Amine this we reviewed a consecutive series of 100 prostate needle biopsies, 68% (68 of 100) of which had cancer, and in which synoptic reporting was not used. On review we found a 100% completeness rate for Gleason grade and score, number of cores involved, extent of involvement (measured as % of tissue), as well as the presence of perineural invasion (only reported when present). Gleason group was not reported at the request of our clinicians. Although a variety of formatting features have been described that can improve either the speed or accuracy of information extraction by clinicians, these features are not consistently applied in the CAP products. Indeed, the separation of the components of grading onto separate lines clearly impedes information extraction by the clinician. Thus, the greatest benefit that synoptic reports for PNBs might offer in our system would be the construction of a structured data set. However, this would only be of value if a structured data set could not be constructed from the original biopsy reports themselves.

To examine this we wrote a Python (Python.org) script by using regular expressions to extract a structured data set from the original reports of this same set of prostate needle biopsies. Cases of adenocarcinoma were identified by the presence of the word “Gleason.” For each such case, the number of positive cores was extracted by counting the incidence of the word “Gleason” minus any cases in which the word “Gleason” was immediately followed by the word “pattern” (in which case the pathologist was describing a tertiary pattern). The Gleason grade and score were identified by a regular expression consisting of a 1-digit number, a “+” sign, a 1-digit number, and an “=” sign and a subsequent 1- or 2-digit number. Since Gleason group is not an independent pathologic feature, it was simply calculated from the Gleason grade and score. The presence of perineural invasion was identified by searching for the word “perineural.” The percentage of tissue involved in a single core was identified by searching for the numeric value before “% of tissue,” and taking the largest such value. Finally, in our system each core is submitted as a single specimen and is identified by a capital letter followed by a period (e.g., A., B.), so the total number of cores was identified by identifying the last capital letter followed by a period and correlating this with its position in the alphabet. Obviously this method would be inaccurate if more than 1 biopsy was submitted per specimen. This simple program extracted a structured data set of prostate needle biopsies with and without cancer with 100% accuracy for the presence or absence of cancer; Gleason grade, score, and group; number of positive cores; largest percentage core involved; total number of cores; and perineural invasion. These data suggest that prostate needle biopsy reports are easily amenable to structured data extraction without the need for a separate synoptic report.

As we have documented previously, we strongly support synoptic reporting when it can lead to a benefit for pathologists, clinicians, or researchers. Indeed, it is possible that the publication of the synoptic protocol for prostate needle biopsies by the CAP would allow the pathologist to provide more complete reports simply by serving as a reference standard. However, implementation of synoptic reports by definition means more work for the pathologist and does not come without additional costs. These costs can include additional errors in the surgical pathology report, and these errors can lead to patient harm. As a result, the rationale for including synoptic reports is unclear if the same information can be obtained simply by using a different automated process to extract the information. There is no reason why all structured data sets from pathology reports need to be constructed by using a single method. Indeed, as we have documented previously, our system for structured data set construction from synoptic reports is highly effective and relies on free text searches of the final report rather than the upfront construction of these data sets that the eCC uses. Since synoptic reports for prostate needle biopsies already have a history of being problematic to implement, and our data suggest that there is essentially no benefit to implementing them when pathologists are using a consistent format for their reports, the members of the CAP would be better served if the CAP directed their efforts at expanding the use of synoptic reports in areas with better cost/benefit ratios.

Andrew A. Renshaw, MD; Edwin W. Gould, MD

Departments of Pathology, Baptist Hospital and Miami Cancer Institute, Miami, Florida


Accepted for publication March 25, 2019.

The authors have no relevant financial interest in the products or companies described in this article.


In Reply to “Malignant Mesothelioma and Its Nonasbestos Causes”

In recent years, coinciding with cosmetic talc litigation, Dr Finkelstein has written a number of correspondence letters regarding peer-reviewed scientific literature in which he espouses various claims regarding cosmetic talcum powder, asbestos exposure, and mesothelioma. In each case, the authors of those publications have
First, with respect to interpreting fiber burden analyses, it is widely accepted that asbestos, as a collective group, is one among many minerals that are ubiquitous in the ambient atmosphere and that there is no evidence that these exposures have any significance with respect to the development of any disease. The scientific evidence correlating cumulative asbestos exposure with disease has been extensively established in occupational settings that are many orders of magnitude above background ambient exposure levels.9,10,11 Numerous analytic laboratories have made correlations between retained amphibole asbestos fiber concentrations in lungs of asbestos-exposed workers and asbestos-related disease. Control reference ranges should be established within laboratories performing fiber burden analyses, and the significance of an individual exposure may then be determined by benchmarking the case to the established laboratory control population.12,13 The control population represents, most closely, only subjects with ambient exposure and no increased risk of asbestos-related disease.

