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Growth rate of clinically diagnosed superficial basal cell carcinoma and changes in dermoscopic features over time

Abstract

Background/Objectives: Basal cell carcinoma (BCC) is the most commonly occurring skin cancer. BCCs have been found to generally grow slowly. Data is limited on how the dermoscopic characteristics of BCCs evolve. We set out to determine the growth rate of superficial BCCs (sBCC) and assess the change in dermoscopic features over time.

Methods: A retrospective review was performed of clinically diagnosed sBCC. Images, demographic and dermoscopic data were collected by a melanographer. Mixed effects linear regression models were used to investigate sBCC growth and associations between size and dermoscopic/demographic variables. We tested differences in trends over time in dermoscopic features using non-parametric trend tests.

Results: 100 individual sBCC were evaluated in 70 patients (mean age 62; 59% male), 69% had Fitzpatrick skin phototype 1 or 2, and 81% had some degree of actinic damage. sBCC were present on the back in 58% and 22% of men and women, respectively. The median surface area was 41.9 mm^2 with a growth rate of 0.81mm^2/month. Males had larger sBCC than females. There was no association between sBCC size and Fitzpatrick skin phototype, history of skin cancer, or family history of melanoma. There is some evidence larger sBCC gain shiny white structures (p=0.053) over time.

Conclusions: sBCC grow at a rate unlikely to adversely affect patient outcomes associated with long wait times. Our data suggests that dermoscopy can aid in appropriate treatment selection for sBCC.

Keywords: basal cell carcinoma, superficial, sBCC, growth, dermoscopy, dermoscopic, skin cancer

Introduction

New Zealand has one of the highest rates of skin cancer in the world[1]. Basal cell carcinoma (BCC) represents the majority of these cancers with one study finding 73% of non-melanoma (keratinocytic) skin cancers in New Zealand were BCCs[2]. In New Zealand, there is no mandatory reporting of BCC to the National Cancer Registry but a histological examination study in 2008 found an annual BCC incidence rate of 1,177 per 100,000 population in Auckland, the largest city in New Zealand[1,2]. The actual rate of BCCs is likely to be higher given that superficial BCCs (sBCC) are often diagnosed clinically and treated without histological confirmation. A significant burden is placed on the health system to manage these BCCs, with a UK study finding the treatment of choice is surgical excision in 58% of cases[3,4]. Delays can arise in accessing appropriate treatment within a suitable timeframe. There have been few studies examining the growth rate of BCCs to observe if delays in treatment result in poor outcomes for patients. Several studies have investigated the growth rate in patients awaiting surgical excision of BCCs. It has generally been accepted that BCCs grow slowly with two prospective studies finding a median increase in major diameter of nodular BCC of 0.5mm over a mean time of 10 weeks[5,6]. However, one study found an increase in major diameter size of 10mm over 19 weeks whilst another found periocular BCCs increased their surface area by a mean rate of 11.2mm^2 every 30 days[7,8]. We were unable to find any reports of growth rates of BCCs over periods longer than 12 months and none specifically looking at the growth rate of sBCC.

Dermoscopy is a validated method to confirm the diagnosis of BCC[9-14]. The International Dermoscopy Society have established BCC dermoscopic diagnostic criteria on Dermoscopedia[9]. Many studies have described the correlation between BCC dermoscopic features and histological findings[10-14]. We were unable to identify any studies looking at the change in dermoscopic features in a population of BCCs over time.

The aim of this study was to determine the growth rate of sBCC and the change in dermoscopic features over time through a retrospective review of clinical and dermoscopic. We hypothesise that sBCC in non-cosmetically sensitive areas exhibit a rate of growth unlikely to impact on patient outcome due to long wait times and acquire dermoscopic features in keeping with growth and invasion. We also wished to investigate whether demographic factors affect sBCC growth rates.

