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The sensitivity and specificity of optical coherence tomography for the assisted diagnosis of nonpigmented basal cell carcinoma: an observational study

M. Ulrich,[1,2] T. von Braunmuehl,[3] H. Kurzen,[4] T. Dirschka,[5] C. Kellner,[6] E. Sattler,[3] C. Berking,[3] J. Welzel[7,*] and U. Reinhold[6]

[1]Private Dermatology Office/CMB Collegium Medicum Berlin GmbH, Luisenstraße 54/55, 10117 Berlin, Germany
[2]Department of Dermatology, Charité Universitätsmedizin Berlin, Berlin, Germany
[3]Department of Dermatology and Allergology, University Hospital Munich, Munich, Germany
[4]Private Dermatology Office, Freising, Germany
[5]Private Dermatology Office Prof Thomas Dirschka, Wuppertal, Germany
[6]Dermatology Center Bonn Friedensplatz, Bonn, Germany
[7]Department for Dermatology and Allergology, General Hospital Augsburg, Augsburg, Germany

Summary

Background The diagnostic criteria for basal cell carcinoma (BCC) using optical coherence tomography (OCT) have been described previously, but the clinical value of these findings remains unknown.
Objectives To investigate the diagnostic value of OCT for BCC in a typical clinical setting. The primary efficacy end point was a diagnosis of BCC for each lesion. Secondary end points were the diagnosis of other possible conditions.
Methods This was an observational, prospective, multicentre study in which consecutive patients with nonpigmented pink lesions suspicious for BCC underwent clinical assessment, dermoscopy and OCT, with the diagnosis recorded at each stage. Once all diagnoses had been recorded, the histological results were disclosed. In total 164 patients with 256 lesions were recruited. Histology was missing for 21 lesions, leaving 235 lesions in 155 patients for analysis.
Results Sixty per cent of lesions (141 of 235) were identified as BCC by histology. A slight increase of sensitivity was noted following OCT, which did not reach statistical significance. The specificity increased significantly from 28·6% by clinical assessment to 54·3% using dermoscopy and to 75·3% with the addition of OCT ($P < 0·001$). The positive predictive value for the diagnosis of BCC using OCT was 85·2% [95% confidence interval (CI) 78·6–90·4], and the negative predictive value was 92·1% (95% CI 83·6–97·0). The accuracy of diagnosis for all lesions increased from 65·8% with clinical evaluation to 76·2% following additional dermoscopy and to 87·4% with the addition of OCT.
Conclusions OCT significantly improved the diagnostic specificity for BCC compared with clinical assessment and dermoscopy alone.

Correspondence
Martina Ulrich.
E-mail: m.ulrich@collegiummedicum.de

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Conflicts of interest
M.U. has been paid for lectures for Michelson Diagnostics Ltd; is a stakeholder in CMB Collegium Medicum Berlin GmbH; has been involved with clinical trials for LEO Pharma and has performed paid lectures for Almirall, Galderma, LEO Pharma and Mavig GmbH. T.B. has received speaker's honoraria from Agfa HealthCare GmbH, LEO Pharma and Roche Pharma; and has been involved in clinical trials sponsored by Agfa HealthCare GmbH and Mavig GmbH. H.K. is a paid advisor to Michelson Diagnostics Ltd; has received speaker's honoraria from Michelson Diagnostics Ltd, Almirall Hermal, AbbVie, Galderma and LEO Pharma; and has been involved in clinical trials for Eli Lilly Pharma, Novartis and AbbVie. T.D. has received advisory board honoraria from Almirall Hermal, Biofrontera, Galderma, Meda Pharma, Scibase and Allergan; and has received speaker's honoraria from Almirall Hermal, Biofrontera, Galderma, Meda Pharma and Janssen-Cilag. C.B. has received speaker's and advisory board member's honoraria from, and has been involved in clinical trials sponsored by Almirall

Hermal, Biofrontera, Galderma and LEO Pharma. U.R. has received speaker's honoraria from Michelson Diagnostics. M.U., T.B., E.S., C.B. and J.W. have used the VivoSight® OCT system lent by Michelson Diagnostics Ltd.

