Photodiagnosis and Photodynamic Therapy 27 (2019) 481–486

Contents lists available at ScienceDirect

Photodiagnosis and Photodynamic Therapy

journal homepage: www.elsevier.com/locate/pdpdt

# OCT in the diagnosis of head and neck pre-cancerous and cancerous cutaneous lesions: An immediate *ex vivo* study

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ARTICLE INFO

*Keywords:*
Optical diagnostics
Optical biopsy
Skin cancer
Optical coherence tomography
OCT

ABSTRACT

*Background:* Optical coherence tomography (OCT) has been shown to reliably identify skin changes with the combined advantage of resolution and penetration depth. The objective of this study was to assess the accuracy of OCT in diagnosing various skin pathologies, using pre-set diagnostic criteria, by two reviewers blinded to the actual diagnosis.

*Patients and methods:* This immediate ex-vivo study included skin specimens from 103 patients with suspicious skin lesions. In total, 110 lesions were scanned using OCT immediately following surgical resection. Two experienced OCT reviewers assessed these OCT diagnostic parameters blindly at two different intervals based on the parameters of the pre-set criteria. Furthermore, based on the diagnostic suggestions of the two reviewers, the sensitivity and specificity were calculated along with the kappa agreement statistic.

*Results:* A variety of lesions were diagnosed, as part of this study, including actinic keratosis (AK), basal cell carcinoma (BCC), cutaneous squamous cell carcinoma (SCC), lentigo maligna (LM) and malignant melanoma (MM). Using the previously set diagnostic criteria, a sensitivity and specificity for AK was reported as 97.5% and 100%, respectively. For BCC it was 98% and 95.3%, respectively; while for cutaneous SCC was 83.3% and 94.9%, respectively. The sensitivity and specificity for LM was reported as 55% and 89.5%, respectively; while for MM it was 43.8% and 76.2%, respectively. High overall levels of intra- and inter-observer agreements were shown for most of the evaluated diagnostic parameters.

*Conclusion:* This study indicates that OCT shows good promise as an optical diagnostic technique in diagnosing skin pathologies. The sensitivity in diagnosing actinic keratosis and basal cell carcinomas was impressive, with satisfactory results in diagnosing cutaneous squamous cell carcinoma. The sensitivity in diagnosing lentigo maligna and malignant melanoma remains poor and require further studies. Experienced OCT reviewers are required to improve diagnostic accuracy.

## 1. Introduction

Skin cancer continues to be the most common cancer in the Caucasian population [1,2]. It mainly affects the sun-exposed skin of individuals who are more sunburn prone. In the last few decades, there appears to be an increase in the incidence of skin cancer. As a result, skin cancer is becoming a major public health problem [3]. The gold standard diagnosis remains pathology following a surgical biopsy.

Over the past two decades, researchers around the world started assessing the possibility of diagnosing tissue pathologies by using optical systems. A light of a specific wavelength is passed through the tissue and the reflected light is measured and can give a specific definition to the changes occurring in that tissue (i.e. cellular and subcellular changes in elastic scattering spectroscopy, molecular vibration in Raman spectroscopy, surface morphology by microendoscopy and biochemical changes from tissue fluorescence) [4].

Optical coherence tomography (OCT) is an optical diagnostic tool that has been applied to study tissue pathologies with variable success. Principally, OCT is analogous to ultrasound with capability to present cross-sectional high-resolution images of structures below the tissue

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https://doi.org/10.1016/j.pdpdt.2019.07.019
Received 9 June 2019; Received in revised form 24 July 2019; Accepted 26 July 2019
Available online 27 July 2019
1572-1000/ 

