HIGH-PERFORMANCE DUAL-ENERGY IMAGING
WITH A FLAT-PANEL DETECTOR

by

Nicholas Andrew Shkumat

A thesis submitted in conformity with the requirements
for the degree of Master of Science
Graduate Department of Medical Biophysics
University of Toronto

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2008

ABSTRACT

Mounting evidence suggests that the superposition of anatomical clutter in x-ray chest radiography poses a major impediment to the detectability of subtle lung nodules. Through decomposition of projections acquired using different x-ray energy spectra, dual-energy (DE) imaging offers to dramatically improve lung nodule conspicuity. The development of a high-performance DE chest imaging system is reported, with design and implementation guided by fundamental imaging performance metrics. Analytical and experimental studies of imaging performance guided the optimization of key acquisition technique parameters, including x-ray filtration, allocation of dose between low- and high-energy projections, and peak-kilovoltage selection. To minimize anatomical misregistration between images, a cardiac gating system was designed and implemented to direct x-ray exposures to within the quiescent period of the heart cycle. The instrumentation and optimal imaging techniques have been incorporated in a DE imaging prototype system now deployed in a clinical study to evaluate the diagnostic performance of DE imaging.
To all those I hold dear

My parents, my grandparents, my sisters, my brothers, my nephews, my niece

My friends
ACKNOWLEDGEMENTS

I am grateful to everyone who has made this work possible.

First and foremost, I would like to acknowledge my supervisor, Dr. Jeff Siewerdsen. He has graciously provided me with this opportunity, helping cultivate it from a simple proposal to something tangible, something (possibly) beneficial, and something I am sincerely proud of. I am grateful for his support, dedication, and unwavering enthusiasm. He has single-handedly injected me with a passion for Medical Physics, one I should only hope to maintain throughout my career.

On that same note, I would also like to thank the members of my supervisory committee, Drs. John Rowlands and Anne Martel. Always willing to lend a hand, they both offered support throughout my endeavors as a graduate student, and have infused this work with a fresh perspective.

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<tbody>
<tr>
<td>BSF</td>
<td>Backscatter Fraction</td>
</tr>
<tr>
<td>Bx</td>
<td>Biopsy</td>
</tr>
<tr>
<td>CBCT</td>
<td>Cone-Beam Computed Tomography</td>
</tr>
<tr>
<td>CR</td>
<td>Computed Radiograph</td>
</tr>
<tr>
<td>CS</td>
<td>Czechoslovakian Lung Cancer Study</td>
</tr>
<tr>
<td>CSA</td>
<td>Cascaded Systems Analysis</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>CXR</td>
<td>Chest Radiography</td>
</tr>
<tr>
<td>DE</td>
<td>Dual-Energy</td>
</tr>
<tr>
<td>DQE</td>
<td>Detective Quantum Efficiency</td>
</tr>
<tr>
<td>DR</td>
<td>Digital Radiograph</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>ELCAP</td>
<td>Early Lung Cancer Action Project</td>
</tr>
<tr>
<td>ESD</td>
<td>Entrance Surface Dose</td>
</tr>
<tr>
<td>FPD</td>
<td>Flat-Panel Detector</td>
</tr>
<tr>
<td>HR</td>
<td>Heart-Rate</td>
</tr>
<tr>
<td>kVp</td>
<td>Peak Kilovoltage</td>
</tr>
<tr>
<td>LAT</td>
<td>Lateral</td>
</tr>
<tr>
<td>LDCT</td>
<td>Low-Dose Computed Tomography</td>
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<tr>
<td>mAs</td>
<td>Product of the x-ray tube current (mA) and the exposure time (s)</td>
</tr>
<tr>
<td>minDCT</td>
<td>Minimum-Dose Computed Tomography</td>
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<tr>
<td>MLP</td>
<td>Mayo Lung Project</td>
</tr>
<tr>
<td>MR</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>NEXT</td>
<td>Nationwide Evaluation of X-ray Trends</td>
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<tr>
<td>NG</td>
<td>Nasogastric</td>
</tr>
<tr>
<td>NLST</td>
<td>National Lung Cancer Screening Trial</td>
</tr>
<tr>
<td>NPS</td>
<td>Noise Power Spectrum</td>
</tr>
<tr>
<td>NSCLC</td>
<td>Non-small Cell Lung Cancer</td>
</tr>
<tr>
<td>PA</td>
<td>Posterior-Anterior</td>
</tr>
<tr>
<td>PACS</td>
<td>Picture Archiving and Communications System</td>
</tr>
<tr>
<td>PET</td>
<td>Positron Emission Tomography</td>
</tr>
<tr>
<td>QDE</td>
<td>Quantum Detection Efficiency</td>
</tr>
<tr>
<td>ROI</td>
<td>Region of Interest</td>
</tr>
<tr>
<td>SCLC</td>
<td>Small Cell Lung Cancer</td>
</tr>
<tr>
<td>SD</td>
<td>Signal-Difference</td>
</tr>
<tr>
<td>SDNR</td>
<td>Signal-Difference to Noise Ratio</td>
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<tr>
<td>SNR</td>
<td>Signal to Noise Ratio</td>
</tr>
<tr>
<td>US</td>
<td>Ultrasound</td>
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Chapter I: Introduction
1. The Chest

