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1 **Imaging of periocular basal cell carcinoma (BCC) using *en-face* optical coherence**
2 **tomography (OCT)-A Pilot Study**

3

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36

37 **ABSTRACT**

38

39 **Aim**

40 To use *en-face* optical coherence tomography (OCT) imaging to identify features of
41 tumour tissue and their correlation with histopathology, and to assess the effect of
42 different wavelengths and resolutions of OCT in identifying tumour boundaries and
43 features.

44 **Methods**

45 Excision specimens of consecutive biopsy-proven periocular BCCs (n=8) were assessed
46 by OCT performing *in vitro* cross section scans and *en-face* scans of the tissues. Images
47 were collected from three different machines; systems 1 & 2 had a wavelength of 1300
48 nm and system 3 had a wavelength of 840 nm. System 2 used high numerical aperture
49 (NA) interface optics which determines higher magnification and hence allows higher
50 transversal resolution. All 8 specimens subsequently underwent routine histopathology
51 examination.

52 **Results**

53 Three common features of tumour tissue were observed in all three systems: (i) lobular
54 pattern of abnormal architecture, (ii) dilated blood vessels and (iii) high reflective
55 margins. We compared the three systems based on their ability to pick up the three
56 above mentioned tumour features. In this respect, system 2 had the highest capability in
57 picking up feature (i), followed by systems 1 and 3. In terms of feature (ii), similar
58 results were obtained with all three systems. System 3 was unable to pick up feature
59 (iii), whereas Systems 1 and 2 performed equally.

60

61 **Conclusion**

62 *En-face* OCT imaging has the potential to identify tumour tissue from healthy tissue. It
63 also showed correlation with corresponding histopathology findings. Non contact OCT
64 imaging of the skin is a non invasive and convenient method and can be useful for
65 demarcating BCCs on the face and eyelids. Future larger studies on *in vivo* BCCs using
66 *en face* ultra high resolution OCT should provide information on sub typing of BCCs.

67

68 **INTRODUCTION**

69 Basal cell carcinoma (BCC) is the most frequently occurring periocular malignancy,
70 with a rapidly increasing incidence worldwide, both because of increased sun exposure
71 and longevity.¹ Surgical excision with predetermined margins², or Mohs' surgery where
72 available^{3,4,5}, is recommended to ensure complete tumour removal.

73

74 Several non invasive diagnostic methods have been reported so far but none have yet
75 proved to be practical. High frequency ultrasound, terahertz imaging and magnetic
76 resonance all offer limited resolution.^{6,7,8} Reflectance confocal microscopy produces
77 high quality images but it has the disadvantage of requiring contact with the tissue, and
78 having a limited field and depth penetration. Ultrasound provides better penetration, but
79 has a lower resolution when compared to confocal microscopy.⁹

80

81 Optical coherence tomography (OCT) is a novel imaging technology¹⁰ used to
82 determine the structure of translucent objects. It combines a high axial resolution with
83 good tissue penetration. Whilst well established for retinal imaging¹¹, the equipment

84 currently used in ophthalmology clinics does not provide reliable skin images. OCT has
85 been successfully used for high resolution imaging of structures in other parts of the
86 body^{12,13} and has been successfully employed to identify tumour features and abnormal
87 skin architecture.¹⁴ In this paper we assess the use of *en-face* OCT, a time domain
88 variant of the OCT technology to identify and delineate periocular BCCs.

89

90 **METHOD**

91 **Clinical Study**

92 A pilot study to assess the capability of OCT to delineate tumour from normal tissue
93 was performed. Ethical approval for the study was obtained from both the Ethics
94 Committee of the Faculty of Science Technology and Medical Studies, University of
95 Kent and the West Kent Ethics Committee. The research described adhered to the
96 tenets of the Declaration of Helsinki.