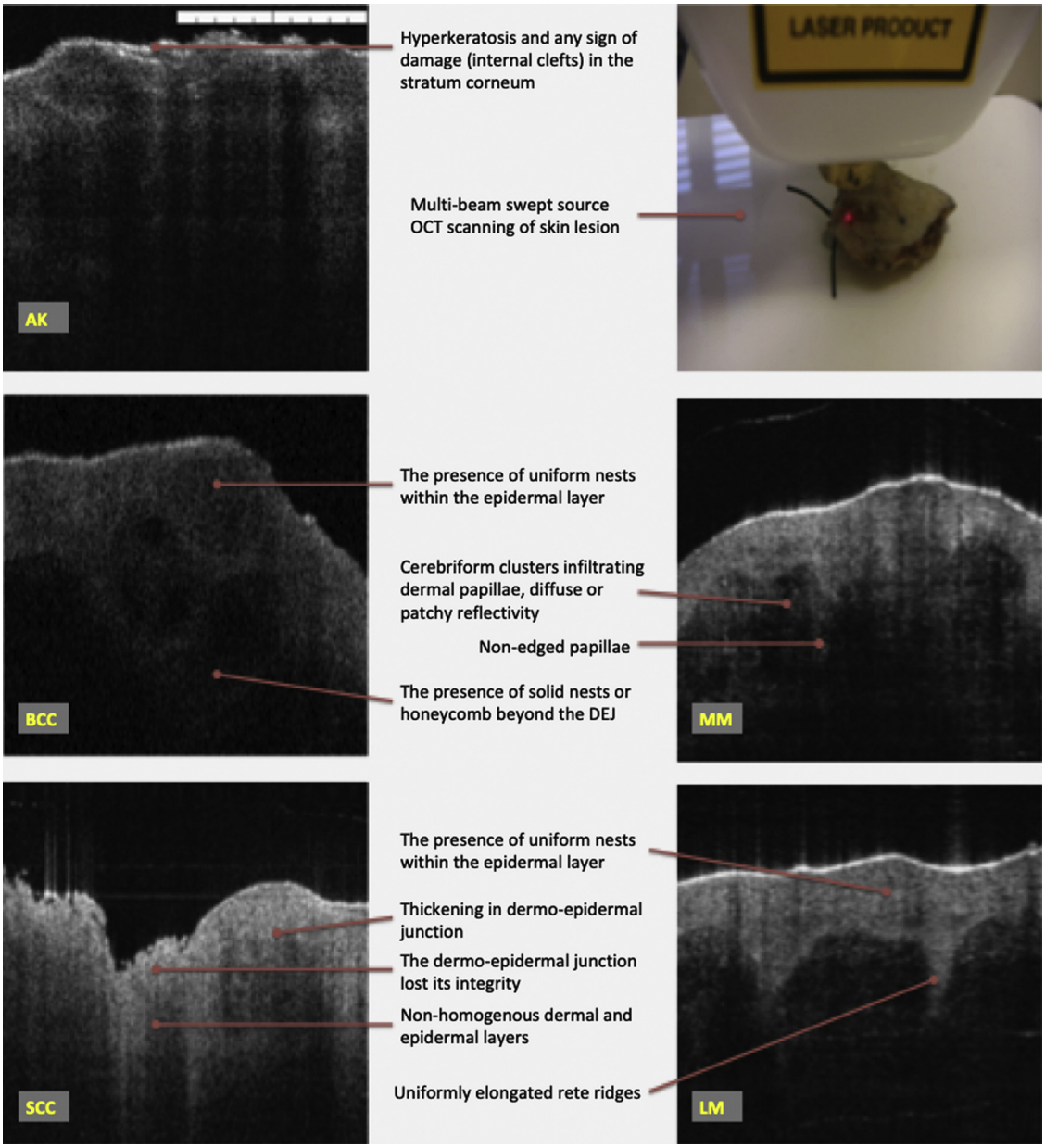


**Fig. 1.** Some of the features in the pre-set OCT-based diagnostic criteria used by the reviewers to assess the OCT images.

surface in analogy to histology. First applied in 1991 by Huang et al., as non-invasive interferometric (superimposing or interfering waves) tomographic imaging modality which allows millimetre penetration with micrometer-scale axial and lateral resolution [5]. Many studies, involving OCT, have been conducted on cancerous tissues. However, there is no consensus regarding diagnostic criteria for diagnosing each pathological category [6,7].

