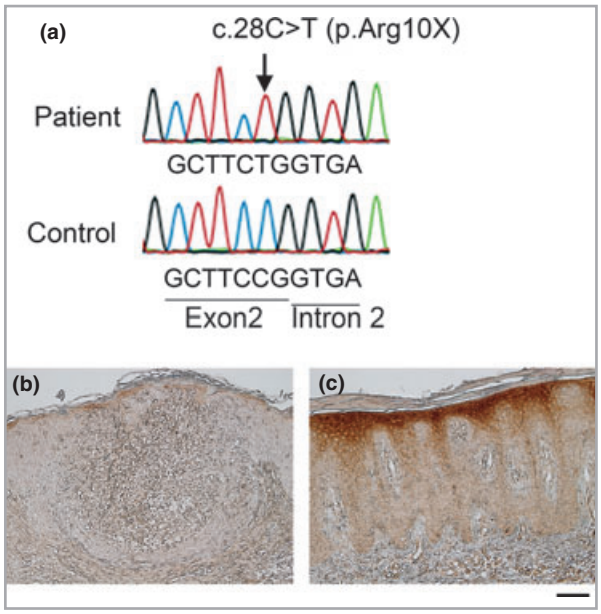

Fig 2. Sequence data of *IL36RN* and expression of IL36RN on the lesion of generalized pustular psoriasis (GPP). (a) Sequence data of *IL36RN* in the patient and control; the arrow indicates the heterozygous mutation c.28C>T (p.Arg10Ter). C at nucleotide position 28 is two bases upstream from the C′ end of exon 2 (the exon 2–intron 2 boundary) of *IL36RN*. (b) Immunohistochemistry of the GPP lesion with anti-IL1F5 (IL36RN); staining was almost negative. (c) Immunohistochemistry of a skin lesion of a patient with psoriasis vulgaris with anti-IL1F5 (IL36RN); staining was strong in keratinocytes in the upper layers. Scale bar = 100 μm.

In addition, it is noteworthy that no GPP cases with *IL36RN* mutations, including the present case, have been associated with PV or PPP,[1,2] and the absence of PV and PPP is a clue in identifying patients with GPP with *IL36RN* mutations.

We believe it is very important to discriminate familial GPP cases with *IL36RN* mutations from the other GPP cases, not only for genetic counselling but also because we expect familial GPP will be treatable with customized therapy that targets IL-36 signalling in the near future.

Departments of [1]*Dermatology,* [3]*Laboratory Medicine, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan*
[2]*Department of Dermatology, Inazawa City Hospital, 1-1 Gokusho-cho, Inazawa 492-8510, Japan*
E-mail: kazusugi@med.nagoya-u.ac.jp

K. Sugiura[1]
T. Takeichi[1,2]
M. Kono[1]
Y. Ogawa[1]
Y. Shimoyama[3]
Y. Muro[1]
M. Akiyama[1]

References

1 Marrakchi S, Guigue P, Renshaw BR *et al.* Interleukin-36-receptor antagonist deficiency and generalized pustular psoriasis. *N Engl J Med* 2011; **365**:620–8.
2 Onoufriadis A, Simpson MA, Pink AE *et al.* Mutations in *IL36RN/IL1F5* are associated with the severe episodic inflammatory skin disease known as generalized pustular psoriasis. *Am J Hum Genet* 2011; **89**:432–7.
3 Mulero JJ, Pace AM, Nelken ST *et al.* *IL1HY1*: a novel interleukin-1 receptor antagonist gene. *Biochem Biophys Res Commun* 1999; **263**:702–6.
4 Smith DE, Renshaw BR, Ketchem RR *et al.* Four new members expand the interleukin-1 superfamily. *J Biol Chem* 2000; **275**:1169–75.
5 Dinarello C, Arend W, Sims J *et al.* IL-1 family nomenclature. *Nat Immunol* 2010; **11**:973.
6 Debets R, Timans JC, Homey B *et al.* Two novel IL-1 family members, IL-1 delta and IL-1 epsilon, function as an antagonist and agonist of NF-kappa B activation through the orphan IL-1 receptor-related protein 2. *J Immunol* 2001; **167**:1440–6.
7 Towne JE, Garka KE, Renshaw BR *et al.* Interleukin (IL)-1F6, IL-1F8, and IL-1F9 signal through IL-1Rrp2 and IL-1RAcP to activate the pathway leading to NF-kappaB and MAPKs. *J Biol Chem* 2004; **279**:13677–88.
8 Sahashi K, Masuda A, Matsuura T *et al.* *In vitro* and *in silico* analysis reveals an efficient algorithm to predict the splicing consequences of mutations at the 5′ splice sites. *Nucleic Acids Res* 2007; **35**:5995–6003.
9 Blumberg H, Dinh H, Trueblood ES *et al.* Opposing activities of two novel members of the IL-1 ligand family regulate skin inflammation. *J Exp Med* 2007; **204**:2603–14.

