

Letters

RESEARCH LETTER

Effects of Ex Vivo Skin Microbiopsy on Histopathologic Diagnosis in Melanocytic Skin Lesions

Currently, histopathologic analysis represents the practical reference standard for the diagnosis of melanocytic skin lesions. However, there are limitations particularly related to the morphologic nature of the histopathologic interpretation and the influence of the clinical information on the final diagnosis.¹ To provide lesional tissue from melanocytic proliferations for molecular analysis without jeopardizing the conventional histopathologic diagnosis, we invented a miniaturized biopsy device with a total width of 0.35 mm, containing a sample chamber 0.15 mm wide. This device penetrates approximately 250 μm in healthy skin (ie, superficial dermis) to collect approximately 1600 cells.² This microbiopsy device can be used without local anesthetic, and there is no need for a suture. Our hypothesis is that the minimal skin damage caused by the microbiopsy does not interfere with the subsequent histopathologic diagnosis.

Methods | Five patients scheduled for suspicious pigmented lesion removal at the dermatology department of the Princess Alexandra Hospital, a public tertiary hospital in Brisbane, Australia, were recruited. Consent was obtained from all participants with approval from The University of Queensland/Princess Alexandra Hospital Human Research Ethics Committees. Clinical images of the lesions were taken before surgery and immediately after excision. Each excised lesion was bisected, and 5 microbiopsy specimens were applied ex vivo to one of the halved lesions. The microbiopsy site locations were documented, and the specimens were labeled accordingly. All specimens were sectioned in the hospital's pathology laboratory according to routine protocol.



Editorial page 1023

Results | All sections were examined by a dermatopathologist (D.L.) for the histopathologic diagnosis, with special emphasis on the microbiopsy defect. The mean (SD) size of the microbiopsy defect was 113 (50) μm wide and 146 (37) μm deep ($n = 4$). These defects are comparable, albeit not identical, to processing artifacts in nonmicrobiopsied specimens ranging from 20 to 2100 μm wide and 70 to 600 μm deep. Histopathologic diagnoses in both halves, while examined separately, were exactly the same in all lesions. Diagnoses included compound nevus, junctional lentiginous nevus, compound dysplastic nevus, junctional dysplastic nevus, and solar lentigo.

From the 5 lesions included in the study, 2 are displayed herein clinically and histopathologically. Patient 1 was an 88-year-old man with a history of metastatic melanoma, who had a deep shave excision of a new nevus identified on his left flank. One of the microbiopsy defects identified within the melanocytic region was 132 \times 74 μm in size (**Figure 1**). The diagnosis was a compound dysplastic nevus. Patient 2 was a 56-year-old woman with history of nonmelanoma skin cancer, who presented with a changing nevus on her left scapula. One of the microbiopsy defects found outside the lesional region was 145 \times 201 μm and reached the superficial dermis (**Figure 2**). Diagnosis of this lesion was junctional lentiginous nevus.

Discussion | Over the years, many microdevices have been developed to obtain tissue samples,³⁻⁵ but interestingly enough none of these microdevices are specifically engineered for skin lesions. Because of the new exciting developments of targeted molecular therapies in patients with melanoma,⁶ there is a need for a minimally invasive biopsy device enabling small tissue collection with minimal adverse effects to perform downstream molecular diagnosis of melanocytic skin lesions.

The size of microbiopsy defects measured in this study was comparable to other artifacts more or less commonly seen in routine sectioned specimens. The potential diagnostic difficulties for the dermatopathologist encountered with the histopathologic assessment of a microbiopsied melanocytic skin lesion can easily be overcome by ordering multiple levels. All 5 melanocytic lesions included in this study were not difficult to assess, and therefore the diagnostic process was not hampered by the microbiopsy-induced artifacts; however, on the basis of the size of the microbiopsy artifacts, we foresee that the diagnostic process, even in equivocal cases, will not be influenced. The data from this study support the hypothesis that minimal skin damage caused by the microbiopsy does not affect the histopathologic diagnosis.