The objective of this study was to assess the accuracy of OCT in diagnosing various skin pathologies, using pre-set OCT-based diagnostic criteria, by two reviewers blinded to the actual diagnosis.

## 2. Patients and methods

In this study, 103 patients (110 lesions) with suspected skin pre-cancer/cancer were recruited at the Head & Neck Centre, University College London Hospital. The patients presented with non-healing skin ulcers or pigmented lesions or other lesions of which there was a high degree of suspicion. The anatomic location of these lesions affected a number of areas in the head and neck. All the 110 lesions required full surgical excision.

The study protocol was approved by the Moorfields & Whittington Local Research Ethics Committee of Human Research, in agreement with the Declaration of Helsinki. Informed consent was obtained from each patient. Inclusion criteria included patients being over 18 years of age. All the removed lesions have been scanned with OCT, but only malignant and premalignant lesions of up to 1 cm in diameter were included, as confirmed on the histology. Lesions with vesicle or bullae or both were excluded from the study as well as inflammatory skin diseases. In total 110 lesions, from 103 patients, were included in this study after satisfying the inclusion/exclusion criteria.

A “pre-made proforma” was used to collect clinic-pathological and optical data from each patient included in this study. The researchers were very accurate in record keeping which later on facilitated statistical analysis and study results. All surgical resections were performed under local anaesthesia. Depending on the diagnosis, patients were either followed-up in head & neck clinic or discussed in a multi-discipline meeting in case further investigations or management were required (this was the case in lentigo maligna and malignant melanoma

patients).

The lesions were immediately subjected to optical coherence tomography scanning following surgical resection (immediate *ex vivo*). In this study, we used a Swept-Source Frequency-Domain Optical Coherence Tomography microscope (Michelson Diagnostics EX1301 OCT Microscope V1.0). The light source used is a Santec HSL-2000, with an imaging wavelength of 1310 nm; axial optical resolution of < 10 μm and lateral optical resolution of < 10 μm. The system provide an image resolution 5.3 μm/pixel with a maximum image width of 6 mm and sub-surface imaging depth of 1.5 mm and a focal depth of 1 mm. Samples can be manipulated to see the full quality results on the screen instantly, with an image capture time of < 100 ms and refresh rate of > 1 Hz. Images were acquired by two modes: black and white and inverted colour mode.

The device utilises a novel optical set-up involving multiple optical channels, which does not suffer from loss of sensitivity or other serious drawbacks. The idea is to partition the depth of field into sub-fields, and provide a separately focused beam for each sub-field. All acquired OCT images were correlated with the corresponding histopathology images to ensure an accurate diagnosis and appropriate co-localisation of abnormal lesion on both OCT image and pathology slide. This was achieved in every resected lesion.

The OCT instrument captured b-mode scans of the tissue. Each of examined skin specimens were placed under the OCT imaging beam and scanned in the immediate *ex-vivo* phase as the transverse virtual line between the two landmarks. To provide a linear focal trough, a series of images were taken from edge to edge along the whole length of the specimen. The main scanned areas were (1) the centre of the lesion (macroscopically tumour-involved area) and the (2) periphery of the specimen (macroscopically tumour-free area). Histopathology slides were constructed from these scanned areas, as well as other areas depending on clinical significance and the pathologist's experience. All the pathology slides were examined and the most obvious architectural changes were recorded.

A clinical photograph has been taken pre and post lesion resection and during OCT scanning. This aided clinical description of the lesion during the blind OCT images analysis and served as an additional guide for OCT scanning of lesion's most suspicious areas. Also it aided histopathology plane cutting in a manner to correlate with OCT scanning. To exactly register the OCT images with the corresponding histological sections, the backs of specimens were tattooed by dark toluene blue to ensure correct orientation in the paraffin-embedding process. Marking sutures have been used to guide microtome cutting of the same scanned planes in order to provide an exact matching between the histopathology and the OCT images.