An important rule in evaluating fiber burden studies is that, at a minimum, an elevation above background is required before considering whether a given case might represent an asbestos-related disease. Another fundamental principle of interpreting fiber burden analyses, ignored by Dr Finkelstein, is that absent contamination, the mere detection of a mineral confers no more significance than prior exposure. It is not possible to infer the specific source or timing of exposure (unless this correlates closely with a clear exposure history) or any etiologic significance absent a comparison with the laboratory control reference population, and preferably a comparison with established disease-specific ranges for that laboratory.

Dr Finkelstein makes no attempt to correlate fiber detection with any causal significance. However, Roggli (in Srebro et al19) has previously published his laboratory controls so such comparisons could have been undertaken. In fact, as Roggli points out (in Krayne et al11), many of the female subjects with malignant mesothelioma have asbestos fiber burdens and asbestos body counts that fall within his laboratory control reference population. Thereby, there is no mineralogic evidence of significant above-background exposure and no evidence for any increased mesothelioma risk from mineral fibers in these North American women with malignant mesothelioma as determined by the fiber burden database cited by Dr Finkelstein. Although we did not use the fiber burden database in our article, these results support our original proposition, which was based on published literature review stating that “in North America few mesotheliomas in women at any site are attributable to asbestos.”

Additionally, it is recognized that various elongate mineral particles can be detected in human lung samples by electron microscopic analysis with energy-dispersive x-ray spectrometry. Although potentially satisfying the definition for a fiber (an elongate mineral particle with an aspect ratio of at least 3:1 and roughly parallel sides), it has been suggested that a minimum 10:1 or preferably 20:1 aspect ratio be used as one criterion for determining asbestiform fibers from elongate particulates of non-asbestiform cleavage fragments.17,18 This has biologic significance, as cleavage fragments of non-asbestiform minerals have not been associated with asbestos-related disease nor are they regulated as asbestos by the Occupational Safety and Health Administration. As Roggli et al19 noted for persons with asbestos-related disease, lung fiber burdens of commercial amphibole forms of asbestos (amosite and crocidolite) show that almost all are greater than 10 μm and their diameter is nearly always less than 1 μm. This contrasts with the noncommercial amphibole minerals (tremolite, actinolite, and anthophyllite) whose aspect ratio is lower, with wider fiber diameters and shorter fiber lengths corresponding to the presence of the more commonly detected cleavage fragments rather than the rarer asbestiform habits of the amphibole minerals.

We recognize that there exists scientific debate regarding the precise nature of accessory minerals in cosmetic talcum products. This was discussed in detail by Keeton et al in response to precisely the same commentary made by Dr Finkelstein. We do not consider there is any purpose in simply rehearsing the same discussions.

Dr Finkelstein seeks to attempt to develop a conclusion from his reanalysis of Roggli’s fiber burden data-

Letters to the Editor

respectsfully disagreed with Dr Finkelstein’s assertions, although he has since repeated the same claims.4,6 We now would like to respond to his commentary that addresses statements we made in our publication regarding spontaneous mesothelioma in North American women.7,8

Dr Finkelstein questions 2 statements in our article, both in reference to spontaneous mesothelioma. First, that most mesotheliomas not clearly attributable to asbestos are spontaneous. Second, that in North America few mesotheliomas in women at any site are attributable to asbestos. We made clear our scientific methodology and peer-reviewed reliance literature, which enabled us to conclude in the manner we did.

Dr Finkelstein argues that there is common occult asbestos exposure arising from use of some talcum powders, something that we did not discuss, and therefore it was inappropriate to conclude in the manner we did. That being so, one would expect Dr Finkelstein would set out the appropriate to conclude in the manner we did. That being so, one would expect Dr Finkelstein would set out the contrary scientific basis with literature supporting his assertion that consumer usage of cosmetic talc, even if contaminated by amphibole minerals (asbestiform or non-asbestiform), poses any risk of malignant mesothelioma.

Dr Finkelstein actually provides no contrary peer-reviewed scientific literature that challenges our 2 statements. Instead, he relies first, on data from Statista, a German market research company, for US purchasing patterns of body and baby powder use between 2011 and 2017,9 and second, on a misrepresentation of a fiber burden database obtained without permission through litigation and published without consent from one of us. Dr Finkelstein is unable to draw any conclusion beyond a commentary on present-day consumer usage of body and baby powder, which as Keeton et al8 highlight, is not specific to products containing talcum powder.