Materials and Methods

Dermoscopic imaging

The study was a retrospective review of clinical and dermoscopic images taken by an experienced melanographer in patients attending a skin mapping service between August 2005 and August 2018. Consecutive patients were included as potential participants where a clinical diagnosis of sBCC was made by an experienced teledermatologist using the pattern recognition method for flat non-pigmented lesions[15]. The diagnostic report is sent to the patient to action with their usual treating physician/general practitioner. To be included in the study, the sBCC must have been present on at least two separate occasions with no evidence of treatment between visits. Exclusion criteria were clinically non-superficial BCCs when first imaged, poor-quality images, and large tumours in which the lesion was not fully contained within a single dermoscopic view. High-quality images of each lesion containing macroscopic, polarised, and non-polarised dermoscopic views were included. Additional data included lesion location, demographics (age at each visit and sex) and skin cancer risk factor data (history of non-melanoma/melanoma skin cancer, family history of skin cancer, Fitzpatrick skin phototype, actinic damage (based on dermatologist designed rating scale: 0 – none, 1 – pigmentary change, 2 - <50% sun exposed sites affected with actinic keratoses, 3 - >50% sun exposed sites affected with actinic keratoses), as assessed by the experienced melanographer, history of immunosuppression, and occupational sun exposure) for each patient. The body location for each lesion was recorded and the long axis (mm), short axis (mm), and surface area (mm^2) were measured using proprietary software (MoleMapView). Measurements were performed by the same researcher (AS) three times and a mean value was recorded. Each imaged BCC was assessed for dermoscopic features of BCCs as defined on

Dermoscopedia by the International Dermoscopy Society (Appendix table 1) using descriptive terminology for dermoscopic features of BCCs[9].

Statistical analyses

Mixed effects linear regression models were used to account for repeated observations per person. Three continuous dependent variables were investigated: (1) long axis measurements (mm^2); (2) short axis measurements (mm^2); (3) surface area measurements (mm^2). The relationships between these three dependent variables were investigated with time of follow-up in months and (a) various dermoscopic variables (Appendix 1) and; (b) various demographic and skin cancer risk factor variables (Appendix table 1). Complete case analysis was performed.

Associations of size with dermoscopic variables and time

The relationships between the three dependent variables and the dermoscopic variables were first examined separately for each dermoscopic variable without further adjustment. Secondly, the relationship of each dependent variable with each independent variable was examined adjusting only for the time of follow-up in months. Thirdly, for each dependent variable, the independent variables with an association with $p \leq 0.1$ were entered into a final adjusted model. The dermoscopic variables considered were shiny white structures, lines radial connected to a common base, lines radial converging, clods brown/blue concentric, clods blue large clustered, clods blue small, short fine superficial telangiectasia, microerosions, and ulceration.

Associations of size with demographics

Univariable relationships between the demographic and cancer risk factor variables and the three dependent variables were assessed. The demographic and cancer risk factor variables with $p \leq 0.1$ were then entered into an adjusted model for each of the three dependent variables to investigate whether demographic variables affect carcinoma growth. The demographic variables considered were gender, skin type, family history of melanoma, personal history of non-melanoma skin cancer, personal history of melanoma, actinic damage, presence of sunburn, sunbed use, history of immunosuppression, and occupational exposure.

Dermoscopic features over time

To investigate how dermoscopic features change over time, we tabulated the features for sBCC at baseline, 1 year, and 2 years, classifying the sBCC by size (< or ≥41.9mm^2 surface area). We tested the differences in trends in dermoscopic features over time using non-parametric trend tests.

Ethics approval

This study was deemed, by the Health and Disability Ethics Committees as being out of scope and therefore not requiring their review as no patient-identifiable data was collected.

Results

Characteristics

In total, 100 individual sBCC were assessed in 70 patients with a mean age of 62 years (interquartile range 52–70). The median number of treatment visits for each BCC was 2 (range 2–7). Males represented 59% of the population, 69% of participants had Fitzpatrick skin phototype 1 or 2, and 81% had at least some degree of actinic damage (severe in 14%). A personal history of melanoma was reported in 17% and a family history in 25%, with 56% having a history of non-melanoma skin cancer (Table 1). Table 2 shows the body location

for the studied sBCC in males and females. Most of the BCCs in males were located on their backs (58%), whilst this was the case for only 22% of females. The majority (54%) of the observed BCCs in females were on their limbs, while only 17% of BCCs in males were located on the limbs. Histological examination was available for 16 of the 100 lesions (16%) and sBCC was confirmed in 14 out of the 16 lesions (88%). One lesion was histologically consistent with morphoeic BCC, whilst the other was micronodular invasive BCC.