97

98 In this study, excision biopsies were performed on periocular BCCs by members of the
99 Ophthalmology Department at Maidstone and Tunbridge Wells NHS Trust. Patients
100 attending the Ophthalmology department at Maidstone Hospital were recruited to the
101 study after informed consent was obtained. All 8 patients recruited had a biopsy-proven
102 BCC within the periorbital region. After routine surgical excision using predetermined
103 tumour margins the tissue was marked with sutures at superior, medial and lateral
104 margins using 5/0 silk (Ethicon).

105

106 Within 3 hours of excision, the samples were transported in formaldehyde to the
107 Applied Optics Group Lab within the University of Kent for OCT imaging. The

108 technology required for OCT imaging of skin is at a much earlier stage of development
109 than that for retinal imaging. All samples were scanned by three different OCT
110 machines. These are experimental prototypes, thereby allowing *in vitro* examination
111 only. The origin of the samples and patient details were single masked from the group
112 performing the OCT scans.

113

114 For scanning, the samples were fixed onto pieces of polystyrene board to align the
115 longest ends of the samples along the horizontal direction. Images were obtained *in*
116 *vitro* using each of the three OCT systems. Multiple *en-face* scans were obtained at
117 steps of 25 μm in depth and horizontal cross section scans were obtained by moving the
118 sample in the *en-face* plane (mostly along the vertical direction). On each of the three
119 OCT machines, the scanning process took between 45 to 60 minutes, including the set
120 up time. All the tissue samples were kept hydrated during the scanning process using
121 drops of formaldehyde. This part of the protocol was agreed with the histopathologist
122 prior to starting the study, ensuring preservation of the tissue for accurate
123 histopathological analysis. On completion of the OCT scans, the tissue samples were
124 stored in formaldehyde and processed for routine histological analysis, undertaken by a
125 single histopathologist. After fixing the specimen, it was transversely sectioned “bread
126 sliced” into several pieces which were processed and embedded in paraffin wax. 2-3
127 micrometer slices were obtained and stained with haematoxylin and eosin. The
128 histopathological sections were therefore orientated in the axis of the OCT cross section
129 scan. The pathologist was masked from the findings of the OCT scans, until routine
130 histology reporting was done. Once histopathological analysis was completed on all 8
131 specimens, the OCT team and histopathologist examined all histopathology sections, to
132 identify a section that correlated with the OCT image for each sample. Where it was not

133 possible to exactly match the histopathological section to the OCT image, a section was
134 chosen that displayed corresponding morphological features.

135

136 **OCT instrumentation**

137 OCT is based on a Michelson interferometer¹⁰, where the light emitted by a source is
138 split into an object beam and a reference beam using a beam splitter. The reference
139 beam is reflected back from a reference mirror. Both beams are combined and the
140 interference pattern read by an interferometer. Depth scanning is achieved by moving
141 the reference mirror, lateral scanning is performed by moving the scan beam laterally,
142 using a dual scanning head (equipped with two galvanometer scanners) and a lens. *En-*
143 *face* OCT as used here generates lateral reflectivity profiles, called T-scans, obtained by
144 scanning the beam horizontally over the target.¹⁵ Multiple T-scans acquired at 500 Hz,
145 are recorded for sequential values of the vertical coordinate to form an *en-face* OCT
146 image (a 2D map, termed as a C-scan, or constant depth image). The vertical scanning is
147 obtained by driving the frame galvo-scanner in the dual scanning head to move the
148 beam vertically at 2 Hz. By changing the position of the reference mirror, C-scan
149 images at different depths can be obtained, and for sufficient dense sampling of the
150 tissue, 3D volumes can be reconstructed. *En-face* OCT has the advantage that by simple
151 re-routing of the signals driving the two scanners, the system can be switched from C-
152 scan into B-scan regime. A B-scan is obtained by stopping the frame scanner and by
153 moving the reference mirror to explore the object in depth. In this way, B-scans are built
154 as 2D-assemblies of T-scans repeated at sequential depths. B-scans represent cross
155 section slices in the tissue, they are orthogonal on C-scans and represent the traditional
156 OCT view. However, the *en-face* OCT method provides the added advantage of
157 producing images with the orientation of microscopy images (C scans). Features with

158 *en-face* orientation allow easier identification of tumour margins when compared to B-
 159 scan OCT images. All three systems used here can be operated in either C-scan or B-
 160 scan regime and their details are specified in Table 1.

