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Non-invasive Digital Disease Severity Scoring Compared to CAILS in early-stage Mycosis Fungoides

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Introduction

The Composite Assessment of Index Lesion Severity (CAILS) score is widely used in clinical trials of Mycosis Fungoides to I) assess lesion severity and II) evaluate response to treatment. However, CAILS is subjected to substantial inter-rater variability and limited sensitivity.

Objectives

To explore the performance of novel non-invasive imaging techniques to enable digital disease monitoring in CTCL-MF

Methods

Exploratory, single-centre, deep phenotyping study to describe MF characteristics and explore novel biomarkers.

- 21 early-stage (Ia/Ib) MF patients included and 11 healthy volunteers (HV)
- Observational part A: visits at week -6 and 0 without treatment (excl washout beforehand)
- Interventional part B: visits at week 4, 8, 12 and 16 of chlormethine (CL) gel 0.016% treatment
- Objective quantification of digital measures for erythema, desquamation, hypo- or hyperpigmentation, plaque elevation

Table 1. Demographics

	Overall (N=21)
Sex	
Female	9 (42.9%)
Male	12 (57.1%)
Race	
Asian	1 (4.8%)
Mixed	2 (9.5%)
White	18 (85.7%)
Age (years)	
Mean (SD)	52.9 (14.3)
Median [Min, Max]	55.0 [19.0, 72.0]
CAILS Score Lesion 1	
Mean (SD)	15.7 (3.17)
Median [Min, Max]	16.0 [11.0, 22.0]
mCAILS Score Lesion 1	
Mean (SD)	14.2 (2.55)
Median [Min, Max]	14.0 [9.00, 19.0]
mSWAT Score	
Mean (SD)	10.3 (7.52)
Median [Min, Max]	9.00 [3.00, 35.0]

Results

To clinically validate our candidate digital biomarkers for MF we investigated:

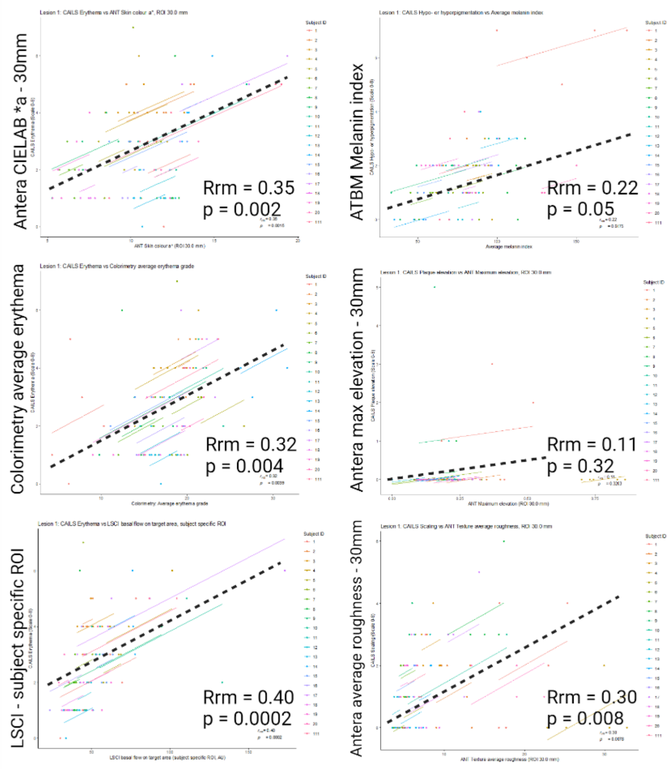
- **Tolerability** Mean burden (IQR) on a scale of 100 was low for all devices, specifically for imaging (e.g. automated total body mapping (ATBM), Antera multispectral imaging (ANT), colorimetry) with 7.8 (1.5-11), 5.7 [0-8] for Optical Coherence Tomography (OCT) and 5.1 [0-6] for Laser Speckle Contrast Imaging (LSCI).
- **Repeatability (Table 2):** Almost all candidate digital biomarkers showed low (<10%) intra-patient variance by coefficient of variation (CV) and good to excellent reliability by intraclass correlation coefficient (ICC). However, repeatability for LSCI and OCT was moderate to poor, respectively.
- **Differentiate diseased vs non-diseased skin (Table 2):** Group differences are displayed in Table 2. All candidate biomarkers quantifying erythema, besides OCT, could significantly discriminate lesioned from non-lesioned skin. For pigmentation quantification, ATBM melanin index was able to detect clear group differences, whereas ANT melanin was not. ANT maximum elevation and roughness could not differ between lesioned versus non-lesioned and healthy skin.
- **Correlation current existing endpoint: CAILS score (figure 1):** Fair correlations with CAILS erythema score were detected for erythema measured by ANT and colorimetry CIELAB *a and LSCI basal flow . A poor positive correlation was found between CAILS pigmentation and ATBM melanin index. CAILS desquamation scoring was fairly correlated to ANT average roughness. For other candidate digital endpoints no correlation was observed.

