

## Researcher Profile: Farhood Farjah, MD, MPH



Dr. Farhood Farjah

**L**ung cancer is the leading cause of death from cancer among men and women, and it is responsible for more deaths than breast, prostate, and colorectal cancer combined.

There are many misperceptions about this disease fueling pessimism and neglect. For instance, many perceive lung cancer to solely be a disease of smokers, but lung cancer in patients

who have never smoked is the sixth most common cause of cancer death in the U.S. Many also believe that lung cancer is incurable. This belief is fueled by the fact that overall five-year survival rates have been dismal (~15%), and these survival rates have been constant for over three decades despite significant advances in diagnostic and therapeutic tools. The reason for poor overall patient outcomes has been presentation of disease at a late stage when curative intent therapy is no longer feasible.

However, a landmark study – the National Lung Screening Trial – published in 2011 has ushered in a new era of early-detection and cure through annual screening of high-risk patients with low-dose computed tomography. Recently, the US Preventative Services Task Force endorsed lung cancer screening

effectively requiring all commercial insurers to cover the costs of screening, and shortly thereafter the Center for Medicare and Medicaid Services followed suit. These policy changes will have a substantial positive impact extending beyond a few hundred thousand lung cancer patients each year to millions of at-risk persons. More than any other time in history, the spotlight on lung cancer now extends along the entire cancer continuum from prevention to survivorship with significant implications for population health.

Dr. [Farhood Farjah](#), Assistant Professor, Division of Cardiothoracic Surgery, is interested in improving the delivery of health care to populations at-risk for lung cancer, lung cancer patients, and lung cancer survivors with an eye towards improving individual and population health.

### Understanding the effectiveness, safety, and costs of lung nodule evaluation

The benefits of early detection of lung cancer must be weighed against the risks of excessive testing, particularly since only 10% of people with an incidentally detected pulmonary nodule have lung cancer. Under-evaluation may result in a missed opportunity to cure lung cancer; over-evaluation unnecessarily exposes people to the risks of diagnostic procedures and increases the costs of care. Practice guidelines intended to optimize nodule evaluation recommend varying intensities of diagnostic work-up depending on risk.

A recent study found that only 55% of individuals with an incidentally detected lung nodule received guideline concordant nodule evaluation. The investigators recommended designing system-level interventions to increase guideline concordance. However, doing so assumes that practice guidelines will lead to better outcomes – an assumption that may not be valid. Better understanding the relationship between practice guidelines and outcomes would help determine whether resources should be invested in improving guideline concordance or developing new strategies to evaluate nodules – for instance with risk-prediction models, biomarkers, and/or centralized, multi-disciplinary nodule clinics.

**“Dr. Farhood Farjah is passionate about research examining how doctors deliver care to lung cancer patients in the United States. The goal of his work is to improve care delivery so that all patients have the best possible outcome. Other goals of his work are to increase the quality and value of thoracic oncologic care.”**

Until recently, an important barrier to studying the relationship between guideline concordance and outcomes was an inability to identify a cohort of individuals with lung nodules. Researchers at Kaiser Permanente (KP) recently developed a natural language processing (NLP) algorithm to scour CT radiology reports to identify health plan members with a lung nodule. Dr. Farjah received funding and support through the [Cancer Research Network \(CRN\)](#) Scholars Program and a CRN Pilot Grant to evaluate the performance of this NLP algorithm at another CRN site – Group Health (GH). Findings from this investigation revealed that NLP is reliable and portable across CRN sites and that its principal value is decreasing the burden of chart abstraction by up to 75%. The implication of this work is that a multi-center study investigating the effectiveness, safety,

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and costs of guideline concordant nodule care is feasible. Dr. Farjah is currently seeking funding to conduct this investigation in collaboration with scientists from GH, KP, and the [Fred Hutchinson Cancer Research Center \(FHCRC\)](#).

### Predicting nodal disease in individuals with suspected or confirmed lung cancer

Of the 224,000 patients with newly diagnosed non-small cell lung cancer (NSCLC) each year, two-thirds (~158,000) will not have metastatic disease on presentation. For these patients, it is imperative to determine the extent to which (if any) cancer has spread to lymph nodes because the decision to recommend one of several vastly different treatment options (e.g. surgery alone versus definitive chemo-radiation) hinges on nodal status. Findings from CT and positron emission tomography (PET) are used to predict nodal disease and guide the use of invasive staging procedures (e.g. mediastinoscopy, endobronchial ultrasound-guided biopsy, etc.).

Practice guidelines have been developed to direct the use of invasive staging procedures based on radiographic findings. Although recommended selection criteria are highly sensitive (100%), they have poor specificity (35%) resulting in unnecessary use of invasive procedures in up to two-thirds of patients who are truly node-negative. In the absence of better imaging modalities, other ways to improve prediction are through better use of existing information and/or the use of novel risk factors for nodal disease.



Dr. Farhood Farjah consults with his patient at the [Seattle Cancer Care Alliance \(SCCA\)](#). Watch the video [here](#).

Risk-prediction models are one way to make better use of existing information. During his clinical fellowship at [Memorial Sloan Kettering Cancer Center \(MSKCC\)](#), Dr. Farjah developed and internally validated a prediction model for nodal disease based on six clinical risk factors available prior to treatment in a population of NSCLC patients without evidence of distant or mediastinal disease by PET. This model was recently externally validated in a

similar population from the University of Washington Medical Center (UWMC). Simulation shows that had the prediction model been used in practice at UWMC, the accuracy of patient selection for invasive staging procedures would have been substantially higher and the use of invasive procedures would have been substantially lower (by 50%). The practical implication of this finding is that use of the risk-prediction model may increase the value of care. Funding is being sought for a pilot randomized trial comparing the use of risk-prediction to guide invasive staging versus usual care with an intent to eventually conduct a multi-center, pragmatic randomized trial in collaboration with participants from [CERTAIN's Washington State Lung Cancer Quality Improvement Collaborative](#).

In order to develop a prediction model for the much broader population of 150,000 patients without metastatic disease, a novel risk-factor would have to be identified that would complement or outperform PET findings – the overwhelmingly dominant predictor of nodal disease. Vascular endothelial growth factor (VEGF)-C is a marker of nodal disease that can be measured in plasma. Basic research demonstrates that VEGF-C is essential for lymphangiogenesis – a mechanism by which epithelial tumors are believed to spread to lymph nodes. Epidemiologic research shows elevated plasma levels of VEGF-C in node positive NSCLC patients compared to node-negative patients, individuals with benign nodules, and health volunteers.

A unique collaboration with investigators from the FHCRC Lung Biorepository (Dr. David Madtes) and the [Mulligan Lab](#) (Dr. [Michael S. Mulligan](#)) allowed for a pilot study of patients with suspected or confirmed, non-metastatic NSCLC staged by PET. The goal of this investigation was to determine whether VEGF-C improves the predictive performance of PET, and the study findings showed that it did. This pilot study led to funding from the [CHEST Foundation](#) to develop a prediction model for nodal disease using *multiple* radiographic risk factors and VEGF-C, and to determine whether the prediction model outperforms practice guideline selection criteria for invasive staging. This study is currently underway and is expected to be completed in 2016.