A pre-set OCT-based diagnostic criteria built from our databank was used to aide the diagnosis of the skin lesions in this study (Fig. 1). This included specific features per pathology:

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- Actinic keratosis (AK): hyper parakeratosis/hyperkeratosis and/or stratum corneum disruption.
- Basal cell carcinoma (BCC): single or multiple nodules in the form of a solid or honeycombed compartment (nest) in case of nodular BCC. While an empty space below dermo-epidermal junction (DEJ) is a diagnostic feature for cystic BCC
- Cutaneous squamous cell carcinoma (SCC): DEJ that have lost their integrity with/out the presence of small bright clusters in the papillary dermis and damage to the superficial epidermal layers (honeycombed, broadened, cobblestone).
- Lentigo maligna (LM): predominantly uniformly elongated rete ridge. Also, uniform nests within the epidermis.
- Malignant melanoma (MM): loss of the typical bright horizontal linear structures with architectural disarray and diffuse or patchy reflectivity, non-edged papillae with cerebriform clusters infiltrating dermal papillae and intact DEJ.

The principal investigator performed all OCT scans, while two reviewers interpreted the OCT image readings independently in a blinded way. Both reviewers were experienced in reading OCT images. To calibrate the reviewers' ability to identify abnormal pathological features on OCT and to reduce inter-observer variation, 10 OCT images (2 x BCC, 2 x AK, 2 x SCC, 2 x LM, 2x MM) and their correlated histopathology images were carefully chosen (by the principal investigator) and were studied by both reviewers and both agreed on the normal and pathological features in these images, guided by the previously mentioned OCT-based diagnosed criteria.

No other imaging processes was involved and original OCT images were used for the reviewing purposes. The reviewers were asked to report any abnormal features in the OCT images that may indicate pathology and also to provide an exact diagnosis. The reviewers were, also, asked to comment on specific features, including:

- Hyperkeratosis and any sign of damage (internal clefts) in the stratum corneum.
- The presence of uniform nests within the epidermal layer.
- The integrity and presence of thickening in dermo-epidermal junction (DEJ) with/out protruding clusters. As well as, DEJ ridges status (elongated or atrophied rete ridges).
- The presence of solid nest or honeycomb beyond the DEJ.

The diagnosis was then compared to the gold standard histopathology. Each reviewer was asked to comment on every acquired OCT image at 2 different intervals (2 weeks apart). The data was then used to calculate the inter- and intra-observer agreements as well as the sensitivity and the specificity of OCT.

Data analysis was carried out using the SPSS statistical package (release 10.0.06; SPSS Inc, Chicago, Illinois) and Stata statistical software (release 10.0; Stata Corp LP; College Station, Texas). We computed the k statistics for evaluation of inter- and intra-observer agreement by calculating the Cohen k statistics measure for each descriptor and considering $P < 0.001$ as significant. The value of kappa (k) = 1 indicates perfect agreement while k = 0 indicates agreement obtained by chance alone. The value of k < 0.20 to represent poor agreement, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as good and values above 0.81 represent very good agreement.

## 3. Results

A total of 110 surgical specimens (from 103 patients) were included in this study as per our inclusion/exclusion criteria. Patients comprised 64 (62.1%) women and 39 (37.9%) men. Three-quarters of the participants were Caucasians, 23% Asians, and 2% Afro-Caribbeans. Fifty-five of them had Fitzpatrick type III skin, 37 were type II and 8 were type I. The mean age was 67 years (range 39–95). Lesions characteristics are presented in Table 1.

Of the 110 lesions that were scanned, 54 were identified by histologic examination as basal cell carcinomas (BCC), 23 actinic keratosis (AK), 15 as cutaneous squamous cell carcinomas (SCC), 10 lentigo maligna (LM), and 8 malignant melanomas (MM). 110 scans were collected from each of the five skin pathologies regardless of the number of lesions. This was mainly employed to facilitate data analysis and comparison. These measurements were standardized and validated by interval sampling. Clinico-pathological details of all the 110 lesions of the five studied skin pathologies are shown in Table 2.