M.U. and T.B. contributed equally to this study.

J.W. and U.R. acted as joint senior authors.

**For the German Working Group of Diagnostic Methods in Dermatology*

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What's already known about this topic?

- The diagnostic criteria of basal cell carcinoma (BCC) by optical coherence tomography (OCT) have previously been defined.
- Recent studies have also described the OCT criteria of actinic keratoses.

What does this study add?

- The results of this study support the additional diagnostic value of OCT for the diagnosis of pink patches.
- The diagnostic specificity for BCC may be increased by the use of OCT.

Nonmelanoma skin cancer (NMSC) is the most common cancer affecting white-skinned individuals worldwide. Although the real incidence and prevalence of NMSC are not exactly known, as it is not always reported in cancer registries, the incidence is thought to have increased annually by 3–8% since 1960.[1] Basal cell carcinoma (BCC) is the most common NMSC, with the incidence increasing by as much as 10% per year, suggesting that its prevalence will soon equal that of all other cancers combined.[2–5]

Rogers *et al.*[6] used another approach, analysing reimbursement data in the U.S.A. and using the number of procedures for NMSC as a proxy for the actual number of NMSCs, and extrapolating the Medicare figures to the rest of the US public. This calculation suggested there were a total of 3 743 315 new cases in 2009, with the number increasing by an average of 4·2% per year from 1992 to 2006.[5,6] This analysis is still an underestimate as it does not capture those using topical agents.

BCC is usually diagnosed clinically and is verified by biopsy and histological examination. However, as noninvasive therapeutic approaches are increasingly being used for superficial lesions, noninvasive diagnostic methods have the advantage of avoiding pre- and post-treatment biopsies, and can be used to monitor therapy. Superficial or early lesions are difficult to diagnose based on clinical examination only, but dermoscopy can assist through identification of distinct vessel patterns or formation of grey–blue globules seen in the pigmented variation.[7]

Dermoscopic evaluation can help to differentiate BCC from other epidermal lesions such as actinic keratosis (AK), irritated seborrhoeic keratosis (SK) or amelanotic melanoma.[8–10] However, even with dermoscopy, diagnosis of BCC is not always straightforward.[11,12] Diagnostic uncertainty often leads to a cautious approach by the physician, who first takes an invasive biopsy and then decides on a noninvasive treatment if indicated. However, a noninvasive approach from the outset would be preferred by the patients because wounding and scarring could then be avoided completely.

Optical coherence tomography (OCT) is a noninvasive optical imaging procedure that generates cross-sectional images of tissue, enabling visualization of altered skin architecture present in superficial skin lesions.[13,14] Promising results have already been demonstrated in the diagnosis and delineation of NMSC,[15–17] and diagnostic criteria for BCC have been established.[13,14,18–20]

However, earlier studies were unable to show that OCT could reliably discriminate between BCC and other skin lesions.[13,21] Improvements now allow detailed imaging of structures within the uppermost layers of the skin, and recent studies have been able to identify morphological criteria for different subtypes of BCC.[19,22]

The aim of this study was to investigate the sensitivity, specificity and diagnostic value of OCT for BCC in a typical clinical setting and to compare these with clinical and dermoscopic evaluation. Only clinically unclear lesions were included that were suspicious for BCC and where biopsy was being considered for confirmation of diagnosis.

Materials and methods

This was an investigator-initiated, phase IV, observational, prospective, multicentre trial carried out in six institutions from April 2013 to March 2014. Michelson Diagnostics Ltd (MDL; Orpington, Kent, U.K.) part sponsored the study and provided OCT equipment.