Funding sources: this study was supported in part by a Grant-In-Aid for Scientific Research, (C) 23591617 (to K.S.) and (A) 23249058 (to M.A.) from the Ministry of Education, Culture, Sports, Science and Technology of Japan.

Conflicts of interest: none declared.

The utility of the 'book biopsy' in Mohs micrographic surgery

DOI: 10.1111/j.1365-2133.2012.10967.x

Madam, By virtue of its tissue-sparing properties and enabling assessment of 100% of the surgical margin, Mohs micrographic surgery (MMS) is considered the gold standard in the surgical treatment of high-risk facial skin cancer.[1–3] Clinicians may often initially perform diagnostic biopsies to confirm the diagnosis (if doubt exists) and also to enable histopathological assessment of any high-risk features such as an infiltrative growth pattern or the presence of perineural invasion.

In order to guide the size of the first Mohs layer, the surgeon typically marks out the clinical extent of the tumour on the skin. However, in patients with significant actinic damage, it may be very difficult clinically to determine the tumour margins. Overestimating the clinical extent of the tumour will result in a surgical defect larger than required; however, not including 'suspicious' areas may result in several stages of surgery, a longer procedure for the patient and an increase in the tissue-processing burden for the Mohs laboratory technicians.

Under such circumstances the 'book biopsy' (BB) may be of value. Figure 1 illustrates the preoperative appearance of a 69-year-old man with a biopsy-proven infiltrating basal cell carcinoma on the lower left nasal dorsum. A previous inci-