The overall sensitivity and specificity for OCT in diagnosing basal cell carcinomas was 98% and 95.3%, respectively. The false negative was identified in one OCT image out of 54, when compared to the exact co-localised histopathology slide. The overall accuracy was 96.5%. When it comes to actinic keratosis, the overall sensitivity was 97.5% with 100% overall specificity. One reviewer's results led to the identification of one false negative when compared to histopathology, with overall accuracy of 99.5% (Table 3).

**Table 1**
Patients' demographics and clinico-pathological features.

| | No. (%) | | No. (%) |
|---|---|---|---|
| Gender (103 patients) | | Clinical features (110 lesions) | |
| Male | 39 (37.9) | Papule | 20 (18.1) |
| Female | 64 (62.1) | Erosion | 32 (29) |
| | | Ulcer | 18 (16.3) |
| Skin type (103 patients) | | Nodule | 33 (30) |
| Type I | 8 (7.7) | Others | 7 (6.3) |
| Type II | 37 (35.9) | | |
| Type III | 55 (53.3) | Colour (110 lesions) | |
| Type VI | 3 (3.1) | Mixed | 40 (36.3) |
| | | Red | 22 (20) |
| Main symptom (110 lesions) | | Brown | 8 (7.2) |
| Itchiness | 23 (20.9) | Black | 5 (4.5) |
| Symptomless | 20 (18.1) | White | 5 (4.5) |
| Scaly | 25 (22.7) | Non specific | 30 (27.2) |
| Lumpy | 30 (27.2) | | |
| Bleeding | 12 (10.9) | Histologic diagnosis (110 lesions) | |
| | | BCC | 54 (49) |
| Location (110 lesions) | | AK | 23 (20.9) |
| Cheek | 30 (27.2) | SCC | 15 (13.6) |
| Nose | 25 (22.7) | LM | 10 (9) |
| Ear | 16 (14.5) | MM | 8 (7.2) |
| Forehead | 13 (11.8) | | |
| Lip | 13(11.8) | | |
| Neck | 8 (7.2) | | |
| Mastoid | 5 (4.5) | | |

**Table 2**
Clinico-pathological details of all the 110 lesions of the five studied skin pathologies.

| | Basal cell carcinoma | Actinic keratosis | Squamous cell carcinoma | Lentigo maligna | Malignant melanoma |
|---|---|---|---|---|---|
| Number of lesions | 54 | 23 | 15 | 10 | 8 |
| Size (cm) | | | | | |
| ≤1 | 54 | 23 | 15 | 10 | 8 |
| Thickness (mm) | | | | | |
| < 0.5 | 8 | 3 | 6 | 9 | 6 |
| 0.5–0.99 | 32 | 20 | 7 | 1 | 2 |
| 1–1.99 | 14 | 0 | 2 | 0 | 0 |
| Location | | | | | |
| Cheek | 15 | 3 | 6 | 4 | 2 |
| Nose | 20 | 1 | 2 | 2 | 0 |
| Ear | 12 | 1 | 2 | 1 | 0 |
| Forehead | 3 | 6 | 1 | 1 | 2 |
| Lip | 3 | 6 | 1 | 1 | 2 |
| Neck | 0 | 5 | 0 | 1 | 2 |
| Mastoid | 1 | 1 | 3 | 0 | 0 |
| Disease length (by patient) | | | | | |
| < 4 weeks | 19 | 6 | 12 | 8 | 8 |
| > 4 weeks | 35 | 17 | 3 | 2 | 0 |
| History | | | | | |
| Primary lesion | 54 | 23 | 15 | 10 | 8 |
| Recurrence | 0 | 0 | 0 | 0 | 0 |
| Treatment | | | | | |
| Surgical resection | 54 | 23 | 15 | 10 | 8 |

