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Title of the paper: "Three-Dimensional Nail Imaging by Optical Coherence Tomography: a novel biomarker of response to therapy for nail disease in psoriasis and psoriatic arthritis".

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Nail disease is common in psoriasis and psoriatic arthritis (PsA) and its objective assessment is challenging with no tissue biomarkers available. Outcome measures include the Nail Psoriasis Severity Index (NAPSI) or the modified NAPSI (1). Optical Coherence Tomography (OCT) is a novel technique able to detect changes in psoriatic nails and may be potentially useful for therapy evaluation (2-4). Here we report the preliminary development of OCT imaging as an outcome measure for nail disease.

All fingernails of four consecutive psoriatic patients attending the Leeds Combined Psoriatic Service, were imaged by OCT at baseline and 6 months following Apremilast therapy, which has known efficacy in psoriatic nail disease (5), using Vivosight OCT scanner (Michelson Diagnostics Ltd, Kent, UK). Three scans were collected from each fingernail (1 transverse, from the lateral to the medial side, and 2 longitudinal–proximal and distal-from the lunula to the distal nail) totalling 240 scans (each of 120 slices) that allowed post-processing 3D nail reconstructions. Scored features are reported in Table 1. A dermatologist blinded to OCT findings scored the NAPSI at the same time-points. The patient clinical characteristics and results are reported in Table 2. Clinical and imaging nail outcomes were concordant in confirming improvement or worsening. Moreover, OCT detected: improvement in two fingernails scored as "stable" by NAPSI at 6 months (case 1); persistence of mild abnormalities in three fingernails scored as "normalised" by NAPSI at 6 months (case 3); abnormalities in a higher number of fingernails at baseline in case 4, in which all appeared mildly involved by OCT while NAPSI detected changes in only two nails. Representative OCT images of fingernails are shown in Figure 1.

These observations suggest the potential of OCT for longitudinal assessment of nail psoriasis, in this case after apremilast-treatment. Our group previously compared OCT and ultrasound in nail psoriasis and showed that OCT has a potential for the systematic characterisation of nail changes (2).

Although NAPSI/mNAPSI is the most commonly used tool for evaluating psoriatic nails, it does not offer information about nail structure. Due to the small sample size, we could not perform any statistical analysis however OCT images clearly showed changes over-time and the OCT score used, allowed a semiquantitative measurement blinded to NAPSI score.

Limitations of this report include the lack of comparison of OCT with ultrasound as this was a case series attending the Leeds Combined Psoriatic Service in which OCT was performed as part of clinical assessment. Compared with NAPSI, OCT is more expensive and currently not available in most centres. By contrast, OCT is not time-consuming (<60 seconds each scan), non-invasive and non-painful procedure, and shows excellent reliability with no specific experience required (4). Advantages include the objective evaluation and 3D reconstruction of nail structure, the pre- and post-treatment image storage, the possibility to measure nail thickness (Figure 2).

OCT identifies all common psoriasis nail changes and may have validity for outcome measure in clinical trials. Further studies with larger numbers and comparing OCT with other imaging tools are needed to validate its potential role as a nail biomarker.

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Figure legends:

Figure 1 (a-d). Representative Optical Coherence Tomography (OCT) longitudinal distal (a-b) and transverse (b-c) scans of four different nail cases. Each panel shows two representative slices of each scan at baseline (left) and follow-up (right) i.e. before and after 6 month-treatment with Apremilast. Corresponding nail pictures are shown in each panel. Each three dimensional scan volume measured 6 x 6 x 2 mm (length x width x depth). Pitting/localised surface irregularities (*) were seen as irregularities of the superficial nail plate, sometimes associated with an underlying shadow (a-d). Diffuse surface waving (≈) was visualised as waving of the superficial profile of the nail plate (a, b). Hyporeflective area with well demarcated border (#) was noted in some nails, interpreted as separation of nail plate from the nail bed and therefore scored as onycholysis. This may represent a putative subungual micro abscess (b). Onycholysis appeared as hyporeflective irregular area underlying the nail plate (↔) showing separation from the nail bed (a-d). Leukonychia / white spots were visualised as linear regular stripes (⇔) and circumscribed hyperreflective lesions (⇒) sometimes seen as multiple lesions, respectively (a, d). Subungual hyperkeratosis (→) appeared as hyperreflective linear subungual lesions (c-d). Right panels show resolution and/or improvement of most of the lesions present at baseline (left panels).

Figure 2 (a1-b1; a2-b2; c1-4). OCT scans showing multiplanar views of representative nails. (a1), (b1), (c1) panels show vertical view of longitudinal OCT scans of 3 nails with green line indicating depth from the surface. Corresponding horizontal view of the same scans at the indicated depth is shown in (a2), (b2), (c2). Blue line in horizontal view indicates the corresponding slice shown in vertical view. Representative measure scale is shown in (a1) and (c2) and can be used to measure any structure and lesion including nail thickness. (c3-4): Three dimensional reconstruction of the longitudinal distal scan (c3) of the case shown in c1-2 and corresponding nail picture (c4).

Table 1. Optical Coherence Tomography scoring system of fingernails.

OCT features	Score range each scan*	Total score range per fingernail^
	0-5	0-15
Leukonychia/white spots	0/1	0-3
Pitting/localised surface irregularities	0/1	0-3
Diffuse surface waving	0/1	0-3
Onycholysis	0/1	0-3
Subungual hyperkeratosis	0/1	0-3

*0=absent; 1=present. ^score calculated on 3 images (transverse, longitudinal proximal and longitudinal distal).

Table 2. Clinical characteristics, total NAPSI and OCT imaging scores at baseline and six months after Apremilast treatment in four cases with psoriatic nail disease.

Case	Sex	Age	Psoriasis*	Psoriatic Arthritis*	NAPSI baseline	NAPSI 6 months	OCT score baseline	OCT score 6 months
					(score range: 0-80)		(score range 0-150)	
1	M	48	1	1	46	24	93	63
2	M	39	1	0	27	54	61	71
3	M	64	1	0	47	19	100	43
4	F	60	1	1	6	0	51	24

*0=absent; 1=present.