The median long axis measurement of the sBCC on presentation (baseline) was 8.7mm with a median short axis measurement of 6.2mm. The median surface area was 41.9mm^2. Table 1 also shows the prevalence of dermoscopy features displayed within the BCCs on initial presentation. Lines white perpendicular was the most common feature recorded (46%), with branched blood vessels present in 32% of participants.

Associations of size with dermoscopic variables and time

Table 3 shows multivariable associations between sBCC size and dermoscopic variables for longitudinal axis, short axis, and surface area. Appendix tables 2a-c gives further results of these analyses. In univariable analyses, we found a longitudinal axis growth coefficient of 0.07 mm/month (95% confidence interval [95% CI]: 0.06, 0.09), or 0.84 mm/year, a short axis growth rate of 0.06 mm/month (95% CI: 0.05, 0.07), 0.72 mm/year, and a surface area growth rate of 0.96 mm^2/month (95% CI: 0.078, 1.14), or 11.5 mm^2/year. In multivariable analyses we found growth rates of 0.07 mm/month (95% CI: 0.05, 0.08), or 0.84 mm/year, for the longitudinal axis, 0.04 mm/month (95% CI: 0.03, 0.05), or 0.48 mm/year, for the short axis, and 0.81 mm^2/month (95% CI: 0.64, 0.99), or 9.7mm^2/year, for the surface area.

For the multivariable analysis with long axis measurement as the outcome, we found that shiny white structures and clods brown/blue concentric were positively associated with long axis size, whilst presence of short fine superficial telangiectasia was negatively associated with long axis size. Presence of shiny white structures, clods brown/blue concentric, clods blue clustered, clods blue small, microerosion were all positively associated with short axis measurement size. The multivariable analysis showed positive associations between surface area measurement and presence of shiny white structures, clods brown/blue concentric, clods blue small, and ulceration.

Associations of size with demographics

Males had larger BCCs than females in the multivariable analyses of surface area and short axis measurements, with a weaker association in the analysis of long axis measurements (Table 4 and appendix tables 3a-c). There was no association between size of sBCC and Fitzpatrick skin phototype, history of skin cancer (melanoma and non-melanoma), or family history of melanoma for any of the measurements. There was some evidence that sBCC in patients with severe actinic damage had a larger short axis measurement. The growth rate coefficients for each of the measurements were unchanged when additionally adjusting for demographic variables.

Dermoscopic features over time

Table 5 demonstrates that over time there is some evidence that larger sBCC (≥41.9cm^2) gain shiny white structures (p=0.053), whilst there is no evidence for increase in dermoscopic features over time for smaller sBCC (<41.9cm^2).

Discussion

Our study into the growth of clinically diagnosed sBCC supports previous research showing that BCCs are slow growing[5,6,16]. The majority of sBCC occur in non-cosmetically sensitive sites (trunk and limbs) and therefore a change in surface area of less than 1mm^2 per month should not have significant consequences to patients experiencing delays in diagnosis and appropriate management[17,18].

We found that surface area measurements of sBCC in males tended to be larger than in females. This might be explained by differences in the location of the sBCC. For males, most of the recorded sBCC were on their backs, whilst in females most of the sBCC were on their limbs. The causal mechanism underpinning this difference in sBCC distribution is unknown. It is unclear if differences in the growth rates of sBCC at different anatomical locations may account for males having larger sBCC at presentation than females. Similar sex differences have been found when studying the distribution of melanoma, with men more likely to have a primary melanoma on the back and women more likely to have one on the lower limbs[19,20]. It has been hypothesised that this difference in location is due to the style of clothing with a bare torso being more common in men while women are more likely to have bare limbs[19].

We found the most common features to be 'shiny white structures', 'short fine telangiectasia' (arborising or serpentine vessels), and microerosions. Larger sBCC size (>41.9cm^2) was associated with having 'shiny white structures', 'clods brown/blue concentric', and 'clods blue small'. Scalvenzi et al. described the dermoscopic features and their prevalence in sBCC in 2008 and found that shiny white areas, short fine telangiectasia, and erosions were associated with sBCC[21].

The correlation between dermoscopic features and underlying histology has been studied previously[11,12,14]. 'Clods blue clustered' and 'clods blue small' are linked to melanin-containing cells located within the reticular dermis, while 'lines radial connected to a common base at edge' (maple leaf-like area), 'lines radial converging' (spoke-wheel structure), and 'clods brown/blue concentric' are linked with melanin-containing cells within the papillary dermis[1]. sBCC, by definition, are confined to, or are contiguous with, the epidermis and should not invade the reticular dermis[22]. Our study shows that superficial BCCs gain signs of deeper dermal involvement as they enlarge with minimal presence of these features in the initial lesions.