The main inclusion criterion was the presence of a clinically unclear erythematous papule or plaque ('pink lesion') with clinical suspicion of BCC and that required a diagnostic biopsy. These could be either reddish macules, patches or small papules with or without scale. Lesions with the typical clinical appearance of BCC on clinical examination (such as the presence of a pearly border, central ulceration and obvious telangiectasias), as well as pigmented lesions, were excluded from the protocol. Inclusion was based on clinical assessment alone, without the assistance of dermoscopy. Patients had to be at least 18 years of age and needed to give their written informed consent before inclusion in the study. Patients with unstable or uncontrolled clinically significant medical conditions were excluded.

OCT was used as an adjunct to clinical examination, dermoscopy and histology for the evaluation of suspicious skin

lesions prior to excisional or diagnostic biopsy. OCT assessments were performed after clinical and dermoscopic evaluation. All assessments were documented before the histological results were available and made known to the investigator in order to avoid potential bias. The local ethics committees approved the research protocol and all research was conducted according to the principles of the Declaration of Helsinki.

Examination

A clinical examination, prior to dermoscopy, had already identified the lesions as suspicious for the diagnosis of BCC. Alternative diagnoses included AK, Bowen disease (BD), squamous cell carcinoma (SCC), lesions such as inflamed SK, eczema, psoriasis and an open category of 'others'. The clinical assessment was recorded.

For each lesion dermoscopy was then carried out using a Dermlite ProHr (3Gen Inc., San Juan Capistrano, CA, U.S.A.), attached to a Sony Cybershot DSC-W710 camera (Sony, Tokyo, Japan) (supplied by MDL). As polarized light was used, no preparation of the area under examination was necessary. One dermoscopy photograph was taken for each lesion and a diagnosis was made based on the procedure.

Following dermoscopy, lesions were scanned with OCT (Vivosight® OCT Scanner, MDL) over an area of 6 × 6 mm, depth 1·2–2 mm, with an optical resolution of < 7·5 μm laterally and < 5 μm axially. The function 'multi-1' setting automatically provided 60 lateral scans of 6-mm length every 100 μm. Again no preparation of the skin surface was required and no oil or ointment was used with the device. The OCT images were assessed by naked eye for features affecting the epidermis, the dermoepidermal junction and the dermis.

After the OCT images had been reviewed, the clinician again recorded the suspected diagnosis. All centres were regular users of OCT, with at least 3 months of practical experience with the device. Nonetheless, all centres received training before participating in the study.

Diagnostic criteria for the three different diagnostic methods included the following patterns.

(i) Clinical examination: pink or red lesions that could be either macules, patches or small papules with or without scale. (ii) Dermoscopy:[23] a scattered vascular global pattern with loose haphazard distribution. Shiny white to red structures with or without chrysalis-like structures. Small fine telangiectasias appearing as fine, kinked vessels of small calibre, with length < 1 mm in superficial BCC and larger arborizing vessels in more invasive BCC (nodular/infiltrative). (iii) OCT: since the study was designed, some literature on OCT features has been published.[22] However, the following criteria were used in this study. Epidermis: protrusions into the dermis with shadowing; dermoepidermal junction: lack of definition or rupturing; and dermis: signal-poor ovoid structures, dark rims, ovoid structures with bright centres, dilated vessels, black areas or cysts, bright stroma and small ovoid signal-poor structures ('fish shoal').

Finally, a biopsy or excision of the lesion was taken and sent for histological analysis. All diagnostic steps had to be completed before histological confirmation was made.

Efficacy end points

The primary efficacy end point was a diagnosis of BCC for each lesion using the following techniques: clinical examination, dermoscopy, OCT and histology. Secondary end points were the diagnosis of conditions other than BCC: AK, SK, SCC or inflammatory conditions, using the same diagnostic techniques.

Study objectives

The primary objective was to determine the sensitivity and specificity of OCT for the diagnosis of BCC. Secondary objectives were to determine the sensitivity and specificity of OCT for the diagnosis of AK, SK, SCC and inflammatory skin conditions such as psoriasis, and to derive positive predictive values (PPVs) and negative predictive values (NPVs) of OCT diagnosis for BCC. BCC subtypes were also recorded sequentially for all three diagnostic modalities.

