Coronary CT Angiography and Incidental Pulmonary Nodules

Running title: Bluemke; CCTA and incidental lung nodules

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Incidental findings are an important topic in diagnostic imaging. Because of the comprehensive nature of computed tomography (CT) scanning, incidental findings are found seemingly on almost every CT scan performed for a wide variety of reasons in a radiology department. Many of these incidental findings are benign and immediately dismissed, such as a liver cyst. Other findings require more extensive interpretation and management. In regards to coronary CT angiography, a similar problem exists. Even though we have a primary interest in the heart, the CT scanner delivers radiation to all tissues of the chest, such as the bones, lung parenchyma and breast tissue. Extracardiac findings are reported to occur in 15% to 67% of CCTA examinations\(^1\) and the vast majority (about 80%) represents pulmonary nodules.

For diagnostic radiologists, evaluation of all tissues in the x-ray path has long been the standard of care. If an x-ray of the shoulder includes the lateral lung fields, the diagnostic radiologist evaluates that portion of the lung for an infiltrate or lung mass. Similarly for CT scanning, if the primary request is to evaluate for pulmonary embolus (pulmonary arteries) or lymphadenopathy (mediastinum), we also expect the radiologist to evaluate all tissues that are exposed to the x-ray beam, including the lungs.

Cardiologists who interpret coronary CT angiography (CCTA) examinations may not have training that allows diagnostic evaluation of all tissues within the field of view of the x-ray beam. This results in two different strategies to deal with extracardiac tissues beyond the coronary arteries:

1) The CCTA images can undergo a separate evaluation by a radiologist for interpretation of extracardiac tissues. This approach requires additional time/effort that may not be fully reimbursed. Some office based practices may not have radiology expertise available. A potential solution is to acquire sufficient training to allow confident handling of such findings.
2) Tissues beyond the heart can be (mostly) removed in an automatic manner by the CT scanner software (Figure 1). Noncardiac data may be digitally discarded. This digital deletion approach is only partially successful, since some lung tissue invariably remains in the field of view. According to an expert consensus statement, the digital deletion approach reduced the number of incidental noncoronary findings from 20% to 2%.

The justifications for options (1) or (2) tend to be along medical and/or ethical lines of reasoning. For example, medically there may be no clinical indication to look at the lungs in the first place -- the ordering physician asked only that the coronary arteries to be evaluated. In this scenario, evaluation of the lungs requires additional effort that may not be reimbursed by payers.

The study by Goehler et al. in this issue of Circulation approaches the problem of incidental pulmonary nodules from an economic and, indirectly, an ethical perspective to estimate the potential cost burden to society to evaluate incidental pulmonary nodules on CCTA scan. They used data from a CCTA clinic at the Massachusetts General Hospital (MGH) as the basis for the MGH Lung Cancer Policy Model. The Lung Cancer Policy Model projected the development and progression of lung cancer over time as well as the likelihood of detection of nodules with diagnostic follow-up care and therapeutic treatment. The economic model takes into account death not only from lung cancer, but also other causes such as coronary artery disease. At the MGH, 591 of 3665 (16%) patients undergoing CCTA had pulmonary nodules that required follow up. Even though 5.8% of patients were projected to have lung cancer, the majority (94%) were projected to die from other causes including coronary artery disease. Thus as viewed from an economic perspective, the work-up of a pulmonary nodule had little consequence in improving the health of society. The work up of all patients to find the minority 6% who were at greatest risk was costly, between $129,800 to $154,700 per quality adjusted life year (QALY). The authors concluded that
this cost was greater than the generally accepted threshold for approval or payment of medical interventions, which the authors refer to as $100,000 per QALY.