Dermoscopic examination of sBCC can inform treatment decisions[23]. Options for sBCC are wider than for the other histological subtypes and include topical and surgical treatment. Topical treatment for sBCC has previously been reported to have a high failure rate, possibly due to clinical under-diagnosis of the depth of the tumour[24]. We therefore suggest that surgical excision be considered if dermoscopic signs of dermal involvement are present. If topical treatment is used, close follow-up is essential to ensure resolution, with consideration of biopsy or excision of the lesion should it persist or acquire features suggesting dermal invasion.

Several patients were noted to have lesions persisting for a few years without evidence of treatment — the longest in the cohort was observed for 7 years (Figure 1). The reasons for delay in treatment were not reported in these cases and are unknown. Van Egmond et al. found that patients have a preference for dialogue with their diagnosing physician[25]. Clear explanation of the diagnosis and treatment options is essential for patients who want to participate in a shared decision-making model. The skin mapping service in this study uses store-and-forward teledermatology for diagnosis and treatment recommendations. There is no discourse between the diagnosing dermatologist and the patient. Lesion location may contribute to delay in treatment. Most lesions occurred on the back, a difficult area to self-monitor.

Strengths and limitations

To our knowledge, this study is the first to track the growth of sBCC using multiple types of measurement. Limitations to our study include demographic data, which was largely self-reported and is therefore subject to recall bias; we were unable to confirm the history provided by the patient. Histological confirmation of sBCC was only available for 16% of the lesions but did confirm the initial clinical diagnosis of sBCC in 88% of these. Whilst this number is low, it does reflect that the diagnosis of sBCC is largely clinical and treatment is commonly non-surgical. The high histological confirmation of the clinical diagnosis supports the algorithm used in this study. Dermoscopy has previously been shown to have a sensitivity and specificity of 81.9% and 81.8% respectively[26]. It is possible that lesions which clinically appeared to be sBCC were another histological

subtype confounding our results, as the growth and dermoscopic features of each histological subtype of BCC are likely to be unique. Lesions that had been treated were not included in the study.

Conclusions

Our study supports the belief that sBCC is slow growing at a rate of less than 1mm^2 per month. Therefore, delays in treatment of sBCC, due to long wait times, are unlikely to affect patient outcome in non-cosmetically sensitive sites. This is reassuring news for patients. We have found that dermoscopic signs of dermal involvement develop as larger sBCC enlarge. This knowledge should aid in planning the appropriate treatment modality.

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Figure 1: Annual dermoscopic images of single lesion located on the back in one patient followed over seven years showing persistence in lesion despite exhibiting clinical (not shown) and dermoscopic features of sBCC (short fine telangiectasia, clods blue clustered, shiny white structures - shown).

Table 1: Baseline patient characteristics and measurements for each BCC

	Median (Interquartile range)
Long axis measurement at baseline (mm)	8.7 (6.5, 11.1)
Short axis measurement at baseline (mm)	6.2 (4.7, 8.4)
Surface area measurement at baseline (mm^2)	41.9 (22.7, 73.6)
Age (years) at baseline photo	62.0 (52.0, 70.5)
	N = 100 (%)
Fitzpatrick skin phototype:	
1	8 (8%)
2	61 (61%)
3	30 (30%)
4	1 (1%)
Male	59 (59%)
Personal history of melanoma	17 (17%)
Personal history of non-melanoma skin cancer	56 (56%)
Family history of melanoma	25 (25%)
Degree of actinic damage	
Non-significant	19 (19%)
Some (pigmentary change)	48 (48%)
Moderate	19 (19%)
Severe	14 (14%)
Dermoscopic variables	**N = 100 (%)**
Shiny white structures	50 (50%)
Lines radial connected to a common base	15 (15%)
Lines radial converging	7 (7%)
Clods brown/blue concentric	14 (14%)
Clods blue clustered	9 (9%)
Clods blue small	17 (17%)
Short fine superficial telangiectasia	43 (43%)
Micro erosion	26 (26%)
Ulceration	5 (5%)

Table 2: Location of BCC by gender

Location	Male [N = 59] (%)	Female [N = 41] (%)
Arm	2 (3%)	9 (22%)
Leg	8 (14%)	13 (32%)
Chest	8 (14%)	3 (7%)
Back	34 (58%)	9 (22%)
Head	5 (8%)	4 (10%)
Neck	2 (3%)	3 (7%)

Table 3: Univariable and multivariable associations of dermoscopic variables with the long axis, short axis, and surface area measurements*. Full tables of adjusted coefficients are given in the appendix.

