



## Proteocyte Developing AI-Based Oral Cancer Predictor, Initiates Additional Clinical Validation

Mar 16, 2018 | [Leo O'Connor](#)

NEW YORK (360Dx) – Proteocyte AI is developing a prognostic test that informs physicians about a patient's five-year risk of developing oral cancer, an area that some researchers and physicians believe has a clear unmet need for better testing.

Proteocyte's test, Straticyte, combines machine learning-based artificial intelligence, protein biomarker S100A7, and biopsy imaging.

The company has made it available on a complementary basis for the past 18 months to build awareness and obtain samples for future clinical testing, and will begin offering a laboratory-developed test in the second quarter of this year, John Davis, its president and CEO, said in an interview.

In Proteocyte's first [study](#), published in March 2017 in the journal *Oral Surgery, Oral Medicine, Oral Pathology and Oral Radiology*, the authors concluded that "by quantitatively assessing S100A7, Straticyte better defines the risk for developing oral squamous cell carcinoma than histopathological dysplasia grading alone."

The test's sensitivity was 95 percent and its specificity 85 percent in that retrospective 150-patient study, Davis said. Straticyte was 20 percent more sensitive than the comparator method, histopathological dysplasia testing using an haematoxylin and eosin stain (H&E), which is the standard of care for diagnosing oral lesions, he added.

A second paper published on Straticyte in August 2017 in *Oral Oncology* reflected results of a retrospective 51-patient study. In response to a reader's request for clarification, the authors noticed a statistical error, Davis said. Because of the error, the author's reduced the test's sensitivity numbers from 71 percent in the published study to 48 percent, he said.

The journal said the reduction in sensitivity and the negative predictive value was too great and they decided to retract the paper, Davis said, adding that the authors have taken full responsibility for the statistical error, though they feel the paper's conclusions still hold value.

At first glance, "the correction from 71 percent to 48 percent appears to be significant," Davis said, "[but] the number only has meaning when you compare it to ... the sensitivity of the H&E test, which was only 3 percent and therefore [reflected] a 16 [times] improvement for Straticyte." In the study, the revised negative predictive values for Straticyte matched that of H&E at 36 percent, he said.

Proteocyte reviewed its numbers, shared updated statistics with the journal, and is looking to have revised numbers published, Jatin Shah, a senior attending surgeon and professor of surgery at Memorial Sloan Kettering Cancer Center, said in an interview. Shah said that he

is an advisor to Proteocyte AI but does not have a personal stake in the company's success, and he has not been involved in developing or validating the test.

Some of the questions about the published performance numbers emerged from a concern that a single-protein biomarker might not be able to produce the levels of sensitivity and negative predictive values published in the journal, he noted.

The new numbers still "show a statistically significant improvement" over the standard-of-care for diagnosis and analysis of oral lesions, he said. However, the development of the test "should be considered a work in progress," he said, adding, "I can't at this point call it the new standard of care, because we need new validation studies."

Based on a biopsy, the Proteocyte test combines and quantifies S100A7-positive cells using proprietary algorithms. According to the firm, it produces an index that's converted to a risk score, which the system compares with a reference database consisting of information from more than 150 annotated oral dysplasia cases with five-year outcomes. The system then calculates a score that indicates a patient's probability of a cancer occurring within five years, and whether the lesions are at a low, medium, or high risk of progressing to cancer.

In practice, Straticyte uses S100A7 immunohistochemistry on slides cut from a biopsy sample used for standard histopathology. The standard-of-care H&E test accurately shows whether a patient has cancer, Davis said, but the current grading system that clinicians use to calculate the risk of progression to cancer is subjective. The Straticyte test can be viewed as complementary to standard histopathology, he added.

In the *Oral Surgery, Oral Medicine, Oral Pathology, and Oral Radiology* study, 14 of the 65 patients that had been identified with mild dysplasia went on to develop cancer. Straticyte reclassified 13 of the 14 to a higher risk category. In the *Oral Oncology* study, 10 of the 16 patients that had been identified with mild dysplasia went on to develop cancer. Straticyte reclassified all 10 patients to a higher risk category, Davis said.

He noted that the firm plans to begin two clinical trials during the next 30 to 60 days, one at the University of Maryland and another at the University of Alabama, Birmingham, and that the firm intends to use the results of those clinical studies to further validate the test and apply for regulatory approvals.

The Toronto-based firm believes that the test will enable earlier treatment of patients with oral lesions that could progress to cancer, contributing to the patients' quality of life and reducing healthcare costs, Davis said.