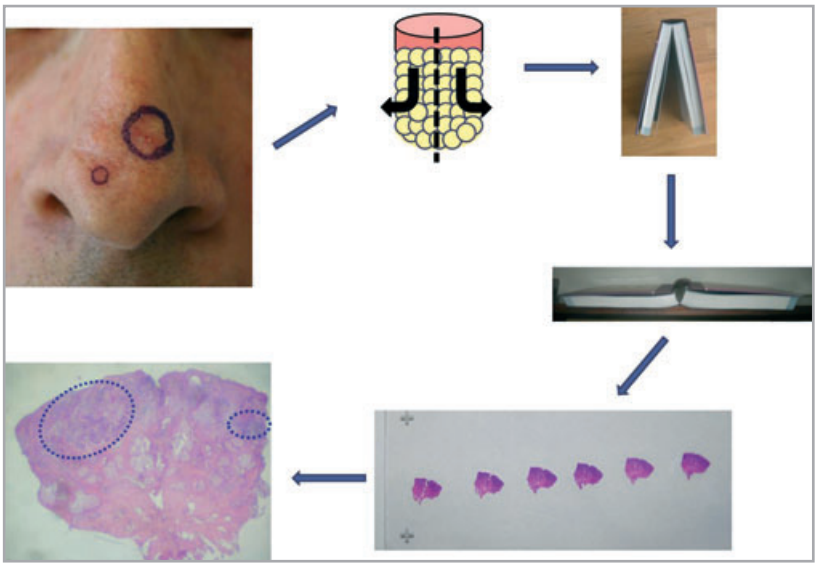

Fig 1. (Clockwise from top left) Clinical margins of an infiltrating basal cell carcinoma on the lower left nasal dorsum (larger circle); there is a suspicious area on the right nasal tip (smaller circle), which was punch biopsied prior to commencing Mohs tumour extirpation. Schematic diagram illustrating how a punch biopsy specimen is partially divided along its longitudinal axis, enabling it to 'open up', similar to an open book as shown. This biopsy specimen may then be laid flat on a microscope slide, akin to a book being laid flat as illustrated; this manoeuvre doubles the surface area available for processing and subsequent histological assessment. Rapid frozen section biopsy slide produced following the punch biopsy of the suspect area on the right nasal tip. Low-power view demonstrating nodular islands of basaloid cells, peripheral palisading and clefting typical of basal cell carcinoma (dotted circles); consequently, the patient's primary Mohs layer encapsulated both the delineated areas on the lower nasal dorsum and right nasal tip, thus increasing the efficiency of the Mohs procedure.

sional biopsy of an erythematous scaly area inferior to this (on the right nasal tip) had been reported at another institution as showing solar elastosis only.

When the patient presented for MMS, despite the previous incisional biopsy result, the clinical features on the right nasal tip were suspicious. Including this area, in the first Mohs layer would significantly increase the defect size (potentially unnecessarily). Not including this area however, could potentially prolong the course of tumour extirpation for the patient.

In order to provide rapid histological guidance, a BB was therefore performed. In this case, the BB involved taking a 3-mm punch biopsy from the suspicious area on the right nasal tip. The cylindrical biopsy was then divided along its longitudinal axis as shown, enabling it to be opened up and laid flat (like a face-down open book) on the biopsy slide. This 'opening up' immediately doubles the surface area available for processing and allows a rapid frozen-section biopsy to be produced (15–20 min on average). This clearly demonstrated basal cell carcinoma and this area was thus included in the first Mohs tissue layer. Tumour-free margins were achieved after two stages and the patient repaired with a single-stage dorsal–nasal flap.

The BB is a useful technique for guiding the Mohs surgeon when extirpating tumours in the presence of significant actinic damage. It is inexpensive and uses equipment readily available to the surgeon. Histotechnicians accustomed to processing frozen section Mohs tissue specimens can rapidly produce the tissue slides for assessment, thus not significantly adding to the time of the procedure. Furthermore, if negative for tumour, a small biopsy defect can either be approximated with a single suture or left to heal by secondary intention, with no significant aesthetic consequences.

Acknowledgments

We are grateful to Christopher Morris and Joshua Christian, Division of Mohs Histotechnology, Leeds Centre for Dermatology, for their assistance in preparing this manuscript.

[1]*Department of Mohs Micrographic and Reconstructive Surgery, Leeds Centre for Dermatology, Great George Street, Leeds LS1 3EX, U.K.*
[2]*Skin Cancer Institute, Tauranga, New Zealand*
E-mail: dr_w_hussain@hotmail.com

W. Hussain[1]
J. Hafiji[2]
P. Salmon[2]

References

1 Rowe DE, Carroll RJ, Day CL Jr. Mohs surgery is the treatment of choice for recurrent (previously treated) basal cell carcinoma. *J Dermatol Surg Oncol* 1989; **15**:424–31.
2 Tromovitch TA, Beirne G, Beirne C. Mohs' technique (cancer chemosurgery). Treatment of recurrent cutaneous carcinomas. *Cancer* 1966; **19**:867–8.
3 Mosterd K, Krekels GA, Nieman FH *et al.* Surgical excision versus Mohs' micrographic surgery for primary and recurrent basal cell carcinoma of the face: a prospective randomised controlled trial with 5-years' follow-up. *Lancet Oncol* 2008; **9**:1149–56.

Funding sources: none.

Conflicts of interest: none declared.

Caution in melanoma risk analysis with smartphone application technology

DOI: 10.1111/j.1365-2133.2012.11046.x

MADAM, The popularity of clinical, diagnostic downloadable applications for use on smartphones and tablet computers is ever increasing. Melanoma risk-assessment tools are recent additions to the market and include programs such as 'MelApp' and 'Skin Scan'. 'MelApp' is designed for use with the iPhone and has not yet been approved by the U.S. Food and Drug Administration. It takes an uploaded image of a lesion and uses an image database from the Johns Hopkins University Medical Center, with pattern recognition software and mathematical algorithms to provide a risk assessment of a mole being a malignant melanoma. There are limited published data on the safety and accuracy of this technology, which is inexpensive and widely available to the public.