Statistical analysis

Prior to the start of the study, statistical calculation of sample size was performed, which resulted in a total sample size of 185 patients being required to show a 90–95% uplift at 80% power. These calculations assume that the diagnosis with each method is a yes/no outcome, thus patients are either diagnosed as having BCC or not. It was decided to aim for a total of 250 patients as a safety margin, particularly as it was anticipated that there would be some patients lost to follow-up, or there would be missing information.

The intention to treat (ITT) set included all lesions with histological confirmation. The OCT, clinical and dermoscopic diagnoses were compared with the result of the histological examination and classified as either true positive, true negative, false positive or false negative.

The specificity of each technique (percentage that test negative when BCC is not present) and sensitivity (percentage that test positive when BCC is present), PPV (percentage of positive diagnoses that are correct) and NPV (percentage of negative diagnoses that are correct) were calculated with exact 95% confidence intervals, using the Clopper–Pearson method.[24] The specificity and sensitivity of OCT for the diagnosis of BCC were compared with the specificity and sensitivity of the other techniques using McNemar's test,[25] which takes into account the paired nature of the data. Similar analyses were carried out for the other possible diagnoses.

The data were analysed by Quantics Consulting Ltd (statistical analysis) and the study authors M.U., J.W. and U.R. (interpretation of data).

Results

Main findings

In total 156 patients and 256 lesions were recruited, with an average number of lesions per patient of 1·55. The median age of the patients was 70 years (range 33–90). Lesions were located mainly on the head (41·0%) and upper body (48·8%).

Histology was missing for 21 lesions, and one case was found to have a combination of both BCC and SK or AK, leaving 235 lesions for analysis in the ITT group. Histology identified 141 of 235 (60%) lesions as BCC.

Sensitivity was high for all three techniques, increasing from 90·0% by clinical examination only to 95·7% with the addition of OCT. However, there was a marked and statistically significant increase ($P < 0·001$) in specificity from 28·6% to 75·3% for OCT (Table 1). However, the sensitivity was not significantly different between OCT and dermoscopy ($P = 0·12$) or clinical assessment ($P = 0·099$).

The PPV and NPV were greatest for OCT, and overall the accuracy of diagnosis for BCC increased from 65·8% (clinical examination alone) to 87·4% with the addition of OCT (Table 1; Figs 1 and 2).

Secondary outcomes

Other diagnoses

Of the 235 lesions, histology identified 32 as actinic keratosis (AK), 17 as BD, six as SK and six as inflammatory diseases such as eczema or psoriasis. The open category of 'other diseases' included 34 lesions and consisted of a large spectrum of other diagnoses such as sebaceous hyperplasia, dermal naevus and microcystic adnexal carcinoma. Following statistical analysis the specificity of OCT was significantly greater than that of clinical evaluation for the diagnosis of AK, BD and inflammatory diseases, and OCT was significantly better than dermoscopy for the diagnosis of BD. Overall, there was no difference in diagnostic sensitivity. Figure 3 shows a BD lesion as visualized by the three different techniques.

Table 1 Detection results and diagnostic accuracy for basal cell carcinoma (BCC)

	Clinical	Dermoscopy	OCT
Number of true positives	126	126	132
Sensitivity[a]	90·0 (83·8–94·4)	90·6 (84·5–94·9)	95·7 (90·8–98·4)
Number of true negatives	26	50	70
Specificity[a]	28·6 (19·6–39·0)	54·3 (43·6–64·8)	75·3 (65·2–83·6)
Positive predictive value[a]	66·0 (58·8–72·7)	75·0 (67·7–81·3)	85·2 (78·6–90·4)
Negative predictive value[a]	65·0 (48·3–79·4)	79·4 (67·3–88·5)	92·1 (83·6–97·0)
Diagnostic accuracy for BCC[b]	152/231; 65·8 (59·3–71·9)	176/231; 76·2 (70·2–81·5)	202/231; 87·4 (82·5–91·4)

OCT, optical coherence tomography. Although each technique analysed 231 lesions, these are different sets in each case. [a]Values are % (95% confidence interval). [b]Values are n/N; % (95% confidence interval).