1.1 Anatomy of the Chest

The chest is the anatomical region of the body enclosed by the thoracic vertebrae, ribs, sternum, clavicles and diaphragm. It contains and protects the principal organs involved in circulation (the heart) and respiration (the lungs). Descending from the Greek word thorakos, and Latin thorax, the chest has throughout history been regarded as the physical and spiritual center of the body, and the location of the soul. The chest consists of four primary components within a flexible skeletal framework of ribs: the lungs, heart, mediastinum, and diaphragm.

1.1.1 The Lungs

The lungs are a pair of large organs located on each side of the thorax, extending from the clavicles to the diaphragm. They are light, porous, and highly elastic. The lungs are an essential part of the respiratory system, responsible for facilitating gas exchange between blood and air. The trachea directs air to and from the lungs through bifurcation into two main bronchi (Fig. 1.1) and further bifurcates into secondary and tertiary structures (bronchioles) that terminate in atria, small structures containing alveolar sacs. Clusters of alveoli (each ~0.1 mm in size) oxygenate the blood through passive diffusion.¹ Alveoli have thin walls of squamous epithelial cells (~0.2 mm thick) allowing for the exchange of gases between air within the alveolar sacs and blood in nearby capillaries.¹ Due to differences in partial pressure, oxygen diffuses into the blood from the inhaled air, whereas carbon dioxide diffuses from the blood to the air, to be exhaled.

The gross anatomy of the lungs is typically characterized in terms of seven regions: the apex, base, two surfaces (costal and mediastinal) and three borders (inferior, posterior, anterior). The apex is located at the base of the neck, normally at the level of the clavicles. The base is a large, concave foundation resting on the diaphragm. The costal surface constitutes the outer edge of each lung, conforming within the chest cavity, whereas the mediastinal surface is located
centrally along the mediastinum and heart, described below. The three borders of the lung separate the costal and mediastinal surfaces from the lung base.

The lungs are divided into lobes by interlobular fissures [Fig. 1.1(a)]. Further subdivisions divide the lobes into lobules, the smallest lung component visible to the naked eye, typically ~3.5 mm in diameter. The right lung consists of three lobes: the upper, middle, and lower. The upper and middle lobes are separated by a depression called the horizontal fissure, whereas an oblique fissure divides the middle and lower lobes. The lower right lobe is elevated slightly to accommodate the liver. The left lung differs from the right as it consists of only two lobes: an upper and lower, divided by an oblique fissure. Also present on the left side is the cardiac notch, an impression found on the left mediastinal surface to accommodate the heart. Bordering the notch is the lingual, a tongue-shaped projection of the anterior aspect of the upper left lobe.

Covering the lungs is a smooth, delicate membrane known as the pleura, separated into visceral and parietal layers. The visceral pleura completely encases the lungs, even dipping into lobular fissures. The parietal pleura lines the chest wall, mediastinum, and diaphragm. Pleural fluid separates the layers and lubricates pleural surfaces, allowing for smooth expansion and compression of the lung volume during respiration. The serous fluid also supplies surface tension between parietal and visceral layers, ensuring cohesion between the pleura and chest wall.
1.1.2 The Heart

The heart lies between the lungs, behind and slightly to the left of the sternum. It is a hollow, conical-shaped organ, typically weighing between 230 and 280 grams. The essential function of the heart is to pump deoxygenated blood to the lungs and circulate oxygenated blood throughout the body by means of steady rhythmic contraction (beats). It is divided into right and left halves, each subdivided into two cavities, an atria and a ventricle. The atria are located superior to the ventricles and act as collecting reservoirs for blood returning to the heart. The ventricles are responsible for pumping blood out of the heart, to the lungs (right ventricle) and to the body (left ventricle).