Variable	Univariable coefficient (95% CI)	P-value	Multivariable coefficient (95% CI)	P-value
Endpoint: Long axis measurement (mm)				
Time (in months)	0.07 [0.06, 0.09]	<0.001	0.07 [0.05, 0.08]	<0.001
Shiny white structures	0.65 [0.11, 1.19]	0.018	0.55 [0.04, 1.06]	0.036
Clods brown/blue concentric	0.98 [0.26, 1.69]	0.008	0.97 [0.27, 1.66]	0.007
Short fine superficial telangiectasia	-0.96 [-1.50, -0.42]	0.001	-0.90 [-1.44, -0.35]	0.001
Constant term			8.92 [8.22, 9.62]	
Endpoint: Short axis measurement (mm)				
Time (in months)	0.06 [0.05, 0.07]	<0.001	0.04 [0.03, 0.05]	<0.001
Shiny white structures	0.59 [0.17, 1.01]	0.006	0.74 [0.34, 1.14]	<0.001
Clods brown/blue concentric	0.77 [0.21, 1.34]	0.007	0.85 [0.31, 1.40]	0.002
Clods blue clustered	0.49 [-0.09, 1.08]	0.098	0.56 [-0.01, 1.13]	0.056
Clods blue small	0.47 [-0.01, 0.94]	0.053	0.48 [0.02, 0.94]	0.042
Microerosion	0.48 [0.11, 0.85]	0.011	0.55 [0.19, 0.90]	0.002
Constant term			5.88 [5.31, 6.46]	
Endpoint: Surface area measurement (mm^2)				
Time (in months)	0.96 [0.78, 1.14]	<0.001	0.81 [0.64, 0.99]	<0.001
Shiny white structures	7.11 [1.74, 12.49]	0.009	7.26 [2.10, 12.44]	0.006
Clods brown/blue concentric	8.35 [1.18, 15.52]	0.022	8.07 [1.03, 15.11]	0.025
Clods blue small	6.14 [0.23, 12.05]	0.042	6.76 [0.85, 12.66]	0.025
Ulceration	11.15 [0.52, 21.77]	0.040	10.39 [-0.06, 20.85]	0.051
Constant term			43.82 [36.60, 51.04]	

CI: Confidence interval

*Only including the variables with $p<0.1$ in the univariable analysis that were entered into the multivariable analysis.

Table 4: Univariable and multivariable associations of demographic variables with the long axis, short axis, and surface area measurements*. Full tables of adjusted coefficients are given in the appendix.

Variable	**Univariable coefficient (95% CI)**	**Multivariable coefficient (95% CI)**
Endpoint: Long axis measurement (mm)		
Time (in months)	0.07 (0.06, 0.09)	0.07 (0.06, 0.09)
Male	1.22 (-0.11, 2.55)	1.27 (-0.04, 2.59)
Endpoint: Short axis measurement (mm)		
Time (in months)	0.06 (0.05, 0.07)	0.06 (0.05, 0.07)
Male	1.34 (0.13, 2.55)	1.52 (0.33, 2.71)
Actinic damage		
No significant	Comparator	Comparator
Some	0.71 (-0.80, 2.22)	1.00 (-0.48, 2.48)
Moderate	0.85 (-0.99, 2.69)	1.00 (-0.79, 2.79)
Severe	1.80 (-0.16, 3.75)	1.97 (0.07, 3.87)
Endpoint: Surface area measurement (mm^2)		
Time (in months)	0.96 (0.78, 1.14)	0.96 (0.78, 1.13)
Male	18.36 (3.17, 33.55)	18.72 (3.43, 34.02)

CI: Confidence interval

*Only including the variables with $p<0.1$ in the univariable analysis that were entered into the multivariable analysis.