Basal cell carcinoma subtypes

In addition to the diagnosis of BCC/no BCC, the evaluators were also asked to document the BCC subtypes. Within the study population 168 lesions were classified as BCC by OCT, compared with the 141 that were histologically confirmed. Of the 168 lesions in the subset of OCT-diagnosed BCC, 132 were confirmed by histology to be BCC, while 36 were another diagnosis. Fifty lesions were classified by OCT as nodular BCC, 75 as superficial BCC, 29 as sclerosing BCC and the remaining 14 as other or unspecified BCC. The surgical procedure was punch biopsy, shave/curettage or excision as documented in the case report form. The histological outcomes and frequencies, with breakdown of the BCC subtypes, are shown in Table 2.

Discussion

In this study we found a high diagnostic accuracy of 87·4% for BCC, with the addition of OCT to clinical examination and dermoscopy. The sensitivity for the diagnosis of BCC was not significantly increased by OCT, but this was not surprising as there had to be a suspicion that lesions were BCC for them to be eligible for inclusion in the study, and the sensitivity of clinical assessment and dermoscopy were already very high.

However, by using OCT we were able to increase significantly the diagnostic specificity, demonstrating the ability of OCT to discriminate between BCC and other lesions with similar clinical features. In these situations, OCT may be able to decrease the number of unnecessary biopsies. The diagnostic accuracy of OCT was found to be significantly greater than that of clinical or dermoscopic methods on their own. When considering lesions that were classified as 'other diagnosis', OCT was also able to increase significantly the specificity when compared with clinical examination alone, while no change in sensitivity was noted. However, due to the diversity of lesions in this group, the numbers of distinctive lesions were low and further studies with higher numbers are required to confirm these preliminary findings.

The relevance of these findings is that, with early identification of BCC using a noninvasive diagnostic technique such as OCT, wounds and scars from biopsies can be avoided and noninvasive treatment measures can be initiated in a timely manner. As a high proportion of BCC lesions are found on the

