemic Autoimmune Diseases (GEAS) of the Spanish Society of Internal Medicine (SEMI) and SEMAIS (Multidisciplinary Spanish Society of Autoimmunity Diseases).

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