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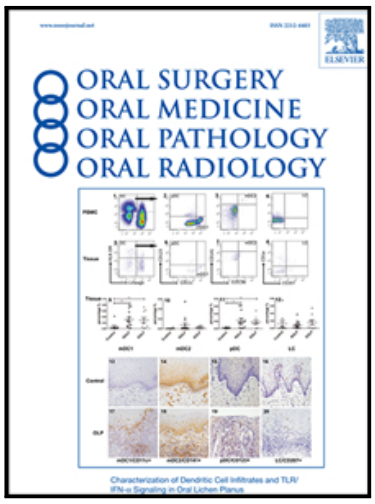

The Promise and Potential Peril of At Home Oral Cancer Testing

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The Promise and Potential Peril of At Home Oral Cancer Testing

Health care delivery continues to undergo dramatic disruptive alterations. The COVID-19 pandemic has further accelerated these changes across many areas of patient care including telemedicine, virtual diagnostic pathology and even remote robotic surgeries. At home cancer testing is another example of our rapidly evolving heath care model, with colon and prostate cancer leading the way. Current oral cancer screening guidelines have found the conventional visual tactile exam continues to be the most effective screening modality.[1-4] The caveat to this recommendation is that this requires widespread patient participation. A National Health Interview Survey found that 60% of the adult United States population visit a dentist on a yearly basis.[5] While this means that patients see their dentist more often than their physician, patient participation can certainly be increased to improve the overall effectiveness of oral cancer screening regardless of the modality employed.

Saliva is diagnostic sample that can be readily collected in a noninvasive manner in both the office setting and at home. The integration of cutting-edge technologies and the realization that saliva contains numerous potential biomarkers in the form of proteins, RNA, and DNA has driven a dramatic growth in the field of salivary diagnostics.[6,7] In fact, “point of care” salivary diagnostics in the clinical setting holds great promise to provide clinicians with real time diagnostic information in lieu of waiting days or weeks for results from the evaluation of a tissue biopsy or blood draw. Conversely, what is the potential utility of an at home saliva-based oral cancer test? Recently, a company working in the gut biome and supplement wellness space began marketing an at home oral cancer test. Using a proprietary combination of transcriptomics, systems biology and artificial intelligence, the company has developed a molecular biomarker signature that may be associated with the presence of oral cancer, with reported sensitivities and specificities of 90%. Conceptually, this may represent another game changing cancer screening test that could be performed in the comfort of one’s home. What is the strength of the evidence that this test can discriminate with high diagnostic accuracy between oral cancer and the many other oral conditions in the real-world setting? The available current data consist of a single manuscript presently under peer review and are limited to the comparison of normal patient controls versus patients with oral cancer.[8]

Screening can be defined as the application of a test or tests to people who are apparently free from the disease in question in order to sort out those who probably have the disease from those who probably do not.[9] Cancer screening is not intended to reach the level of being a

standalone diagnostic result. Importantly, in practice, cancer screening is rarely a binary (benign vs. malignant) result. This is particularly true in the oral cavity. A seminal paper by Dr. Bouquot screened 23,616 patients and reported that more than 10% of United States population had some type of oral lesion.[10] The 30 most common entities represented more than 93% of all reported lesions, with oral carcinoma ranked 24th overall. These 30 distinct pathologic entities represent an extremely wide array of conditions that can be generally categorized as inflammatory, infectious, autoimmune, traumatic, premalignant, malignant or systemic in nature, and potentially involve the oral mucosa, connective tissues and salivary glands. What are the transcriptomic profiles of the 30 most common oral lesions? What percentage of overlap is there between each common oral lesion and the oral cancer profile? How does the presence of one or more of these common lesions, in conjunction with oral cancer, affect the diagnostic accuracy of the test? Unfortunately, we do not know the answers to these and other critical questions because the study was not designed in a manner that is in keeping with Prospective-sample-collection-Retrospective-Blinded-Evaluation (PRoBE) standards. Consisting of five specific phases, PRoBE was developed by the National Cancer Institute's (NCI) Early Detection Research Network (EDRN) to address the issue of unreproducible and insufficiently validated cancer biomarkers.[11-13] In short, without performing an appropriately designed PRoBE compliant study, we simply do not know the true diagnostic accuracy of this test when used in the real-world setting.

Given the paucity of data regarding the ability of this test to discriminate between oral cancer and other common oral lesions/conditions in a real-world setting, one might ask how such a test would be able to reach the market. Most cancer screening devices/tests are handled very differently than drugs/invasive devices by regulatory bodies. For example, the test in question recently received the Food and Drug Administration (FDA) Breakthrough Device Designation. The goal of this voluntary program is to provide patients with timely access to new technologies that may provide more effective diagnostic and treatment options for life-threatening or debilitating diseases, while preserving the statutory standards for premarket approval, 510k clearance, and De Novo marketing authorization.[14] Furthermore, there are significant differences between the 510k paradigm and FDA approval.[15] Unlike FDA approval for novel therapeutics and invasive devices, 510k clearance, regardless of obtaining Breakthrough Device Designation, does not require a rigorous evidence of efficacy. Although bringing any cancer screening device/test without this type of real-world data is technically within the mechanisms allowed by the FDA, I find this business model unfortunate because it affords

companies the ability to market a product without requiring the appropriate data to demonstrate efficacy in a real-world setting. This is even more particularly concerning when considering the field of at home cancer screening testing.

In conclusion, the era of molecular diagnostics has arrived. At home cancer screening tests may address the challenges associated with patient access and compliance. They may also improve our ability to screen, diagnose, prevent and treat many different malignancies including oral cancer. However, just because one can perform a test that is currently available does not necessarily mean that we should do so or advocate for such. All cancer biomarker screening tests should have significant PRoBe compliant, peer-reviewed scientific evidence that it can discriminate between true normal, common non-malignant pathologies and pre-malignant/malignant pathologies with a reasonable degree of diagnostic accuracy. This would seem to be particularly true in the realm of at home cancer testing. The inability of cancer screening tests to demonstrate acceptable diagnostic performance characteristics may have profoundly negative impacts on the patients we are charged with caring for. For an example of how an underperforming oral cancer screening test can result in unfortunate clinical outcomes, I would respectfully ask that you consider the story of a “positive” oral cancer screening test that was recently reported.[16]

DISCLOSURE
None.

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Editor-in-Chief

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