	Central wavelength	Optical bandwidth	Superluminescent diode (SLD) power	Lateral resolution	Axial resolution
System 1	1300 nm	60 nm	<1mW	>15 μm	13.6 μm
System 2	1300 nm	60 nm	<1mW	<5 μm	13.6 μm
System 3	840 nm	50 nm	<1mW	>15 μm	8.8 μm

161 Table 1. Specifications of the three OCT systems used in the study

162

163 RESULTS

164 Three common features of tumour tissue were observed with all the three systems.
 165 These features were: (i) a lobular pattern of abnormal architecture, (ii) dilated blood
 166 vessels in the upper dermis and (iii) high reflective margins of tumour lobules. Table 2
 167 shows detailed results for each system. System 2 showed the best performance in
 168 picking up the abnormal architecture, followed by systems 1 and 3. There was no
 169 difference between systems in exhibiting dilated blood vessels. However, system 3
 170 could not identify high reflective margins in any samples, while systems 1 and 2 could.

	Pick up rate of tumour features		
	(i) Lobular pattern of abnormal architecture	(ii) Dilated blood vessels	(iii) High reflective margins
System 1	5/8 (62.5%)	1/8 (12.5%)	3/8 (37.5%)
System 2	6/8 (75%)	1/8 (12.5%)	3/8 (37.5%)
System 3	2/8 (25%)	1/8 (12.5%)	0/8

Table 2. Pick up rates of tumour features for each of the three OCT systems

174 Fig 1 illustrates the appearance of normal skin in an OCT image in comparison with
 175 histology with haematoxylin and eosin stain. All the scans showed a well defined
 176 epidermis. However, the thickness of the epidermis varied across the samples.

177

178 The typical lobular architecture of BCCs was noted both on histology and on OCT
179 images. Details are as shown in Fig 2.

180

181 Fig 3 shows lobular pattern of abnormal architecture, as well as high reflective bands.
182 Lobular low reflective areas were seen scattered within the tissue at depths beyond 300
183 μm (Fig 2, 3). Multiple lobular low signal areas clumped together were also seen at
184 depths beyond 250 μm . Both the lobular low signal areas and the altered architecture of
185 the skin were seen in the upper dermis area. Dilated blood vessels were seen as oval,
186 lower signal, well defined structures with regular outlines (Fig 4).

187 **DISCUSSION**

188 Previous attempts to produce skin images using OCT have been reported^{14,16} but this
189 technology is still under review. There are a lack of systematic studies which prove the
190 efficacy of OCT as a tool for the diagnosis and delineation of BCC and all the studies
191 undertaken to date have examined B-scan images only. Live *en-face* images provide a
192 transverse view at a desired depth. This allows identification of all four margins at any
193 particular depth of tissue. Combining the interpretation of B-scan and C-scan OCT
194 images, the tumour margins can be better delineated in all three dimensions, as achieved
195 by Mohs' surgery. In the future, this could be further enhanced using computer imaging
196 to produce a 3D reconstruction of the tumour tissue. To the best of our knowledge, this
197 is the first paper to look at *en face* OCT imaging in examining BCCs.

198

199 In this study, we observed the tumour margins as signal intense lines separating the
200 tumour from the surrounding tissue and also dividing the tissue into different lobules.