Cutaneous squamous cell carcinoma results were studied and showed 3 false negatives in one reviewer's results and 2 in the other's out of 15 OCT images co-localised with histopathology confirming the diagnosis. Hence the overall sensitivity was affected and reported at 83.3%, while the overall specificity and accuracy was at 94.9% and 93.3%, respectively. The overall sensitivity for lentigo maligna was fairly poor at 55%, while the overall specificity and accuracy was 89.5% and 85.2%, respectively. Similarly the overall sensitivity for malignant melanoma diagnosis was poor at 43.8%, with 4–5 false negative OCT images out of 8 total images compared and co-localised with histopathology were the diagnosis was confirmed. The overall specificity and accuracy in case of malignant melanoma was at 76.2% and 74%, respectively (Table 3).

Inter-observer agreement was generally lower than intra-observer agreement. The inter-observer agreement for DEJ integrity was good, with a weighted kappa value of 0.89. For the presence of solid nest compartments within the epidermis, the percentage of agreement was high (0.92). However, agreement on the thickening of DEJ with/out protruding clusters was small and the kappa values were 0.60. Higher agreement was obtained for DEJ ridge status (elongated or atrophied), which helped differentiate MM from LM with a k value of 0.55. The k scores ranged from 0.72 for stratum corneum disruption to 0.8 for hyperkeratosis (Table 4).

## 4. Discussion

One of the challenges we faced in this study was the small sample size as well as the inconsistency in patient numbers among the five examined skin pathologies. This was directly related to the referral rate from primary care centres to our tertiary head and neck unit. Although we were able to recruit a relatively good number of patients when it comes to basal cell carcinomas (n = 54) and actinic keratosis (n = 23) but this was not achieved when it comes to lentigo maligna (n = 10) and malignant melanomas (n = 8) which are usually referred to dermatology units.

The gold standard diagnosis of skin lesions remains histopathological analysis. The use of dermoscopy is now widely recommended by dermatologists to aide diagnosis. The emergence of non-invasive optical techniques like reflectance confocal microscopy and optical coherence tomography is becoming more noticeable in the medical literature. The added benefits of these techniques include cost-effectiveness, real-time diagnosis and reduce the need for unnecessary biopsies. The application of these techniques remains at the development stage and full-scale clinical applications needs more high evidence studies [8,9].

When it comes to dermoscopy, Lallas et al. [10] reported that it enhances BCC detection, by facilitating its discrimination from other skin tumors and inflammatory skin diseases. A retrospective analysis by Zalaudek et al. [11], studied the dermoscopic features of facial actinic keratosis, intraepidermal carcinoma (IEC), moderately to poorly differentiated invasive SCC, and well-differentiated SCC of the keratoacanthoma. Many dermatoscopical features were identified and aided diagnosing these lesions and differentiating between them. The study further recommended a progression model of facial AK developing into IEC and invasive SCC, which could aide diagnosis, monitoring and follow-up. A systematic review by Watts et al. [12] came to the conclusion that dermoscopy remains a favourable tool for detecting melanomas early and quickly, and the recent dermatology guidelines attributed a high level of evidence to its general use.

The use of confocal microscopy in detecting skin pathologies, like OCT, remains a developing technology. One of the early studies by Braga et al. [13]on forty benign and malignant pigmented skin lesions revealed that this technology is able to identify nuclear, cellular, and architectural changes in epidermal and superficial dermal layers with high resolution and contrast which could aide diagnosis and monitor treatment. A study by Zalaudek et al. [14]showed that this technology, when correlated with histopathology, is able to identify architectural changes on cellular and subcellular levels which could lead to the accurate diagnosis of actinic keratosis, basal cell carcinomas and other non-melanocytic skin tumours.