Most physicians are very aware of the increasing implementation of low radiation dose CT screening programs for surveillance of patients at high risk for lung cancer. In this case, the pulmonary nodules are not incidental, but rather the goal of the CT scanning. The basis for such programs is the National Lung Screening Trial (NLST) that enrolled 53,454 individuals at high risk for lung cancer, demonstrating that CT screening reduces mortality of lung cancer compared to chest x-ray.3 The NLST trial included patients who were 55-74 years and who had smoked at least 30 pack years in their lifetime. In this trial, a 20% reduction in lung cancer mortality was demonstrated compared to screening with x-ray radiography. The cost of lung cancer screening has been estimated to between $126,000 and $166,000 per QALY when compared with no screening and assuming background quit rates.4 This cost is similar to that identified Goehler et al.2

The acceptance of lung cancer screening programs by CT gaining traction in the United States.5,6 Algorithms such as the MGH Lung Cancer Policy Model are only as good as the data and assumptions that feed the computations. A key data element for the Lung Cancer Policy Model was the Fleischner Society policy statement for evaluation of incidental pulmonary nodules. In 2005, the approach to dealing with incidental pulmonary nodules was significantly influenced by a statement from the Fleischner Society, a think tank of academic chest radiologists with vast expertise in the field. Guidelines exist for both solid pulmonary nodules7 as well as subsolid nodules.8 The MGH Lung Cancer Policy Model used the Fleischner guidelines for the more common solid pulmonary nodule (Table 1). For solid pulmonary nodules, these guidelines divide patients into either low risk patients (minimal or absent history of smoking and of other known risk factors) or high risk patients (history of smoking or of other known risk factors). Overall,
adherence to these guidelines is only moderate, about 35-60% amongst practicing radiologists. 9, 10

The clarity of the Fleischner guidelines (Table 1) is compelling. At my institution, all of our CT scanners can routinely reconstruct a CT image at a slice thickness of about 0.5 mm, resulting in frequent detection of nodules below the 4 mm threshold suggested by the Fleischner guidelines. For low risk patients, the mental relief that a large fraction of detected nodules do not require follow up is very significant to the practicing radiologist. On the other hand, what exactly do we know about the behavior of a 4 mm nodule versus a 5 or 6 mm nodule? Also, the follow-up intervals by the Fleischner guidelines give considerable latitude to the practitioner: should a nodule be followed at 6 month or 12 month intervals, and what is the impact on diagnosis (and cost)? Like other expert statements, the Fleischner guidelines have been generated in part by expert experience when clinical trial data is not available. Validation of these guidelines has not been prospectively been performed.

The foundations of the Fleischner guidelines7 included knowledge about a) the growth rate and biology of lung cancer, b) the relative risk of smoking and c) the characteristics of modern CT scanners. The Fleischner statement authors did not directly evaluate the economic impact of their recommendations using metrics such as QALY. Since both the Fleischner guidelines and the MGH Lung Cancer Policy Model make many assumptions about lung cancer growth rates, a question is if the assumptions are the same in both the guidelines and the model. Assuming no contradictions between the two, the results of Goehler et al. present an interesting opportunity to test the cost effectiveness of Fleischner guidelines. Could economic models help us refine our guidelines in the future? Currently, metrics such as QALY are not employed in appropriate use guidelines from our major professional societies. 11

Besides the Fleischner guidelines, there are other assumptions by Goehler et al. that would
be interesting to subject to a sensitivity analysis. For example, if one presumed that a threshold cost was $100,000 per QALY, what would the costs of the various medical services need to be in order to attain that QALY goal? Alternatively, how sensitive is the MGH model to the success of treatment of lung cancer? In the typical regression model, the beta coefficients characterize the magnitude of the effect sizes. But in the economic model from Goehler et al., the relative contributions of various assumptions are not readily visualized. From their table 2b, the mortality results appear quite dismal: lung cancer mortality was projected at 6.4% without any follow-up of nodules. But medical intervention appears to have little effect – only a reduction of 0.3% if lung nodules are followed-up and intervened upon. At the same time, most patients (94%) die from other causes, including coronary disease. The results of Goehler et al. seem to point to the current futility of treatment of lung cancer combined with the fact that patients die from many other causes (e.g., infections or a wide variety of ailments).