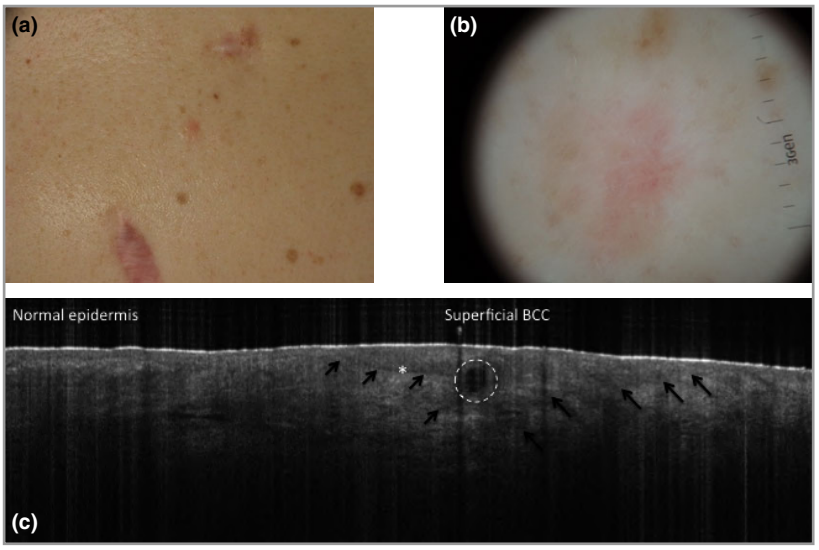

Fig 1. (a) Clinical, (b) dermoscopic and (c) optical coherence tomography (OCT) images of a representative superficial basal cell carcinoma (BCC) from the study. (a) The clinical appearance of a small pink papule on the back (black arrow) with clinical suspicion of BCC, adjacent to scars from previous excisions of BCCs and atypical moles. (b) The respective dermoscopy image with erythema and chrysalis-like structures that were in favour of a diagnosis of BCC. (c) OCT image showing focal thickening of the epidermis (black arrows) with underlying dark border (white asterisk) and a cystic structure in the centre (white dashed circle) confirming the diagnosis of a superficial BCC.

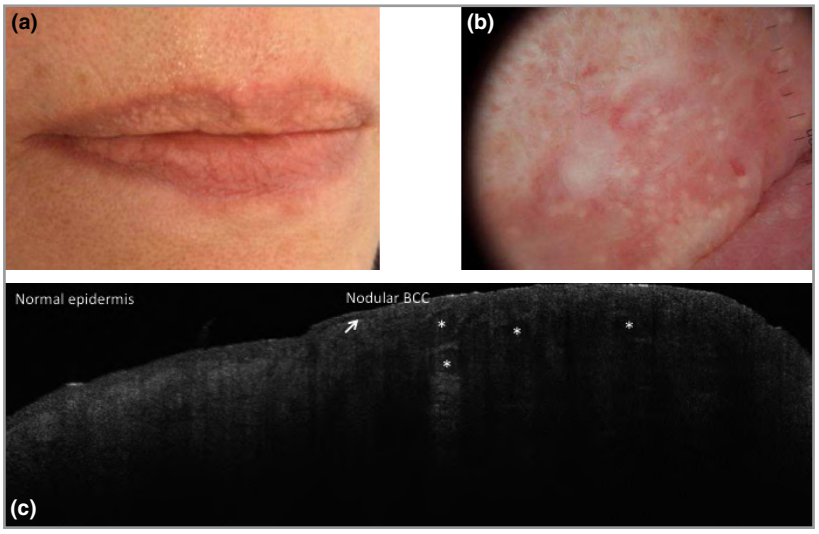

Fig 2. (a) Clinical, (b) dermoscopic and (c) optical coherence tomography (OCT) images of a representative nodular basal cell carcinoma (BCC) from the study. (a) The clinical appearance of a small, skin-coloured to slightly pink papule on the left central portion of the upper lip with clinical diagnosis of a scar/fibrous papule. (b) The respective dermoscopy image with diffuse erythema and a few telangiectasias in the periphery of the lesion, which favoured a dermoscopic diagnosis of BCC. (c) The correspondence of the papule in the right part of the OCT image with thinning of the epidermis (white arrow) and multiple, small ovoid nests (white asterisks) in the dermis that correspond to the OCT diagnosis of micronodular BCC, which was confirmed by histology.

head or neck (41% in our study) the cosmetic impact of diagnosis and treatment is a very important consideration.

In our study the specificities of clinical assessment and dermoscopy were lower than rates reported elsewhere.[26,27] However, the inclusion criteria allowed only unclear lesions that were mostly flat and of a superficial subtype (44·7% of all confirmed BCCs), which tend not to display distinct features on dermoscopy. Typical diagnostic rates without the use of OCT reported in other studies range from 56% to 90% for clinical sensitivity and 87% to 96% for dermoscopic sensitivity, with specificity rates of 75–90% (clinical assessment) and 72–92% (dermoscopy).[12] However, comparisons are difficult to make due to differences in study design. If all suspicious lesions had been included in our study, the sensitivity and specificity for each technique would have been higher, but only cases that were difficult to diagnose were included. This is in contrast to other studies that have commonly included all lesions, regardless of the certainty of clinical diagnosis. Many of these studies were retrospective, therefore it is to be expected that diagnostic accuracy rates would be much higher than in a prospective setting.