Optical coherence tomography is another, developing, optical technology in the world of dermatology [15–17]. A recent systematic review, by Cheng and Guitera [18], which involved 22 studies with 556

**Table 3**
Data analysis of OCT scans studied by both reviewers.

| | TP[a] | TN[a] | FP[a] | FN[a] | Sensitivity (%) | Specificity (%) | PPV[a] (%) | NPV[a] (%) | Accuracy (%) |
|---|---|---|---|---|---|---|---|---|---|
| BCC | | | | | | | | | |
| Reviewer 1 | 53 | 54 | 2 | 1 | 98 | 96 | 96 | 98 | 97 |
| Reviewer 2 | 53 | 53 | 3 | 1 | 98 | 94.5 | 94.5 | 98 | 96 |
| AK | | | | | | | | | |
| Reviewer 1 | 22 | 87 | 0 | 1 | 95 | 100 | 100 | 99 | 99 |
| Reviewer 2 | 23 | 87 | **0** | **0** | 100 | 100 | 100 | 100 | 100 |
| SCC | | | | | | | | | |
| Reviewer 1 | 12 | 91 | 4 | 3 | 80 | 95 | 75 | 96 | 93 |
| Reviewer 2 | 13 | 90 | 5 | 2 | 86.6 | 94.7 | 72 | 97.8 | 93.6 |
| LM | | | | | | | | | |
| Reviewer 1 | 6 | 90 | 10 | 4 | 60 | 90 | 73 | 95 | 85 |
| Reviewer 2 | 5 | 89 | 11 | 5 | 50 | 89 | 31 | 94.6 | 85.4 |
| MM | | | | | | | | | |
| Reviewer 1 | 4 | 77 | 25 | 4 | 50 | 75 | 13 | 95 | 73.5 |
| Reviewer 2 | 3 | 79 | 23 | 5 | 37.5 | 77.4 | 11.5 | 94 | 74.5 |

[a] TP: true positive, TN: true negative, FP: false positive, FN: false negative, PPV: positive predictive value, NPV: negative predictive value.

**Table 4**
Intra-observer and inter-observer agreements.

| | Reviewer 1 (K score)[a] | Reviewer 2 (K score)[a] | Reviewers (K score)[b] |
|---|---|---|---|
| Stratum corneum thickening | 0.95 | 0.9 | 0.8 |
| Stratum corneum disruption | 0.9 | 0.75 | 0.72 |
| Uniform nest within the epidermis | 0.95 | 0.98 | 0.92 |
| Integrity DEJ | 0.9 | 0.95 | 0.89 |
| Thickening of DEJ with/ out clusters | 0.7 | 0.88 | 0.6 |
| DEJ ridges status | 0.8 | 0.8 | 0.55 |
| Solid nest or honeycomb beyond the DEJ | 0.7 | 0.8 | 0.7 |

[a] Intra-observer agreement.
[b] inter-observer agreement.

histologically proven BCCs concluded that OCT is a useful tool in the diagnosis, treatment planning and treatment monitoring of BCC. When it comes to melanocytic lesions, a newly developed speckle-variance OCT (SV − OCT) has been reported to detect vascular changes occurring in these lesions, which can increase detection accuracy [19].

In this immediate ex-vivo study, we evaluated skin resections of five common skin pathologies. All specimens were examined immediately following resection with the aim to prevent cell swelling and rupturing that otherwise would affect OCT image quality. OCT accuracy for the diagnosis of basal cell carcinoma (96.5%) exceeded that of the published rates for physical examination at 92% [20]. Additionally, OCT has the ability to confirm the diagnoses non-invasively and in real-time. Sahu et al. [21] reported, in a recent study, that by using a combined reflectance confocal microscopy-optical coherence tomography, basal cell carcinoma detection could be achieved at high level of sensitivity (100%) and specificity of 75%. The group conclusion, after studying 85 lesions, that this optical technique is that it may prospectively be used to diagnose lesions suggestive of BCC and triage for treatment.