"More than 70 percent of oral cancer patients are diagnosed at stages 3 or 4, and they progress asymptotically and without pain," he said. "Straticyte allows clinicians to obtain early identification of patients that are at risk and develop a customized treatment pathway."

Ross Kerr, a clinical professor in the department of otolaryngology-head and neck surgery at New York University, agreed that standard-of-care histopathology "is not the best predictor" of which oral lesions will progress to malignancy.

"The most important thing related to early detection is to be able to perform a comprehensive examination of your patient," Kerr said. "Unless you're looking for lesions in the mouth, you are not going to find them. When you find one, the question is whether it's cancer or not."

Some of the lesions that clinicians see are categorized as premalignant, he said. They are dysplasias, abnormal cells in the skin-lining the inside of the mouth. About 5 percent of them become malignant, Kerr said, adding, "The question of which lesions will transform

over time is a really important question, so finding new markers and tests that will help us better predict malignant transformation is also really important."

Moderate and severe dysplasia patients generally have their lesions excised, but mild dysplasia patients can be left to watchful waiting or lost to follow up, Davis noted.

Proteocyte is currently working with the University of Western Ontario in London, the University of Alberta in Edmonton, and Mount Sinai Services in Toronto to obtain scanned images of biopsy samples that it processes through Straticyte.

Following the launch of a laboratory-developed test, the firm plans to seek Class III pre-market approval from the US Food and Drug Administration within the next 18 to 36 months, Davis said. It is also developing a platform that would use the same biomarker and artificial intelligence platform for use at the point of care, though Davis noted that the regulatory pathway for the POC device has not yet been determined.

He said that according to the firm's estimates, the global market size for biomarker testing of oral cancer lesions is about \$2.4 billion.

Straticyte is among a few cancer risk tests that the firm is developing using the same technology platform. It has identified biomarkers that are reflective of breast, prostate, and thyroid cancers, Davis said. "As we continue to move forward and grow as an organization, we'll develop products for those areas as well," he added.

While conducting proteomic studies of neck and head cancers, researchers at York University and Mount Sinai Hospital in Toronto discovered protein S100A7 and other candidate biomarkers for oral pharyngeal early neoplasia.

Proteocyte, founded in 2011, licensed use of the biomarkers and added its own intellectual property by combining the biomarkers with a prediction algorithm and the imaging software that it developed, Davis said.

The firm has attracted more than \$4 million in funding from research grants and high-net worth angel investors. It is completing a bridge round of \$600,000 in financing that it expects will close within the next 30 to 60 days. Some of the funds from the bridge round will be used to help Proteocyte develop an economic model that it intends to use to obtain reimbursement from private US payors, the US Centers for Medicare & Medicaid Services, and Canadian agencies.

The firm plans to launch a \$6 million Series A funding round in early Q3, or sooner, which would enable it to "complete some of the necessary requirements to commercialize the test and begin generating revenue," Davis said. He noted that the Series A funds would also permit the company to continue development of additional tests in its pipeline, with a focus on a point-of-care test for oral cancer.

According to Proteocyte, oral cancer affects 450,000 people per year worldwide and, primarily because of late diagnosis, has a five-year mortality rate of about 47 percent in the US and 50 percent worldwide. Early-stage diagnosis of localized disease lowers the mortality rate to 17 percent, it added.

"Based on preliminary numbers, we believe we can save the healthcare system a significant amount of money by identifying patients early and enabling suitable treatments," Davis said.

He said that he expects that when the company launches its lab-developed test, it will be available at \$400 or CA\$450 for patients.

The company recently changed its name from Proteocyte Diagnostics to Proteocyte AI. The artificial-intelligence component of its test "better exemplifies what we are as an organization and our future direction," he said.

Investors tend to consider diagnostic companies as requiring a "long haul" approach to get to market, he noted. But Proteocyte is a prognostic company, and artificial intelligence, an increasing component of its test, "allows us to be more efficient in our delivery model and to scale globally," Davis added.

Kerr said he believes that the challenges of obtaining reimbursement are among the greatest for tests like Straticyte in getting into the US market, but they are not an impediment in a national health system where tests tend to be covered for patients. There are also challenges related to understanding the disease, he said, adding, "Although we are moving in the right direction, not everyone that treats patients with oral lesions really understands the disease and knows when to apply these types of new tests."

Memorial Sloan Kettering's Shah noted that the success of the test in achieving adoption will depend on its ability to show statistically significant sensitivity and negative predictive values in clinical studies.