We disagree with Dr Finkelstein because he ignores basic scientific principles of interpreting fiber burden analyses when seeking to attribute significance to an exposure in the causation of disease, because he relies on incorrect and irrelevant data sources, and because he ignores the wider scientific evidence that consistently concludes that cosmetic talc is not a cause for malignant mesothelioma.
base, namely, that in women, talc and noncommercial amphiboles are detected more frequently than in men, to support his proposition that the consumer usage of cosmetic talc was more common in women and exposed women to noncommercial amphibole minerals. Even if talc is detected on mineral analysis, Dr Finkelstein cannot conclude by his methodology that the talc is from a cosmetic talc source or that talc was the source of any codetected noncommercial amphibole minerals. Talc was the most common non-asbestos mineral fiber that was identified in the reference population.

An understanding of gender differences observed in fiber burdens, fiber counting protocols, and limits of detection in analyzing cases provides a clear explanation for this observation, which Dr Finkelstein ignores. In general, fiber burden studies undertaken on lung digestes from men with asbestos-related disease reflect prior occupational exposures to commercial forms of amphibole asbestos, predominantly amosite. The exposures to asbestos in men are very typically heavier than the exposures observed in women. This fact impacts upon fiber burden detection limits of minerals analyzed. In asbestos-related disease, because of fiber-counting protocols, in heavier exposures (more often reflected in men, following occupational settings) the fiber burdens will be dominated by commercial amphibole asbestos. At low exposures (more typically observed in women), commercial forms of amphibole asbestos are less frequently detected and noncommercial amphiboles and non-asbestos minerals are disproportionately represented. Most importantly, it provides no evidence for the timing or significance of such exposure.

We did not introduce discussions regarding talc (industrial or cosmetic/pharmaceutical grade), its mineralogy, or its biologic significance or any accessory minerals, even if present, or their role, if any, in the development of malignant mesothelioma. This was because we did not consider it as relevant to the scope of our review. However, as this has been raised by Dr Finkelstein, we will now address the issue. First, it is worth noting that there has never been a single confirmed case of malignant mesothelioma in any of the epidemiologic studies of cosmetic talc mine and mill workers conducted in Europe or North America, a finding that is consistent with the fact that these mines did not contain asbestiform amphiboles.21–28 Second, published reviews of subjects undergoing pleurodesis with cosmetic/pharmaceutical-grade talc for various benign pleuropulmonary conditions, which investigated the potential development of mesothelioma, identified no mesotheliomas in any of the more than 300 patients with follow-up ranging from 14 to 40 years.29–31 A weight of evidence review concluded that talc pleurodesis was safe for use with no long-term effects.32 Finally, toxicologic studies of rats exposed to high levels of Italian cosmetic-grade talc showed no asbestos-related effects and no mesotheliomas after either intrapleural injection or inhalation.33,34 Additionally, Syrian golden hamsters showed no mesotheliomas after exposure to Vermont talc.35,36

In the final analysis we are unable to identify any evidence that supports Dr Finkelstein’s propositions regarding our statements about spontaneous mesotheliomas, or cases of malignant mesothelioma arising in US women. We identify no evidence for any causative role of cosmetic talc in malignant mesothelioma. We thank Dr Finkelstein for his comments but respectfully do not agree with them.

Richard L. Attanoos, MBBS, FRCPath1; Andrew Churg, MD2; Francoise Galateau-Salle, MD3; Allen R. Gibbs, MBCchB, FRCPath4; Victor L. Roggli, MD5

1 Department of Cellular Pathology, Cardiff and Vale University Health Board, and Cardiff University, University Hospital of Wales, Cardiff, United Kingdom 2 Department of Pathology and Laboratory Medicine, University of British Columbia, and Vancouver General Hospital, Vancouver, British Columbia, Canada 3 Department of Biopathology, Léon-Bérard Cancer Centre, Lyon, France 4 Department of Cellular Pathology, Cardiff and Vale University Health Board, Cardiff, United Kingdom 5 Department of Pathology, Duke University Medical Center, Durham, North Carolina

19 Roggli VL, Green CL. Dimensions of elongated mineral particles: a study of more than 570 fibers from more than 90 cases with implications for pathogenicity and classification as asbestiform vs. cleavage fragments [published online ahead of print]


External Quality Assurance of Platelet Function Assays: Results of the College of American Pathologists Proficiency Testing Program

To the Editor—We applaud the efforts of the College of American Pathologists (CAP) to provide proficiency testing to improve the quality and reliability of clinical test results. We are pleased to see that PlateletMapping testing available on the TEG 5000 analyzer platform (both Haemometrics Corp, Braintree, Massachusetts) has been included in the program since 2012. We believe that external quality assurance programs improve the use of our devices and align with our commitment to improving product quality.

In the article “External Quality Assurance of Platelet Function Assays: Results of the College of American Pathologists Proficiency Testing Program,” Chandler et al. present and discuss the proficiency testing data for platelet function tests from 2012 to 2016. Given the high visibility of this article and its association with CAP, it would be difficult to take the opportunity to share some more context related to our device. We would also like to challenge some of the interpretation and discussion of the results that we feel could benefit from a balancing view.