An accurate noninvasive diagnostic method in combination with nonsurgical treatments is becoming increasingly important to patients. The efficacy of nonsurgical treatment options

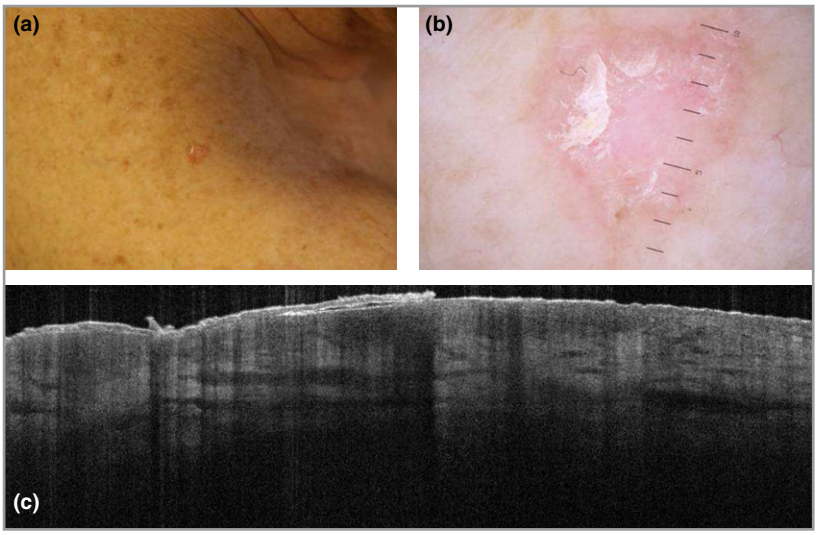

Fig 3. (a) Clinical, (b) dermoscopic and (c) optical coherence tomography (OCT) images of a representative Bowen disease lesion selected from the study. (a) The clinical appearance of a scaly patch on the back of a patient, which was suspicious for superficial BCC on clinical examination. (b) The respective dermoscopy image, with a central pinkish area, scaling and a few telangiectasias surrounding the lesion. Thus, this lesion was diagnosed as BCC by dermoscopy. (c) The corresponding OCT image, which shows disruption of the stratum corneum with scales (two white arrowheads) and the underlying widespread thickness of the epidermis (white arrows), but lacking clefts underneath the irregular epidermal thickening. In areas of hyperkeratosis the visualization of deeper structures is limited (white asterisk). On OCT the lesion was correctly classified as Bowen disease.

Table 2 Histological outcomes of basal cell carcinoma (BCC) detected by optical coherence tomography (OCT), giving a breakdown of BCC by subtype and type of biopsy. Inclusion criteria were any lesion diagnosed as BCC by OCT

Classification following OCT	Histology shows BCC (type of surgical procedure)	Histology shows no BCC (type of surgical procedure)
Nodular BCC	44 (15 punch, 9 shave/cur, 19 excision, 1 NS)	6 (1 punch, 1 shave/cur, 2 excision, 2 NS)
Superficial BCC	59 (6 punch, 39 shave/cur, 14 excision)	16 (2 punch, 8 shave/cur, 2 excision, 4 NS)
Sclerosing BCC	19 (11 punch, 3 shave/cur, 4 excision, 1 NS)	10 (2 punch, 1 shave/cur, 1 excision, 6 NS)
Other or unspecified BCC	10 (5 punch, 1 shave/cur, 2 excision, 1 NS)[a]	4 (2 punch, 1 excision, 1 NS)

Shave/cur, shave biopsy or curettage; NS, not specified. [a]One lesion was a collision tumour, resulting in two diagnoses.

is partly related to depth,[28–32] therefore confirmation by OCT of lesion depth and BCC subtype would be of value in deciding whether it is appropriate to use topical therapeutic agents or surgery.