Parastoo Banan, MD
Lynlee L. Lin, BSc
Duncan Lambie, BDS, MBBS, FRCPA
Tarl Prow, BS, MSc, PhD
H. Peter Soyer, MD, FACP

Author Affiliations: Dermatology Research Centre, The University of Queensland, School of Medicine, Translational Research Institute, Princess Alexandra Hospital, Brisbane, Queensland, Australia (Banan, Lin, Prow, Soyer); Department of Anatomical Pathology, Princess Alexandra Hospital, Brisbane, Queensland, Australia (Lambie).

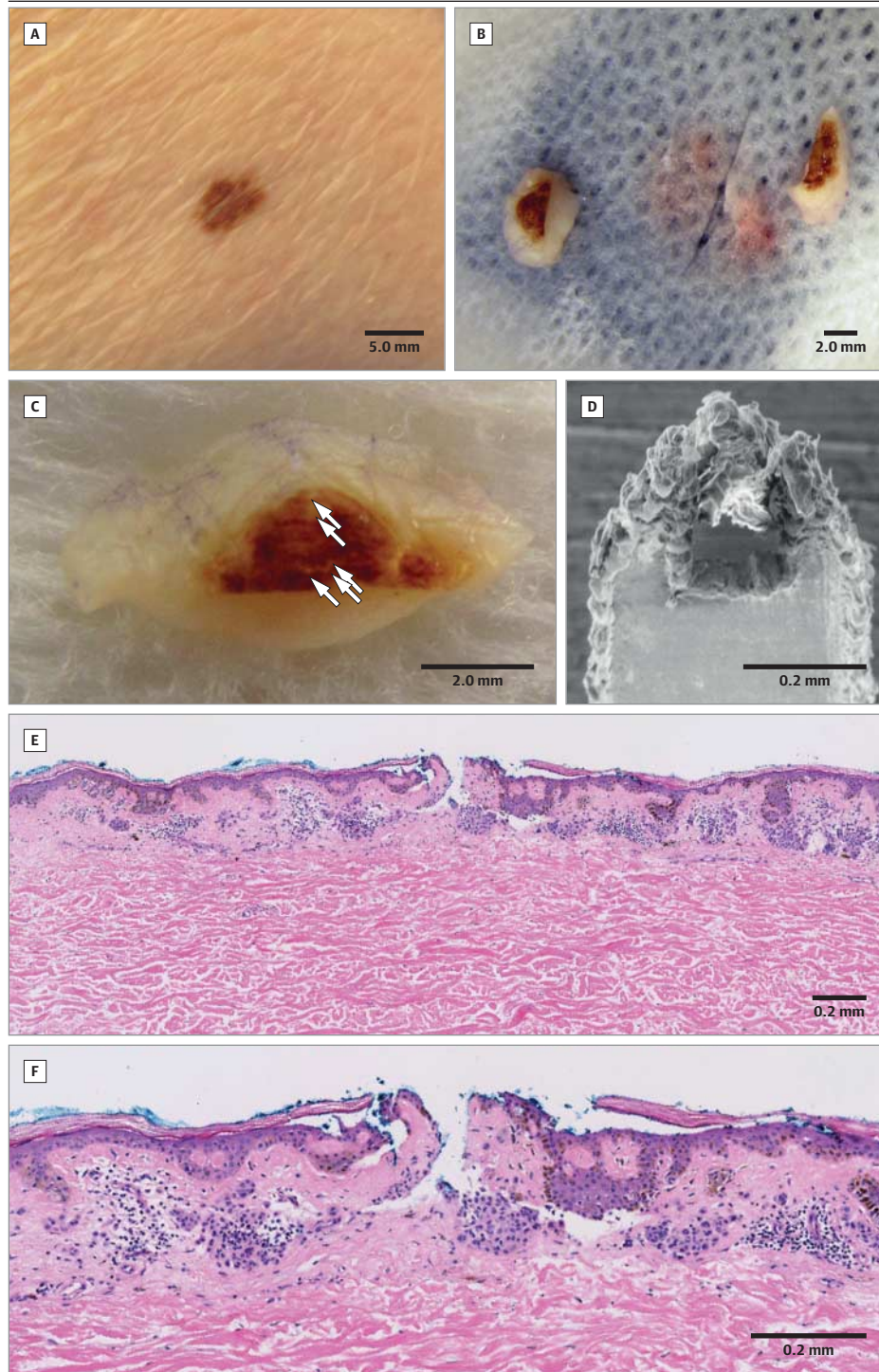
Corresponding Author: H. Peter Soyer, MD, FACP, Dermatology Research Centre, The University of Queensland, School of Medicine, Translational Research Institute (TRI), 37 Kent St, Woolloongabba, QLD 4102, Australia (p.soyer@uq.edu.au).