Table 5: Change in dermoscopic features over time for small (surface area < 41.9 mm^2) compared to large (surface area ≥ 41.9 mm^2) superficial basal cell carcinomas

		Baseline (N = 100)	**Year 1 (N = 100)**	**Year 2 (N = 72)**	
Dermoscopic variables		**Small = 49, Large = 51**	**Small = 49, Large = 51**	**Small = 35, Large = 37**	**P-value***
Shiny white structures	Small	20 (41%)	21 (43%)	14 (40%)	0.963
	Large	30 (59%)	35 (69%)	29 (78%)	0.053
Lines radial connected to a common base	Small	8 (16%)	7 (14%)	5 (14%)	0.784
	Large	7 (14%)	7 (14%)	5 (14%)	0.979
Lines radial converging	Small	4 (8%)	5 (10%)	6 (17%)	0.215
	Large	3 (6%)	5 (10%)	6 (16%)	0.117
Clods brown/blue concentric	Small	6 (12%)	6 (12%)	9 (26%)	0.117
	Large	8 (16%)	8 (16%)	7 (19%)	0.704
Clods blue clustered	Small	4 (8%)	5 (10%)	5 (14%)	0.377
	Large	5 (10%)	5 (10%)	3 (8%)	0.800
Clods blue small	Small	10 (20%)	14 (29%)	12 (34%)	0.153
	Large	7 (14%)	6 (12%)	7 (19%)	0.539
Short fine superficial telangiectasia	Small	22 (45%)	23 (47%)	14 (40%)	0.693
	Large	21 (41%)	26 (51%)	19 (51%)	0.319
Micro erosion	Small	8 (16%)	12 (24%)	8 (23%)	0.428
	Large	18 (35%)	17 (33%)	16 (43%)	0.486
Ulceration	Small	0 (0%)	0 (0%)	0 (0%)	NA
	Large	5 (10%)	6 (12%)	3 (8%)	0.834

*Non-parametric trend test for differences across years in the percentage of patients (either with small or large BCCs at baseline) that have the dermoscopic characteristics

Appendix

Appendix Table 1: Comparison of descriptive and metaphorical terms for BCC dermoscopy features

Descriptive Terminology	**Metaphorical Terminology**
Shiny white structures	Shiny white streaks/crystalline
Lines radial connected to a common base	Leaf-like areas
Lines radial converging	Spoke-wheel area/structure
Clods brown/blue concentric	Concentric globules
Clods blue large clustered	Blue-grey ovoid nests
Clods blue small	Blue globules
Short fine superficial telangiectasia	Arborising vessels
Microerosions	-
Ulceration	-

Appendix Table 2a: Univariable and multivariable coefficients for long axis measurement with dermoscopic variables and time.

	Univariable coefficient (95% CI)	**p-value**	**Univariable coefficient adjusted for time (in months) (95% CI)**	**p-value**	**Multivariable coefficient (95% CI)**	**p-value**
Time (in months)	0.072 (0.058, 0.086)	<0.001	NA	NA	0.070 (0.055, 0.085)	<0.001
Dermoscopic variables:						
Shiny white structures	1.34 (0.78, 1.91)	<0.001	0.65 (0.11, 1.19)	0.018	0.55 (0.37, 1.06)	0.036
Lines radial connected to common base at edge	0.36 (-0.42, 1.13)	0.365	0.24 (-0.46, 0.93)	0.506		
Lines radial converging	0.91 (0.15, 1.67)	0.019	0.43 (-0.26, 1.12)	0.222		
Clods brown/blue concentric	1.08 (0.29, 1.88)	0.008	0.98 (0.26, 1.69)	0.008	0.97 (0.27, 1.66)	0.007
Clods blue clustered	0.51 (-0.29, 1.32)	0.212	0.37 (-0.37, 1.12)	0.326		
Clods blue small	0.34 (-0.33, 1.01)	0.321	0.22 (-0.38, 0.83)	0.468		
Short finest	-0.76 (-1.35, -0.17)	0.011	-0.96 (-1.50, -0.42)	0.001	-0.90 (-1.44, -0.35)	0.001
Micro-erosion	0.74 (0.22, 1.26)	0.005	0.39 (-0.08, 0.85)	0.108		
Ulceration	0.87 (-0.34, 2.08)	0.160	0.43 (-0.67, 1.52)	0.447		
Constant					8.92 (8.22, 9.62)	

CI: Confidence Interval

Appendix table 2b: Univariable and multivariable coefficients for short axis measurement with dermoscopic variables and time.