201 Tumour tissue from the deeper layers of the skin appeared as oval and round, low-signal
202 areas with no clear arrangement. The epidermis was clearly distinguishable from the
203 dermis in samples where skin surface was even and the border was seen as a low
204 reflective band. OCT images showed areas of high reflectivity corresponding to tumour
205 lobules on histology. In addition, scattered high reflective areas surrounded by low
206 reflective areas were observed within the abnormal tissue. Similar observations have
207 been made in a previous study. Bechara et al¹⁶ reported similar morphologic structures
208 and formations both in histology and OCT, in their series of 6 patients with BCC and
209 naevi. In their study the OCT images were taken *in vivo*, prior to lesion excision.
210 Although *in vivo* imaging has obvious clinical benefits, our study was limited to *in vitro*
211 imaging due to the prototype setup of the machines available. Strasswimmer et al¹⁷
212 devised a pilot study using polarization sensitive OCT to identify features of BCC. Prior
213 to surgical excision, they scanned different portions of the tumour. A loss of
214 birefringence was noted in the tumour itself which was more marked in the infiltrative
215 type of BCC. They were unable to correlate exact features of OCT and histology to
216 determine precise lateral tumour extension.

217

218 It is recognised that water content and temperature of the body tissue can affect image
219 quality.¹⁸ Normal skin temperature is 37 degrees Celsius and it contains 60-70% water.
220 These constants are affected in excised tissue and can modify the optical properties of
221 the skin. Since the samples used in our study were examined *in vitro* the temperature
222 difference from normal body conditions might have played a significant part in the
223 modification of tissue optical parameters. Schmitt et al¹⁹ have shown that differences
224 exist in the optical properties when measurements are taken at different temperatures.

225 Also, Bonner et al²⁰ reported that the absorption spectrum of water in the near infra red
226 region depends on temperature.

227

228 Different wavelengths for imaging the BCC samples were selected (1300 nm and 840
229 nm) taking into consideration the fact that the absorption coefficient for different layers
230 of the skin is different. The second OCT system with high NA interface optics, which
231 enables a high transverse resolution of better than 5 μm and axial resolution of 13.6 μm ,
232 was able to image tumours in greater detail. However, higher magnification and better
233 transverse resolution result in a smaller field of view. In our study, the highest tumour
234 detection rate was obtained with system 2 (high NA) followed by system 1 both
235 operating at 1300 nm. System 3, which had a wavelength of 840 nm, did not show
236 significant findings. This may be due to the reduced penetration depth at 840 nm as well
237 as to a variation of contrast with wavelength.

238

239 Previous studies with OCT imaging of BCC showed features similar to those found in
240 our study.^{15,17} Our study examined BCCs exclusively from the face and eyelids, used
241 two different wavelengths and also performed *en-face* scans. Boundaries demarcating
242 the tumour from normal tissue, as well as dividing the tumours into different segments,
243 were clearly visible in the *en-face* images at 1300 nm wavelength. The disappearance of
244 this feature at 840 nm could indicate a reflectivity and absorption profile for the tumour
245 tissue. Altered architecture of the skin was seen very prominently in images from
246 system 2 which had a transverse resolution comparable to what can be achieved in
247 confocal microscopy.

248

249 *En-face* (C) scans and cross sections (B) were performed on all 8 samples, with all three
250 OCT systems; this provided the advantage of being able to correlate information at a
251 particular depth in the C-scans with that along depth in B-scans, guiding us in
252 delineating the margins of the tumour in all directions in 3D volume. B-scan OCT
253 images may lead to missed features across the lateral aspect of the tumour.

254

255 There are no studies currently available which have reported *en-face* scans on basal cell
256 carcinoma. In traditional B-scan OCT images, margins appeared as high reflective
257 bands separating the tissue into segments. No such findings were demonstrated in
258 previous studies on BCC.¹⁷ In this study, altered skin architecture was the most common
259 finding in the majority of the samples and it had varied presentations.

260

261 Given the low contrast of OCT images, the way forward is to combine imaging
262 modalities. Some encouraging results have been reported using fluorescence or
263 polarisation. Thus simultaneous or sequential imaging in different regimes where the
264 hardware allows accurate superposition of images could be a way forward.