Accepted for Publication: May 7, 2013.

Published Online: July 17, 2013.
 doi:10.1001/jamadermatol.2013.5020.

Author Contributions: All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Figure 1. Patient 1



A, Patient 1 clinical photograph; B, excised lesions; and C, microbiopsy sites (white arrows). D, The microbiopsy device with a sample; E, the site of microbiopsy at low magnification; and F, the site at high magnification.

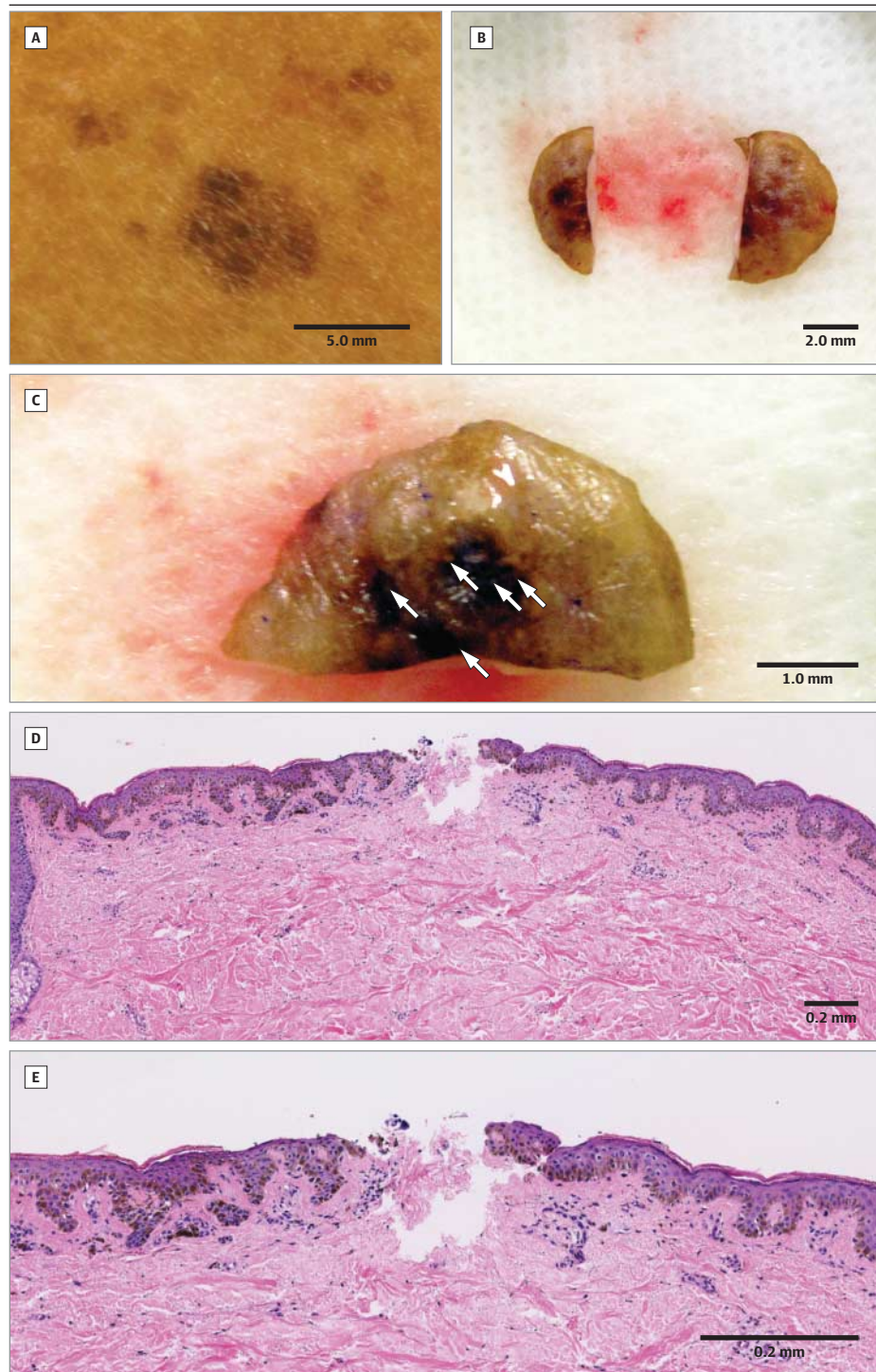
Study concept and design: Lambie, Prow, Soyer.
Acquisition of data: Banan, Lin, Lambie.
Analysis and interpretation of data: All authors.
Drafting of the manuscript: Banan, Lin, Prow.
Critical revision of the manuscript for important intellectual content: All authors.
Statistical analysis: Banan.
Obtained funding: Soyer.
Administrative, technical, and material support: Banan, Lin, Lambie, Prow.
Study supervision: Lambie, Prow, Soyer.