The limitations of a strictly economic approach to pulmonary nodule evaluation are quite straightforward. Given 100 individuals with nodules, the model cannot determine a priori which 6 people will have lung cancer. Those 6 people stand an excellent chance of cure of their lung cancer since it is detected at an early stage. Unfortunately, the MGH Lung Cancer Policy Model says that in order to find those 6 people, we invariably harm 94 people with unnecessary testing and procedures -- at relatively high financial cost to society. Medically, it is difficult to potentially ignore the 6 people we could help. On the other hand, the diagnostic imaging community is probably relatively poor at providing information to the other 94 patients about the ‘risks’ of C ATA testing in relationship to incidental findings.

Although Goehler et al. address the issue of pulmonary nodules,2 we will soon see yet another paradigm shift in CT technology that may be more wide reaching. The latest generation
of CT scanners being delivered to sites in the U.S. and worldwide is so fast that special “coronary
CT” settings may not be required in all cases. In other words, routine screening CT of the chest for
conditions such as adenopathy, infection, etc. will soon contain sufficient information for full 3-
dimensional reconstruction of the coronary arteries at 0.5 mm spatial resolution. Coronary artery
questions could arise frequently: routine CT chest studies are performed at least 100-fold more
frequently than dedicated CCTA studies. Instead of the quandary of cardiologists interpreting
pulmonary nodules, it is conceivable that the general diagnostic radiologist would face a decision
of whether to interpret the coronary arteries seen on a routine chest CT. Currently, the large
vessels (aorta, pulmonary arteries) are evaluated; why not smaller coronary arteries as well? One
could argue that the impact of incidental coronary artery stenosis is much greater than that of
incidental pulmonary nodules: ischemic heart disease has a high prevalence and is the leading
cause of morbidity and mortality world-wide.12 Perhaps we should subject such questions to
economic modeling such as that presented by Goehler et al.2

Overall the work of Goehler et al. is extremely interesting and thought provoking. My own
conclusion is that our current guidelines for treatment and diagnosis of incidental pulmonary
nodules have not caught up with the proliferation of CCTA testing. Should we at least temporarily
ignore the lung findings until therapies for lung cancer therapies improve? As a physician and
radiologist, I am quite biased against that approach. In medicine, a busy practitioner in almost any
discipline encounters dozens of patients a week for which optimal decision patterns are unknown.
For CT scanning, we can digitally delete lung nodules to avoid making decisions, but deletion of
medical information in any other discipline is not considered to be ethically sound. Algorithms
such as those by Goehler et al. present a step forward to help us understand the implications of
various patient management strategies.
Conflict of Interest Disclosures: Dr. Bluemke reports research agreements with Philips Healthcare and Siemens Medical Systems.

References:


Table 1. Fleischner Society Guidelines for solid pulmonary nodules detected incidentally in persons age 35 yrs and older. Adapted from MacMahon et al.7

<table>
<thead>
<tr>
<th>Nodule size</th>
<th>Low risk patient (minimal or absent smoking history or other risk factors)</th>
<th>High risk patient (history of smoking or other risk factors)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤4 mm</td>
<td>No follow-up</td>
<td>f/u CT at 12 months, if unchanged no further follow-up</td>
</tr>
<tr>
<td>&gt;4-6 mm</td>
<td>f/u CT scan at 12 months. If unchanged, no further f/u</td>
<td>f/u CT at 6-12 months then at 18-24 months if no change</td>
</tr>
<tr>
<td>&gt;6-8 mm</td>
<td>f/u at 6-12 months then at 18-24 months if no change</td>
<td>f/u CT at 3-6 months then at 9-12 and 24 months if no change</td>
</tr>
<tr>
<td>&gt;8 mm</td>
<td>f/u CT at about 3, 9 and 24 months, contrast CT, PET and/or biopsy</td>
<td>f/u CT at about 3, 9 and 24 months, contrast CT, PET and/or biopsy</td>
</tr>
</tbody>
</table>

f/u: follow-up

**Figure Legend:**

**Figure 1.** Coronary CT angiogram with circular field of view to automatically exclude extracardiac tissue. Despite the restricted area of visualization, a 10 mm pulmonary nodule was identified at the right lung base (small arrow). A 20 mm nodule was also partially seen at the left lung base (large arrow).
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