265 In terms of ideal parameters, the wavelength of 1300 nm seems the most appropriate.
266 Radiation of longer wavelength may have better penetration, however the water
267 absorption peaks up and the transversal resolution deteriorates. Radiation of shorter
268 wavelength encounters **more** scattering and perhaps this explains our results here with
269 the third machine at 840 nm being less effective. As regards the optimum regime of
270 operation, time domain (TD) versus spectral domain (SD), it is largely accepted that
271 SD-OCT offers better sensitivity than TD-OCT. However, SD-OCT acquires images
272 under a fixed focus and as a consequence it is incompatible with higher magnification
273 which requires focus change in synchronism with depth exploration. Higher

274 magnification is also required for improved transversal resolution. Therefore, the *en-*
275 *face* OCT (a TD-OCT method), which allows focus change, seems better suited to
276 investigations which require higher magnification, despite its lower sensitivity in
277 comparison to SD-OCT. Lastly, considering the issue of image size versus transversal
278 resolution, perhaps different probes with different magnifications may overcome the
279 optics limitation which prevents good transversal resolution when under low
280 magnification.

281

282 There were two main limitations to our study. The first was the small sample size. It
283 was designed as a pilot study to demonstrate proof of concept, with a view to a larger
284 study in the future depending on the results. The technical and logistical difficulties of
285 transporting the samples to a different site for OCT scanning, then back to the lab for
286 histopathological analysis, necessitated a small sample size. The other limitation was
287 the *in vitro* scanning. Ideally, the study would have looked at *in vivo* scanning, as this is
288 where the clinical application of OCT lies, but we were limited by the equipment
289 available to us. A further study is planned to compare the results of *in vitro* versus *in*
290 *vivo*, once the technology is available.

291

292 In conclusion, *en-face* imaging has the potential to demarcate tumour tissue from
293 healthy tissue. It has also showed correlation with corresponding histopathology, as
294 demonstrated in the figures above. Non contact OCT imaging of the skin is a very
295 convenient method and may be very useful for imaging BCCs on the face and eyelids.

296 However, larger studies of BCC *in vivo* are required for better identification of tumour
297 margins and sub typing tumours.

298

299 **COMPETING INTERESTS**

300

301 Adrian Podoleanu: acted as consultant for, and has patents with, Ophthalmic
302 Technology Inc, Canada and University of Kent.

303

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305

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307

308 **REFERENCES**

309

310 1. Allali J, D'Hermies F, Renard G. Basal cell carcinoma of the eyelids.

311 *Ophthalmologica* 2005;219(2):57-71.

312 2. Netscher DT, Spira M. Basal cell Carcinoma: An overview of tumour biology and

313 treatment. *Plast Reconst Surg* 2004;113(5):74-94.

314 3. Mohs FE. Micrographic Surgery for the Microscopically controlled excision of eyelid

315 cancers. *Arch Ophthalmol* 1986;104:901-9.

316 4. Margo CE, Waltz K. Basal cell carcinoma of the eyelid and periocular skin. *Surv*

317 *Ophthalmol* 1993;38(2):169-92.

318 5. Cook BE, Bartley GB. Treatment options and future prospects for the management of

319 eyelid malignancies – An evidence-based update. *Ophthalmology* 2001;108:2088-2100.

320 6. Woodward RM, Wallace VP, Pye RJ, et al. Terahertz pulse imaging of ex vivo basal

321 cell carcinoma. *Journal of Investigative Dermatology* 2003;120(1):72-78.