For protection and lubrication, the heart is enclosed in a fluid-filled fibrous sac called the pericardium. Branching from the heart and pericardium are the “great vessels,” a term collectively used to describe the primary blood vessels with the chest. The great vessels consist of the vena cavae (superior and inferior), pulmonary arteries (right and left), pulmonary veins
(right and left superior, and inferior) and the aorta. These vessels are the largest within the body and are responsible for blood transport directly to and from the heart.

### 1.1.3 The Mediastinum

The mediastinum is a group of structures within the central region of the chest between the lungs, extending from the vertebral column to the sternum. It constitutes all of the viscera in the chest, excluding the lungs. The trachea, esophagus, numerous lymph nodes, the heart, and the great vessels are constituents of the mediastinum. Typically, the mediastinum is separated into two main regions: superior and inferior. The superior section extends from the upper thoracic vertebrae to the manubrium (superior segment of the sternum) and contains the aortic arch, trachea, esophagus, thoracic duct, thymus, nerves, and lymph glands. The inferior mediastinum is further subdivided into anterior, middle, and posterior sections. The anterior component is small, and is located on the left side of the body, containing only a few lymphatic elements, arteries and connective tissue. The middle mediastinum is the largest element of the inferior mediastinum and contains the heart and pericardium, ascending aorta, pulmonary veins, phrenic nerves, and the bifurcation of the trachea and principal bronchi. Lastly, the posterior mediastinum runs parallel to the vertebral column and encompasses the upper descending aorta and other vessels, the vagus nerve, esophagus and lymphatics.

At the mediastinal surface of each lung, slightly above and behind the heart, is the hilum, a triangular impression accommodating the root of the lung. The hilum is the point where the primary bronchus, pulmonary and bronchial vessels, lymphatics, and nerve plexes enter the lung.

Also part of the mediastinum is the thymus, a ductless gland that obtains its full size at early infancy and gradually reduces in size until puberty, at which time it atrophies. It is located centrally along the superior mediastinum and pericardium, and is typically $5 \times 4 \times 0.5$ cm in size. When active during childhood, the thymus assists in the development of the immune system,
stimulating the development of mature T-cells (lymphocytes involved in cell-mediated immunity).

1.1.4 The Diaphragm

The diaphragm is a convex, muscular septum that separates the thoracic and abdominal cavities. It facilitates respiration through contraction and relaxation. During inhalation, the diaphragm contracts, enlarging the chest cavity and reducing the intra-thoracic pressure. This draws air into the lungs. During exhalation, the diaphragm relaxes, the chest cavity reduces, and air is expelled.

1.1.5 The Ribs

The ribs and surrounding connective tissue serve as an osseo-cartilagenous cage that protects the contents of the chest. Humans normally have twelve pairs of ribs, seven with individual connections to both vertebrae and sternum, three “false” ribs that connect individual vertebrae to a common point on the sternum (costal cartilage), and two “floating” ribs that attach only to the T11 and T12 vertebrae [Fig. 1.1(b)].

1.2. Chest Abnormalities

The chest is a common site for disease. The lungs are particularly vulnerable to pathogens and disease due in part to continuous exposure to allergens, toxic chemicals, bacteria, and viruses in the atmosphere. Lung disease is the third largest killer in Canada and is responsible for approximately one in ten deaths. Afflictions include asthma (inflamed/irritated airways), chronic obstructive pulmonary disease, pneumonia (fluid accumulation within alveoli), tuberculosis (myobacterial infection), and cancer (described in detail below).

