UNC study highlights diagnosis of lung cancer subtypes

by Mary Ruth Helms — last modified May 17, 2012 09:24 AM

In the processes of treating most cancers, one of the key pieces of information is the appearance of the tumor under the microscope using a technique called light microscopy. In lung cancer, for example, the appearance of the tumor determines both which chemotherapies are safe and which chemotherapies are effective. In addition, tumor appearance also suggests which patients should be tested for mutations that can be targeted by some of the most effective and safest drugs on the market.

Drs. Juneko Grilley-Olson and Neil Hayes are co-first authors of the study.

Until recently, many of the mutations in lung cancer were unknown and the therapies not available, such that light microscopy was considerably less important for patient treatment. Now that accurate diagnosis of tumors under the microscope has become so important, investigators at UNC wanted to estimate how accurately it can be applied by pathologists (physicians who are experts in light microscopy) and what factors are related to improved diagnosis.

A UNC-led study performed the most extensive review ever of the diagnostic accuracy of classification of tumors of the lung using light microscopy, and identified both areas of concern as well as opportunities for future improvement in the vital process of lung cancer diagnosis. While the study was performed under artificial conditions that do not reflect the full review given to patients in clinical practice, the study identified that a significant fraction of cases were difficult to reproducibly categorize. In brief, when shown the same slide under experimental conditions, 30-40% of slides were assigned competing diagnoses across the set of pathologists in the study. In theory, such disagreements would have resulted in the treating physicians assigning patients to different treatments in the care of the patient's lung cancer. The study evaluated factors that related to increasing agreement in pathologists such as years of experience and subspecialty training in lung cancer.

It is important to note that the study estimates of accuracy are likely an underestimate of the accuracy of diagnosis in clinical practice since many routine components of patient care were intentionally not available to the pathologists in the current study, in order to isolate this key component of the diagnostic process. However, the study does highlight some concerns and emphasizes that improvements in accurate diagnosis could have an immediate impact on assigning patients to the correct therapies.

Juneko Grilley-Olson, MD, co-first author of the study and assistant professor of medicine, says, "Our study is the first to look at the entire (comprehensive) diagnostic classification system as well as the clinically relevant squamous and non-squamous subsets of lung cancer.

"This study is important because we need to know what factors make the specimen slide most useful to pathologists. Of course, in clinical practice, any diagnosis is based on much more information and consultation than just the pathology slide; however, having the most informed pathology data is a key component in the diagnostic process.

"The most significant NSCLC (non-small cell lung cancer) identifier is tumor subtype: squamous cell or non- squamous cell. The subtype shapes treatment decisions, especially important with targeted therapies currently used to treat NSCLC. For

example, we know that patients with squamous type NSCLC are at increased risk for bleeding if given bevacizumab (Avastin), so the drug is used only in patients with non-squamous type NSCLC. Pemetrexed (Alimta) has been proven in clinical trials as less effective with squamous type NSCLC.

“With NSCLC treatment, we’re at a similar place as breast cancer therapy was when the drug tamoxifen was introduced. Tamoxifen was given to many patients, but only some benefited. Once breast cancer sub-types were defined, the drug could be selectively given to those who would most benefit.”

Their report appeared in the May 14, 2012 online issue of the Archives of Pathology & Laboratory Medicine. The study, called, Validation of Interobserver Agreement in Lung Cancer Assessment (VOILA), now has a follow-up study underway that includes more pathologic data in addition to the tumor specimen slides.

The VOILA study involved 24 pathologists recruited from the Pulmonary Pathology Society and community practices. Each was asked to evaluate one tumor sample slide and make a diagnosis. This was then simplified to the key categories, squamous or non-squamous non-small cell lung cancer. The digital slides were developed from a primary resected lung cancer specimen. The pathologists based their diagnosis on criteria established by the 2004 World Health Organization classification system for non-small cell lung cancer.

Study scientists report several variables that can facilitate the diagnostic process including better slide quality, advanced pathology expertise and confidence in their assigned diagnosis.

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