	Univariable coefficient (95% CI)	**p-value**	**Univariable coefficient additionally adjusted for time (95% CI)**	**p-value**	**Multivariable coefficient (95% CI)**	**p-value**
Time (in months)	0.061 (0.050, 0.071)	<0.001	NA	NA	0.042 (0.033, 0.052)	<0.001
Dermoscopic variables:						
Shiny white structures	1.21 (0.75, 1.67)	<0.001	0.59 (0.17, 1.01)	0.006	0.74 (0.34, 1.14)	<0.001
Lines radial connected to common base at edge	0.32 (-0.31, 0.95)	0.327	0.33 (-0.22, 0.87)	0.237		
Lines radial converging	0.75 (0.13, 1.36)	0.018	0.41 (-0.14, 0.95)	0.142		
Clods brown/blue concentric	0.72 (0.08, 1.37)	0.028	0.77 (0.21, 1.34)	0.007	0.85 (0.31, 1.40)	0.002
Clods blue clustered	0.55 (-0.10, 1.20)	0.095	0.49 (-0.09, 1.08)	0.098	0.56 (-0.01, 1.13)	0.056
Clods blue small	0.63 (0.10, 1.16)	0.020	0.47 (-0.01, 0.94)	0.053	0.48 (0.02, 0.94)	0.042
Short finest	0.12 (-0.38, 0.62)	0.641	-0.09 (-0.54, 0.36)	0.686		
Micro-erosion	0.82 (0.40, 1.23)	<0.001	0.48 (0.11, 0.85)	0.011	0.55 (0.19, 0.90)	0.002
Ulceration	0.30 (-0.69, 1.28)	0.553	0.07 (-0.80, 0.94)	0.873		
Constant					5.88 (5.31, 6.46)	

CI: Confidence Interval

Appendix table 2c: Univariable and multivariable coefficients for surface area measurement with dermoscopic variables and time.

	Univariable coefficient (95% CI)	**p-value**	**Univariable coefficient adjusted for time (in months) (95% CI)**	**p-value**	**Multivariable coefficient (95% CI)**	**p-value**
Time (in months)	0.961 (0.785, 1.137)	<0.001	NA	NA	0.815 (0.636, 0.993)	<0.001
Dermoscopic variables:						
Shiny white structures	13.83 (8.02, 19.65)	<0.001	7.11 (1.74, 12.49)	0.009	7.27 (2.10, 12.44)	0.006
Lines radial connected to common base at edge	1.56 (-6.15, 9.28)	0.691	1.22 (-5.67, 8.12)	0.728		
Lines radial converging	8.33 (0.69, 15.98)	0.033	4.28 (-2.60, 11.15)	0.223		
Clods brown/blue concentric	8.77 (0.94, 16.61)	0.028	8.35 (1,18, 15.52)	0.022	8.07 (1.03, 15.11)	0.025
Clods blue clustered	3.62 (-4.14, 11.37)	0.361	1.89 (-5.30, 9.08)	0.606		
Clods blue small	8.61 (2.12, 15.09)	0.009	6.14 (0.23, 12.05)	0.042	6.76 (0.85, 12.66)	0.025
Short finest	-2.60 (-8.61, 3.40)	0.395	-4.52 (-10.04, 0.99)	0.108		
Micro-erosion	66.41 (1.14, 11.68)	0.017	3.22 (-1.45, 7.89)	0.177		
Ulceration	15.32 (3.71, 26.92)	0.010	11.15 (0.52, 21.77)	0.040	10.39 (-0.06, 20.84)	0.051
Constant					43.81 (36.60, 51.04)	

CI: Confidence Interval

Appendix table 3a: Univariable and multivariable coefficients for long axis measurement with demographic variables and time.