Table 2: Systematic evaluation of skin assessments to evaluate suitability as endpoint in clinical trials

Test	Group difference					Repeatability		Effect sizes	
	Lesion Mean	Control NL Mean (n=21)	p-value	Control HS Mean (n=11)	p-value	Within Lesion CV*	ICC	MDES L vs NL	MDES L vs HS
ERYTHEMA									
ANT CIELAB *a	10.03	8.03	0.003	7.56	0.014	8.1%	0.89	2.74	3.31
ANT Hemoglobin average level	25.30	18.02	0.0002	16.67	0.0023	8.9%	0.88	7.04	9.05
Colorimetry CIELAB *a	18.70	13.30	< 0.0001	14.04	0.003	7.0%	0.84	3.75	4.92
LSCI basal flow (AU)	52.57	44.14	0.007	46.26	0.30	10.6%	0.73	15.32	19.98
OCT Average blood flow depths 0.01 – 0.035 (AU)	0.0215	0.0188	0.12	0.0188	0.43	31.7%	0.23	0.01	0.01
PIGMENTATION									
ANT Melanin average level (pixels)	39.17	38.85	0.86	36.01	0.32	4.4%	0.98	12.54	11.18
ATBM melanin index	77.85	69.03	0.02	62.13	0.05	8.8%	0.95	27.13	26.17
ELEVATION									
ANT maximum elevation	0.333	0.255	0.12	0.250	0.25	11.7%	0.91	0.17	0.25
DESQUAMATION									
ANT average roughness	9.04	7.31	0.13	6.12	0.10	17.9%	0.78	8.87	5.90

Colors: Green = suitable; Red = unsuitable; Yellow: indeterminate. Abbreviations: NL: non-lesioned skin (of patients), HS: healthy skin (of healthy volunte of variation; ICC: Intra-class correlation coefficient; MDES: minimal detectable effect size; LSCI: laser speckle contrast imaging, OCT: optical coherence to

Figure 1: Repeated measure correlations for candidate digital CAILS biomarkers



Conclusions

- This study clinically validated:
  - ANT CIELAB *a, hemoglobin average level and colorimetry CIELAB *a for erythema quantification.
  - ATBM melanin index for pigmentation quantification
- We recommend ANT multispectral imaging and the handheld colorimetry device for erythema quantification as secondary endpoint in research and clinical setting.

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CAILS:

Erythema	3
Pigmentation	6
Plaque	2
Scaling	4
Lesion_size	7

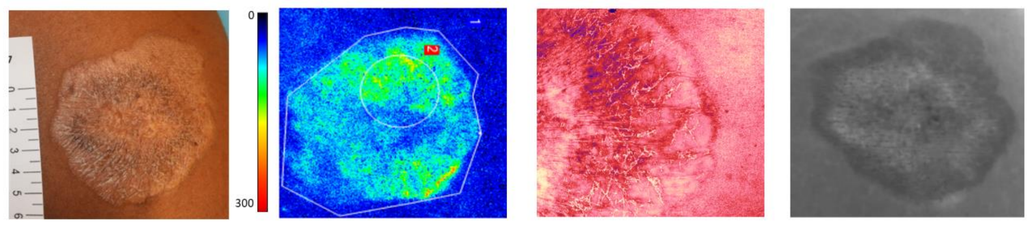

Figure 2: Clinically validated imaging biomarkers. A) CAILS score B) 2D clinical image of hypopigmented MF lesion with images of C) LSCI , D) Erythema and haemoglobin by ANT E) ATBM Melanin index

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