- 322 7. Buchwald HJ, Muller A, Kampmeier J et al. Optical coherence tomography versus
323 ultrasound microscopy of conjunctival and eyelid lesions. *Klin Monatsbl Augenheilk*
324 2003;220:822-9.
- 325 8. Gufler H, Franke FE, Rau WS. High-resolution MRI of basal cell carcinomas of the
326 face using a microscopy coil. *American Journal of Roentgenology* 2007;188:480-4.
- 327 9. Brezinski ME, Tearney GJ, Weissmann NJ et al. Assessing atherosclerotic plaque
328 morphology: comparison of optical coherence tomography and high resolution
329 intravascular ultra sound. *Heart* 1997 May; 77(5):397-403.
- 330 10. Fercher A F , Drexler W, Hitzenberger C K et al. Optical coherence tomography-
331 principles and applications. *Institute of Physics Publishing; Rep. Prog. Phys* 2003;66:
332 239–303.
- 333 11 Podoleanu AGH, Rosen RB. Combinations of techniques in imaging the retina with
334 high resolution. *Progress in Retinal and Eye Research* 2008; 27(4): 464-499
335
- 336 12. Bibas AG, Podoleanu AGH, Cucu RG et al. 3-D optical coherence tomography of
337 the laryngeal mucosa. *Clinical Otolaryngol* 2004;29;713-720
- 338 13. Wang RK, Elder JB. Polypropylene Glycol A Contrasting Agent for Optical
339 Coherence Tomography to Image Gastrointestinal tissues. *Lasers in Surgery and*
340 *Medicine* 2002;30;201-208.
- 341 14. Olmedo J, Warschaw K, Schmitt J. Optical coherence tomography for the
342 characterization of basal cell carcinoma *in vivo*: A pilot study. *J Am Acad Dermatol*
343 2006;55:408-12.

- 344 15. Podoleanu AG, Seeger M, Dobre GM et al. Transversal and longitudinal images
345 from the retina of the living eye using low coherence reflectometry. *J. Biomed.*
346 *Opt.*1998;(3): 12-20
- 347 16. Bechara FG, Gambichler T, Stucker M, et al. Histomorphologic correlation with
348 routine histology and optical coherence tomography. *Skin Res Technol* 2004;10:169-73.
- 349 17. Strasswimmer J, Pierce MC, Park BH et al. Polarization-sensitive optical coherence
350 tomography of invasive basal cell carcinoma. *J Biomedical Opt* 2004;**9**:292–8.
- 351 18. Troy TL, Thennadil SN. Optical properties of human skin in the NIR wavelength
352 range of 1000-2200 nm. *J. Biomedical Opt* 2001;6:167-76.
- 353 19. Schmitt JM, Zhou GX, Walker EC et al. Multilayer model for photon diffusion in
354 skin. *J. Opt. Soc. Am.* 1990;**A7**:2141-53.
- 355 20. Bonner RF, Nossal R, Havlin S et al. Model of photon migration in turbid biological
356 media. *J. Opt. Soc. Am.* 1987;**A4**:423-432.

357

358 **LEGENDS**

359 Fig 1: (A) Horizontal B-scan OCT image obtained with system 1, image depth 1.5 mm
360 measured in air. Boundary between the epidermis and dermis is seen as a low reflective
361 band (arrow); image from normal eyelid skin. (B) Histology image showing normal
362 epidermis and dermis. Arrow indicates the dermo-epidermal junction. Magnification
363 x40, haematoxylin and eosin stain.

364 Fig 2: (A) C-scan OCT image of biopsied tissue, obtained with system 2. Large low
365 reflective lobular structures are seen (white arrow), image size $X = Y = 3.5$ mm, at a

366 depth of 0.45 mm (measured in air). (B) Corresponding histology picture showing BCC
367 lobules. Magnification x20, haematoxylin and eosin stain.

368 Fig 3: (A) C-scan OCT image obtained with systems 1, showing high reflective margins
369 dividing tissue into multiple segments. Image size X = 8 mm; Y = 9.5 mm. at a depth
370 selected ~0.45 mm (measured in air). (B) Corresponding histology with arrow
371 indicating stromal tissue separating lobules of cancerous tissue. Magnification x20,
372 haematoxylin and eosin stain.

373 Fig 4: (A) C-scan OCT image of biopsied tissue obtained with system 3. Dilated blood
374 vessels are seen as multiple low reflective oval structures (white arrow). Image size X =
375 1.37 mm; Y = 1.1 mm, at a depth selected ~0.325 mm (measured in air). (B)
376 Corresponding histology image showing vessels, with red blood cells in the lumen, in
377 the superficial dermis overlying a lobule of BCC. Magnification x20, haematoxylin and
378 eosin stain.







