Editorial

Management of the pulmonary nodule—shifting paradigms and an opportunity for change

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The diagnosis of the pulmonary nodule, has metaphorically, been a diagnostic "Holy Grail" since the advent chest roentgenography over 100 years ago. We know where the pulmonary nodule is but until it is fixed in formalin, stained and placed under a microscope, we do not know what it is much like the proverbial Holy Grail. Although the vast majority of pulmonary nodules are benign, the early and accurate diagnosis of a malignant pulmonary nodule is of profound importance and the science of diagnosing pulmonary nodules has undergone an ever-changing evolution which can be divided into several eras.

The first era began in 1896 with the introduction of roentgenograms. The same period saw the introduction of the rigid bronchoscope by Gustav Killian in Germany and its popularization by Chevalier Jackson in the United States. In 1964, John D. Steele, MD, a professor of surgery at UCLA, published the monograph—*The Solitary Pulmonary Nodule* (1). A total of 1,034 cases of solitary pulmonary nodules less than 6 cm were submitted to this study. The monograph is largely concerned with the radiologic characteristics of benign and malignant pulmonary nodules. A total of 887 male patients underwent resection, 316 of the resections revealed malignancies. However, 65 of the nodules were hamartomas and 474 were granulomas. In other words, 65.5% of the resections were performed for benign disease. Today, such a high rate of pulmonary resections for benign disease would be clearly unacceptable. In tandem with roentgenographic analysis of pulmonary nodules, evaluation using rigid bronchoscopy also had low diagnostic yields.

The next era began in 1972 when computed tomographic (CT) imaging was developed by Godfrey Hounsfield of EMI Laboratories and Alan Cormack of Tufts University, a discovery for which they were later awarded the Nobel Prize for Physiology or Medicine. Initially, this technology was dedicated to imaging of the head but by the mid-1980s it was capable of imaging the entire body and became widely disseminated throughout the world. CTs were far more informative about pulmonary nodules than chest roentgenograms. They gave precise information about the anatomic location of nodules, were able to detect smaller nodules and gave increased information about a nodule's morphology and consistency. In turn, these findings led a higher degree of descriptive accuracy. In addition, improved cytological technologies spurred radiologic interventionalist to increasingly perform fine needle aspirates of peripheral pulmonary nodules. The fiberoptic bronchoscope was developed in 1966 by Shigedo Ikeda and the proliferation of this technology paralleled the proliferation of CTs. Fiberoptic bronchoscopy allowed for access to areas of the lung previously unimagined with rigid bronchoscopes. There was an obvious increase in the diagnostic yield as these technologies combined to evaluate pulmonary nodules and large numbers of unnecessary diagnostic surgeries have been avoided.

Rigid thoracoscopy was originally reported on by H.C. Jacobeus, a professor of medicine, in Stockholm in 1910. This procedure added very little, if anything,

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to evaluation of pulmonary nodules. In the early 1990s, however, fiberoptic thoracoscopy became available and this technology allowed for a visual inspection of most of the thorax and biopsying of visible pulmonary nodules. At the same time, positron emission tomography (PET), although developed much earlier, began to be widely used in the evaluation of pulmonary nodules. For lung cancer, it has an overall sensitivity of 96%, a specificity of 79% and accuracy of 91% (2). Although these numbers are laudatory, there are still wide variations in interpretation of positive results and this study cannot be considered an absolute diagnostic predicator in the evaluation of lung cancer.

The development and broader use of endobronchial ultrasound (EBUS) and navigational bronchoscopy (NB) have made the fiberoptic bronchoscope a much more formidable diagnostic tool. EBUS allows for the accurate biopsying of central lung lesions, and mediastinal lymph nodes. NB is being used with increasing frequency to biopsy nodules in the periphery of the lung as well as placing dye markers into peripheral lung nodules that would otherwise be invisible to a thoracoscopist (3). In institutions that have this technology, it is being used as an adjunct to other procedures—CT guided FNA, VATS, hybrid theatre Dyna-CT, etc. or in some cases employed as the initial diagnostic procedure in the evaluation and work up of the indeterminate pulmonary nodule (4,5). It is reasonably accurate and less likely to cause pneumothoraces than CT-FNAs. NB also allows for the placement of fiducial markers for Stereotactic Radiosurgery in patients with lung cancer who are otherwise not candidates for lung resection (6).

During the transition into the twenty first century, there continues to be significant interest in minimally invasive technologies for the diagnosis of lung cancer especially in its' early stages. Lung cancer screening programs (7) have become increasingly common across the United States in the hope of establishing early diagnosis and improved survivorship in patients with lung cancer. Breath analysis of lung cancer related to volatile organic compound profiles for differentiating malignant from benign nodules is being evaluated (8). Research is being conducted using a serum microRNA signature (the miR-test) to identify pulmonary nodules that are malignant (9). There are a myriad of other studies including serum plasma analysis, circulating DNA, proteonomics and tumor associated antibodies being conducted in the hopes of differentiating benign from malignant lung nodules and achieving early diagnosis (10). Furthermore, as we look to the future, the ability to identify the lung cancer subtype, for example the subtype of adenocarcinoma, from a blood, sputum, FNA, or intra-operative frozen section specimen will become increasingly important as we recognize the difference in prognostic implications and realize other potential therapeutic options other than major lung resection.

The goal of identifying one or more pulmonary nodules as benign or malignant has employed a multitude of tests and technologies in the hope of avoiding a major operation, that frequently includes a lung resection, when it is not really needed. It is unlikely that any one test will ever achieve that goal and in all probability a panel of tests, some non-invasive and some invasive, will always be needed to differentiate the benign from the malignant nodule.

In turn, the mindsets of physicians who deal with this challenging problem will need to undergo profound changes. Pulmonologists, thoracic surgeons, oncologists, radiation oncologists and the many others who treat lung cancer will have to realize that in the case of lung cancer they are not different specialties. They are the same specialty and each act as extension of the others. Specialty ownership of a diagnosis, a technology or a test needs to become a historical concept rather than an actuality. In point of fact, the days of distinction between the historical "barber and apothecary" and the somewhat artificial split that that distinction implies is long over. There has been a clarion call for the development of multidisciplinary teams but even this approach has its downsides. While such an approach, in all probability, represents an improvement, perhaps even a substantive one, often, at the conclusion of a multidisciplinary clinic, the various specialties return to their respective "corners".

To address these issues, it is our perspective that in order to improve the management of pulmonary nodules as well as other pleuropulmonary diseases two concepts need to be developed and more widely deployed. The first concept is the emergence and development of the nurse navigator role-one that is specifically designed to bridge some of the gaps in care as it is now delivered. The second, in so far as we are aware, has not yet been employed or developed. There is a strong and pressing need to develop "trans-disciplinary" teams. While this may seem like mere semantics, the implication is that approaches to complex problems, especially in the current era where the astronomical increase in the magnitude and breath of available data, defies and confounds even the most diligent individual or episodic groups of individuals to deliver consistent, high quality integrated care. To that end, whether the problem is the pulmonary nodule, and one need only look at the breath

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of specialties contributing to this edition, or the myriad of other lung diseases, or for that matter other disease entities involving other organ systems, the need to routinize diverse approaches and perspectives will be critical in advancing disease management well into the foreseeable future.

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Footnote

Conflicts of Interest: Subsequent to the completion of the supplement, Dr. Krimsky is a part-time employee of Medtronic. Prior to that he was a consultant for Medtronic with intellectual property rights. The other authors have no conflicts of interest to declare.

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