Using 'MelApp' on the iPhone we collected risk-assessment data of 35 pigmented skin lesions on 31 patients referred by general practitioners to our urgent suspected cancer clinic. Each lesion was also risk assessed and a clinical diagnosis given by an experienced dermatology consultant physician. Skin biopsies were performed on 17 lesions.

The 'MelApp' program was unable to make an assessment of 14/35 (40%) photographed lesions and the following explanations were given. There was a segmentation error with eight lesions, three lesions had no resemblance to a mole and three lesions could not be assessed due to low contrast. Of the lesions that could be assessed by 'MelApp', three were considered to be high risk, two medium risk and 16 low risk. All lesions classified high risk and medium risk by 'MelApp' were excised on the basis of an independent clinical decision. Table 1 shows the histological diagnoses and patients discharged with clinically benign lesions for each risk assessment. Importantly, one patient was assessed by 'MelApp' as low risk for melanoma and had a histopathological and clinical diagnosis of superficial spreading melanoma (Fig. 1).

When the low- and high-risk assessment for 'MelApp' was compared with a benign and malignant diagnosis, sensitivity for 'MelApp' was calculated at 50% with a specificity of 88%. When 'MelApp' risk assessment was compared with the physician risk assessment for low- and high-risk lesions, the sensitivity for MelApp was 20% and specificity 92%.

These data suggest that smartphone application technology for the risk assessment of melanomas should be utilized with caution and further studies are necessary to assess safety of the technology. These tools may help to promote self-surveillance and highlight the dangers of melanoma to the general population; however, there is concern that a patient may be dissuaded from accessing health care advice if their lesion were to be assessed as low risk. There is also no evidence to suggest that patients would select the most appropriate skin lesion to assess. Viola *et al.*[1] found that 9·8% of incidental lesions identified at clinical consultation by a dermatologist after nondermatology referral were found to be melanomas. In a study of 3827 pigmented skin lesions assessing the accuracy of a computer-based system of the automated diagnosis of melanoma, three melanomas were missed because the nonexpert physicians did not choose them for examination with the automated system.[2]

Table 1 Patients with risk assessment for melanoma from 'MelApp' and subsequent outcome and histological diagnoses

'MelApp' assessment	Outcome	Histological diagnosis	Number of lesions
High risk	Excised	Acral lentiginous melanoma	1
		Benign naevus	2
Medium risk	Excised	Dysplastic compound naevus	1
		Benign, traumatized intradermal naevus	1
Low risk	Excised	Blue naevus	1
		Dysplastic naevus	1
		Superficial spreading melanoma	1
		Seborrhoeic keratosis	2
		Benign naevus	1
	Discharged		10

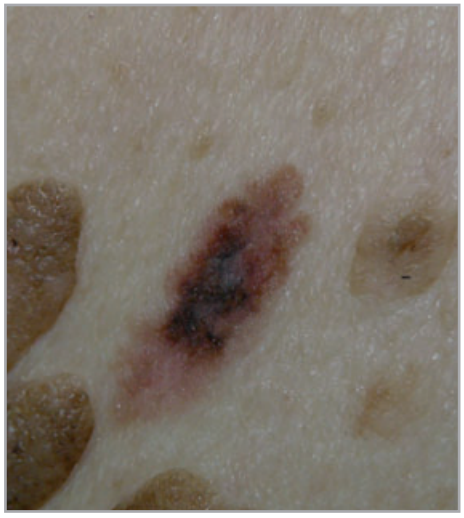

Fig 1. Superficial spreading malignant melanoma risk-assessed as low risk by 'MelApp'.

Dermatology Department, Singleton Hospital Y. ROBSON
Sketty Lane, Sketty S. BLACKFORD
Swansea SA2 8QA, U.K. D. ROBERTS
E-mail: y.robson@doctors.org.uk