Using tumor DNA to refine lung cancer staging and treatment

The treatment of non-small cell lung cancer (NSCLC) is guided by disease stage as assessed by clinical and pathologic criteria. Clinical tumor stage is determined by imaging including computed tomography (CT) scans, magnetic resonance imaging (MRI), positron emission tomography (PET) scan, and evaluation of lymph nodes in the chest using bronchoscopic sampling (camera into the airways). For those patients with NSCLC that can be readily removed surgically the treatment approach often involves an initial surgery. Following surgery the tumor and surrounding lung and lymph nodes are examined under the microscope to determine the pathologic stage.

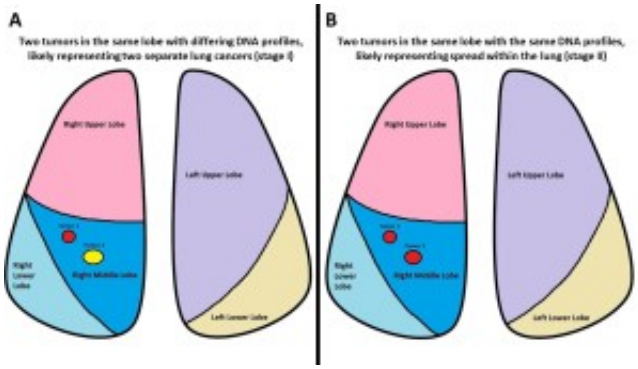

Fig. 1. Graphical depiction of two similar lung cancer presentations separated using genomic profiling.

Due to the high rates of NSCLC recurrence after surgery alone a series of clinical trials tested whether the addition of chemotherapy following surgery (adjuvant treatment) reduces the chance of tumor recurrence and extends patient survival. For patients with stage II and stage III disease there is a clear benefit to adjuvant therapy, however, the benefit for stage I patients is less clear, and some patients may be harmed by adjuvant chemotherapy. A particular problem arises when a patient has two tumors in the same lobe of the lung (see figure) as traditional analyses cannot reliably determine if these are two separate tumors or spread from one place to another within the lung. Therefore, there are likely lung cancer patients being both under-treated, and over-treated using the current staging system, which is an imperfect reflection of tumor biology.

Newer technologies such as comprehensive genomic profiling (CGP) examine tumor DNA for changes in several hundred genes that may be altered in cancers and provide insight into tumor biology and treatment choices. Combining this DNA sequencing technology with microscopic examination may improve tumor staging to guide patient therapies. Using CGP we examined both tumors in a patient with NSCLC and two tumors in the same lobe of the lung, and found that both tumors had identical DNA changes across multiple genes (tumor profiles). This finding strongly argues that both came from the same originating cell and had spread from one place in the lung to

another, likely reflecting more aggressive biology. This finding was used to confirm stage II disease and guide the patient's treatment, and suggests this approach may have broader applications in lung cancer and other tumors.

Publication

The Clinical Use of Genomic Profiling to Distinguish Intrapulmonary Metastases From Synchronous Primaries in Non-Small-Cell Lung Cancer: A Mini-Review.
Klempner SJ, Ou SH, Costa DB, VanderLaan PA, Sanford EM, Schrock A, Gay L, Ali SM, Miller VA.
Clin Lung Cancer. 2015 Sep