	Univariable (95% CI)	p-value	Multivariable (95% CI)	p-value
Time (months)	0.072 (0.058, 0.086)	<0.001	0.072 (0.058, 0.086)	<0.001
Age at first photo	0.01 (-0.04, 0.07)	0.674		
Skin type				
1	Comparator	NA		
2	0.95 (-1.28, 3.18)	0.404		
3	-0.21 (-2.57, 2.15)	0.861		
4	2.50 (-3.95, 8.94)	0.448		
Male	1.22 (-0.11, 2.55)	0.072	1.27 (-0.04, 2.59)	0.057
Hx melanoma	-0.57 (-2.21, 1.08)	0.482		
Hx NMSC	-0.41 (-1.65, 0.83)	0.514		
FHx melanoma	0.47 (-0.95, 1.91)	0.513		
Actinic damage				
No significant	Comparator			
Some	0.14 (-1.52, 1.781)	0.864		
Moderate	0.79 (-1.19, 2.77)	0.435		
Severe	0.63 (-1.51, 2.77)	0.564		
History of sunburn	1.33 (-0.27, 2.92)	0.102		
Sunbed use	1.98 (-4.25, 8.20)	0.534		
Immunosuppression	-2.13 (-8.15, 3.88)	0.487		
Occupational exposure	0.82 (-1.36, 3.00)	0.461		
Constant			8.19 (7.16, 9.22)	

Hx: History of; FHX: Family history of; NMSC: Non-melanoma skin cancer; CI: Confidence interval

Appendix table 3b: Univariable and multivariable coefficients for short axis measurement with demographic variables and time.

	Univariable (95% CI)	p-value	Multivariable (95% CI)	p-value
Time (months)	0.061 (0.050, 0.071)	<0.001	0.060 (0.050, 0.071)	<0.001
Age at first photo	0.02 (-0.03, 0.07)	0.383		
Skin type				
1	Comparator			
2	0.53 (-1.63, 2.68)	0.633		
3	-0.37 (-2.66, 1.92)	0.753		
4	-0.35 (-6.06, 5.37)	0.906		
Male	1.34 (0.13, 2.55)	0.030	1.52 (0.33, 2.71)	0.012
Hx melanoma	-0.78 (-2.32, 0.77)	0.323		
Hx NMSC	-0.75 (-1.96, 0.47)	0.227		
FHx melanoma	0.37 (-0.98, 1.71)	0.594		
Actinic damage				
No significant	Comparator		Comparator	
Some	0.71 (-0.80, 2.22)	0.433	1.00 (-0.48, 2.48)	0.187
Moderate	0.85 (-0.99, 2.69)	0.367	1.00 (-0.79, 2.79)	0.274
Severe	1.80 (-0.16, 3.75)	0.072	1.97 (0.07, 3.87)	0.042
History of sunburn	0.86 (-0.61, 2.32)	0.253		
Sunbed use	-0.55 (-6.00, 4.89)	0.842		
Immunosuppression	-1.63 (-6.91, 3.65)	0.546		
Occupational exposure	0.17 (-1.86, 2.21)	0.867		
Constant			4.83 (3.38, 6.29)	

Hx: History of; FHX: Family history of; NMSC: Non-melanoma skin cancer; CI: Confidence interval

Appendix table 3c: Univariable and multivariable coefficients for surface area measurement with demographic variables and time.

	Univariable (95% CI)	p-value	Multivariable (95% CI)	p-value
Time (months)	0.960 (0.784, 1.135)	<0.001	0.959 (0.784, 1.134)	<0.001
Age at first photo	0.30 (-0.34, 0.94)	0.354		
Skin type				
1	Comparator			
2	7.05 (-19.98, 34.09)	0.609		
3	-3.03 (-31.75, 25.69)	0.836		
4	5.52 (-66.46, 77.49)	0.881		
Male	18.36 (3.17, 33.55)	0.018	18.72 (3.43, 34.02)	0.016
Hx melanoma	-10.25 (-29.60, 9.10)	0.299		
Hx NMSC	-6.50 (-21.78, 8.78)	0.404		
FHx melanoma	4.59 (-12.26, 21.44)	0.593		
Actinic damage				
No significant	Comparator			
Some	2.92 (-16.34, 22.18)	0.766		
Moderate	6.22 (-17.13, 29.57)	0.602		
Severe	14.24 (-10.59, 39.06)	0.261		
History of sunburn	11.67 (-6.75, 30.09)	0.214		
Sunbed use	2.15 (-66.40, 70.70)	0.951		
Immunosuppression	-15.82 (-82.67, 51.03)	0.643		
Occupational exposure	1.98 (-23.58, 27.54)	0.879		
Constant			39.51 (27.56, 51.47)	

Hx: History of; FHX: Family history of; NMSC: Non-melanoma skin cancer; CI: Confidence interval