Conflict of Interest Disclosures: None reported.

Funding/Support: This study was supported in part by Epiderm. Dr Soyer has a National Health and Medical Research Council Practitioner Fellowship.

1. Ferrara G, Argenyi Z, Argenziano G, et al. The influence of clinical information in the histopathologic diagnosis of melanocytic skin neoplasms. *PLoS One*. 2009;4(4):e5375.
2. Lin LL, Prow TW, Raphael AP, et al. Microbiopsy engineered for minimally invasive and suture-free sub-millimetre skin sampling. *F1000Research*.

Figure 2. Patient 2



A, Patient 2 clinical photograph; B, excised lesions; and C, microbiopsy sites (white arrows). D, The microbiopsy site at low magnification; and E, the site at high magnification.

2013;2:120. doi:10.12688/f1000research.2-120.v1. <http://f1000research.com/articles/2-120/v1#reflist>. Accessed May 2, 2013.

3. Cosnier ML, Martin F, Bouamrani A, Berger F, Caillat P. A minimally invasive microdevice for molecular sampling and analysis. *IEEE Trans Biomed Eng*. 2009;56(12):2898-2904.

4. Pflueger DR, inventor; Stryker Puerto Rico Limited, assignee. Micro-invasive breast biopsy device. US patent 6,673,023 B2. January 6, 2004. <http://www.google.com/patents/US6673023>. Accessed January 16, 2013.

5. Cho D, Park SK, Lee AR, et al, inventors; Seoul National University Industry Foundation, assignee. Catheter capable of being equipped with micro biopsy tool. US patent 7,927,289 B2. April 19, 2011. <http://www.google.com/patents/US7927289>. Accessed January 16, 2013.

6. Khattak M, Fisher R, Turajlic S, Larkin J. Targeted therapy and immunotherapy in advanced melanoma: an evolving paradigm. *Ther Adv Med Oncol*. 2013;5(2):105-118.