If surgery is favoured, OCT can provide information on tumour margins and depth so that the surgical procedure can be planned better[33,34] to achieve optimal aesthetic results.[18] A recent study has shown that OCT may be applicable for delineating the thickness of squamous neoplasia and thus may help to improve surgical management by correctly identifying the lateral margins.[35] Another study has suggested that OCT can be used to detect subclinical residual NMSC lesions following photodynamic therapy, providing early detection of residual lesional tissue.[36]

As recent studies have shown a large discordance between the correct diagnosis of the BCC subtype on diagnostic biopsy and complete excision of the tumour,[37] a method that could correctly classify BCCs at the time of diagnosis would improve therapeutic management. Although we recorded the subtype of BCC, our study was designed before this was known and did not allow evaluation of this question, as histological confirmation was done by a variety of methods including punch biopsy, shave/curettage or excision, and not all lesions were completely excised.

Other advantages of OCT may be seen in the management of patients with field cancerization or a large number of suspicious skin tumours. As each OCT investigation takes only a few minutes and is noninvasive, it can easily be used on a high number of lesions without the need for selection of a lesion for investigation or for carrying out multiple biopsies. We do not advocate the use of OCT as a replacement for clinical examination and dermoscopy; its most appropriate role is as an adjunct to these methods, particularly in the case of clinically unclear lesions. OCT can be particularly valuable for difficult cases that are not otherwise amenable to assessment. However, there may also be limitations of OCT as some lesions may not display distinct features and thus appropriate diagnosis may be impossible.

Special caution seems to be necessary in rare cases of amelanotic melanoma, which can present as a pink patch, plaque or nodule and where misdiagnosis may be fatal. Currently, OCT criteria for amelanotic melanoma are largely unknown and further studies are required to determine whether differentiation between amelanotic melanoma and BCC is possible.

Earlier reports of OCT[13,38,39] used devices that operated in the time domain rather than the frequency domain,[40] limiting system sensitivity and resulting in reduced penetration and contrast in the images. In this study we used a Fourier domain OCT device and have demonstrated the improved diagnostic accuracy for different types of NMSC. Fourier domain systems can scan tissue more quickly, which is important in clinical use, and deeper tissue can be visualized with better contrast. The commercial system used in this study had additional optical techniques to enhance resolution and contrast compared with standard Fourier domain systems,[41,42] with an optical lateral resolution of at least 7·5 μm and axial resolution of at least 5 μm.

Another diagnostic technique, reflectance confocal microscopy (RCM), has shown high sensitivity and specificity for the diagnosis of BCC,[43] and recently a retrospective analysis has shown that RCM may also be applied for differentiation of BCC subtypes.[44] RCM has the great advantage of cellular resolution that also allows detection of rare lesions such as amelanotic melanoma.[45] However, RCM evaluation is limited to a depth of 250–350 μm, whereas the OCT system used in our study has a penetration depth of up to 2 mm.

As BCC is the most prevalent type of NMSC, improvements to the diagnostic process have the greatest potential in clinical practice. Current estimates for prevalence are difficult to establish as NMSC is not a reportable disease, but analysis of reimbursement data in the U.S.A. suggested there were 3 743 315 new cases in 2009, with the number increasing by an average of 4·2% per year from 1992 to 2006.[39] Given the 92% NPV demonstrated in this study, the 50% of patients typically biopsied as negative for BCC could be reduced to just 4%, a very significant reduction in surgery. With a corresponding increase in the use of noninvasive therapies, there would be a significant impact on costs and morbidity. Although mortality is very low for BCC, with its incidence increasing at 4% per year a 0·4% mortality rate is significant.

In conclusion, in addition to its high sensitivity of 95·7% for BCC, OCT significantly improved diagnostic specificity, in a challenging population of lesions with uncertain identity, when compared with clinical assessment and dermoscopy alone. Thus, OCT offers an improvement in the diagnosis of uncertain lesions with a suspicion for BCC. The very high NPV of 92% means that many lesions can be spared unnecessary excisional biopsies or surgery.

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