Because it reflects a more holistic view of hemostasis and platelet contribution, it is by nature subject to more influencers than other, more targeted tests. In a recent review of perioperative thrombocytopenia, Nagrebetsky et al. came to the conclusion that the “assessment of viscoelastic properties of blood in vitro (thromboelastography) may also provide useful information on platelet function. However, this technique evaluates the combined effects of many components of hemostasis. Thus, it is not a platelet function test in a strict sense [...]”

Although the PlateletMapping test can be used for the assessment of platelet reactivity in response to medication, such as in the recent CREATIVE trial, a lot, if not most, of its use is in surgeries with high bleeding risk, such as cardiovascular and trauma surgery. This is important to note because the clinical reality of this test is much more heterogeneous than that of other tests that are targeted specifically at the platelet effects of certain drugs (mostly P2Y12 inhibitors). Some of the other tests described in this article present with more than 40 000 data points and more than a decade of experience. PlateletMapping testing has around 2000 data points and was only introduced into the proficiency testing program in 2012. With growing adoption, clinical acumen in using the test increases. The direct comparison with the other platelet function tests is misleading. Other frequently used tests, such as VerifyNow (Instrumentation Laboratory, Bedford, Massachusetts), are missing.

INHERENT LACK OF INTERPRETATION (POSTANALYTIC)

A key finding in the CAP data is that about half of the PlateletMapping tests are returned by the laboratory without an interpretation. Given the above context and the fact that there is no company-provided interpretation guidance for the PlateletMapping test performed on the TEG 5000 (as rightly pointed out in the article), these results are not surprising. If anything, they highlight an opportunity to further train laboratory personnel in the execution of this test, in addition to the already provided end user clinician training. Moreover, they should be provided with more guidance specific to the various therapeutic areas with which they are interacting. In our

claimant and defendants in asbestos litigation. Dr Galateau-Salle has no relevant financial interest in the products or companies described in this article.


External Quality Assurance of Platelet Function Assays: Results of the College of American Pathologists Proficiency Testing Program

To the Editor—We applaud the efforts of the College of American Pathologists (CAP) to provide proficiency testing to improve the quality and reliability of clinical test results. We are pleased to see that PlateletMapping testing available on the TEG 5000 analyzer platform (both Haemometrics Corp, Braintree, Massachusetts) has been included in the program since 2012. We believe that external quality assurance programs improve the use of our devices and align with our commitment to improving product quality.

In the article “External Quality Assurance of Platelet Function Assays: Results of the College of American Pathologists Proficiency Testing Program,” Chandler et al. present and discuss the proficiency testing data for platelet function tests from 2012 to 2016.

Given the high visibility of this article and its association with CAP, it would be difficult to take the opportunity to share some more context related to our device. We would also like to challenge some of the interpretation and discussion of the results that we feel could benefit from a balancing view.

Because it reflects a more holistic view of hemostasis and platelet contribution, it is by nature subject to more influencers than other, more targeted tests. In a recent review of perioperative thrombocytopenia, Nagrebetsky et al. came to the conclusion that the “assessment of viscoelastic properties of blood in vitro (thromboelastography) may also provide useful information on platelet function. However, this technique evaluates the combined effects of many components of hemostasis. Thus, it is not a platelet function test in a strict sense [...]”

Although the PlateletMapping test can be used for the assessment of platelet reactivity in response to medication, such as in the recent CREATIVE trial, a lot, if not most, of its use is in surgeries with high bleeding risk, such as cardiovascular and trauma surgery. This is important to note because the clinical reality of this test is much more heterogeneous than that of other tests that are targeted specifically at the platelet effects of certain drugs (mostly P2Y12 inhibitors). Some of the other tests described in this article present with more than 40 000 data points and more than a decade of experience. PlateletMapping testing has around 2000 data points and was only introduced into the proficiency testing program in 2012. With growing adoption, clinical acumen in using the test increases. The direct comparison with the other platelet function tests is misleading. Other frequently used tests, such as VerifyNow (Instrumentation Laboratory, Bedford, Massachusetts), are missing.

INHERENT LACK OF INTERPRETATION (POSTANALYTIC)

A key finding in the CAP data is that about half of the PlateletMapping tests are returned by the laboratory without an interpretation. Given the above context and the fact that there is no company-provided interpretation guidance for the PlateletMapping test performed on the TEG 5000 (as rightly pointed out in the article), these results are not surprising. If anything, they highlight an opportunity to further train laboratory personnel in the execution of this test, in addition to the already provided end user clinician training. Moreover, they should be provided with more guidance specific to the various therapeutic areas with which they are interacting. In our...