A recent Cochrane review reported that conventional OCT might have a role for the diagnosis of BCC in clinically challenging lesions, with a meta-analysis showing a higher sensitivity and higher specificity when compared to visual inspection plus dermoscopy [22]. Hussain et al. [23] reported that OCT could identify eight architectural changes associated with basal cell carcinoma: disruption of layering, hyporeflective rounded areas surrounded by a hyper-reflective halo ('honeycomb' structures), palisading at margin, dilated vessels, well--circumscribed black/signal poor areas, intact DEJ with underlying dark rounded areas, thinning of the epidermis, and horizontal signal intense cords. Some of these features were accurately described in our study.

Our study demonstrated that OCT diagnosis of actinic keratosis was very accurate. Using experienced reviewers might be one of the reasons of obtaining such high accuracy in distinguishing AK from other skin lesions with 100% specificity and 97.5% sensitivity. In this study, we did not evaluate dark bands specifically, but we identified them in some of our OCT images, suggesting that they may not be a general feature of identifying AK. The decreased penetration depth of OCT in AK that we identified is attributed to the optical properties of hyperkeratosis. Korde and colleagues studied OCT images of sun-damaged skin and AK and reported a sensitivity of 86% and a specificity of 83% in their study [24]. Other studies found similar diagnostic criteria in differentiating AK. The presence of a dark band in the stratum corneum was 79% sensitive and 100% specific for AK in a study by Barton et al [25].

Diagnosis of cutaneous SCC remains a challenge due to the lack of evidence [19]. Nevertheless, our study reported an overall sensitivity of 83.3% and specificity of 94.9%. Reggiani et al. [26] reported that OCT could identify a number of architectural changes associated with cutaneous SCC: destruction of the epidermis and thickened epidermal layer. The fact that these architectural changes do overlap with other skin pathologies may indicate our current sensitivity for detecting this skin pathology. Other features have been examined that could guide towards more accurate diagnosis was reported by Boone et al. [27] and included disruption of the DEJ and disarranged epidermal pattern in the absence of honeycomb structures.

Our study has reported poor OCT sensitivity in detecting lentigo maligna as well as malignant melanoma. The current literature indicates that there is not enough evidence to study the possibility of using OCT in detecting melanoma skin cancers [22] Currently, dermatologists rely mainly on the dermoscopy to get the initial idea about what the entire pathology are. The diagnostic accuracy of dermoscopy for melanoma is lacking and considered to be inferior to other non-invasive skin screening tools [10–12]. There may also be concern that OCT, like dermoscopy before it, is a new technique and has a learning

curve associated with it. Gambichler et al. [28] studied benign naevi and malignant melanoma using high-definition OCT and was able to identify pagetoid cells, fusion of rete ridges, and junctional or dermal nests with atypical cells to be more characteristic of melanomas compared to benign nevi. In our study, we managed to define the characteristics of benign lentigines that distinguish them from melanomas. Nevertheless, it was difficult to distinguish between the different types of melanoma. Junctional activity and the cluster cells were also distinguishable in cross-sectional OCT images. In the diagnosis of lentigo maligna, we could reach sensitivity of 55% and specificity of 89.5%. While OCT sensitivity in diagnosing melanomas was 43.8% and specificity was 76.2%.

## 5. Conclusion

This study indicates that OCT shows a good promise as a useful optical diagnostic technique in diagnosing skin pathologies. The sensitivity in diagnosing actinic keratosis and basal cell carcinomas was impressive, with satisfactory results in diagnosing cutaneous squamous cell carcinoma. The sensitivity in diagnosing lentigo maligna and malignant melanoma remains poor and require further studies. Inter-observer agreement was generally lower than intra-observer agreement. Experienced OCT reviewers are required to improve diagnostic accuracy.

In-vivo OCT is the next step in our research in this discipline. We have already developed a handheld OCT probe, however there are some technical difficulties with regards to the use of the probe in the oropharyngeal region. Also the issue of co-localising the *in vivo* OCT measurements with the formalin-shrunken pathology samples may represent a new challenge to this optical modality.

## Declaration of competing interest

Mr Colin Hopper is advisory board member at Michelson Diagnostics, Kent, UK.

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