Structures within the chest are subject to numerous other afflictions as well. Pneumothorax (accumulation of gas within the pleural cavity) and pleural effusion
(accumulation of water within the pleural cavity) are common chest abnormalities due to acute injury or disease. Pulmonary embolism refers to a blockage of the pulmonary blood vessels usually due to a thrombus that has embolized into the arterial system. Obstructions of the airway are common ailments caused by blockage due to a foreign body, trauma, infection, or allergic reaction. Common diseases of the mediastinum or hilum include mediastinitis (inflammation), pneumomediastinum, and mediastinal masses caused by a vascular anomaly, adenopathy, or cancer. The ribs are subject to bruising, fracture, and distant tumour metastases. Heart disease, of course, is the single greatest killer of mankind (~33% of all deaths\textsuperscript{4}), with aspects of etiology, diagnosis, and treatment beyond the scope of the current thesis.

1.3. Lung Cancer

1.3.1 Lung Cancer Incidence

As the leading cause of cancer death for both men and women, lung cancer presents an enormous burden to society.\textsuperscript{5-7} Worldwide, over 1.1 million people die each year from lung cancer, and the disease has been cited by the World Health Organization as one of the major problems facing the world.\textsuperscript{8} In Canada, the disease accounted for nearly 20,000 deaths in 2007, with 23,000 new cases presenting in the same year.\textsuperscript{9} Lung cancer accounts for 15% of all new cancer cases while contributing to 27% of all cancer deaths.\textsuperscript{9} In Canada, it takes more lives than the next three most common cancers combined – viz., colon (8,700 deaths), breast (5,400 deaths) and prostate cancer (4,300 deaths).\textsuperscript{9} The average lifetime chance of developing lung cancer for both men and women is approximately 1 in 12 and 1 in 19, respectively.\textsuperscript{9} Overall, the incidence of lung cancer has been decreasing over the past 40 years. However, the rate of incidence in women has increased by a factor of 3 to 4 during the same period.\textsuperscript{10,11} Women are more likely to develop lung cancer than men, and are more prone to the disease as non-smokers. While
reduction in future incidence beckons for improved health education (e.g., regarding cigarette smoking), lung cancer poses a healthcare burden that will persist for decades; moreover, there is rising evidence of increased incidence in nonsmokers, particularly women.\textsuperscript{12-14} Moreover, there is rising evidence of increased incidence in nonsmokers, particularly women.\textsuperscript{15-17}

\textbf{1.3.2 Lung Cancer Etiology}

Like most cancers, lung cancer is caused by genetic changes that deregulate cellular replication and/or apoptosis. A diverse range of genetic abnormalities are seen in cancer cells, including the activation of a proto-oncogene (e.g., \textit{ras, EGFR}), deactivation of a tumor suppressor gene (e.g., \textit{p53, Rb}) or telomerase activation (e.g., immortalization of cells and offspring due to the inhibition of apoptosis). In particular, the most frequent genetic abnormality occurring in lung cancer is a mutation in \textit{p53}, an important gene involved in inducing cell cycle arrest, apoptosis and DNA repair. Mutations in \textit{p53} are present in over than 50\% of all lung cancers.\textsuperscript{18} Recent studies have shown that mutations involving \textit{EGFR} and the \textit{ras} family of oncogenes (H-\textit{ras}, K-\textit{ras} and N-\textit{ras}) are occurring more prominently in lung cancers.\textsuperscript{11} The precise role and mechanism for these genetic factors are currently the focus of extensive research.

The primary cause of lung cancer is tobacco smoke, with approximately 85-90\% of lung cancer patients reported to be current or former smokers.\textsuperscript{11} Cigarette smoke contains carcinogens that can lead to the development of cancer, including arsenic, naphthylamine, aminobiphenol, benzene, and vinyl chloride.\textsuperscript{11} As the effect of carcinogens accumulate over time, the risk from smoking remains after cessation, yet can reduce by 20-50\% after cessation.\textsuperscript{11} The risk, however, will never be as low as a non-smoker, and the relative risk of lung cancer in smokers is 20 times greater than that of those who have never smoked.\textsuperscript{10} Genetic factors and age also play a strong role in lung cancer development. Approximately one out of every five smokers develops lung cancer, yet numerous chemical and environmental factors have also been shown to lead to the
disease. These include secondhand smoke, asbestos, radon, chromium, and polycyclic aromatic hydrocarbons.

### 1.3.3 Lung Cancer Types

Because lung cancers develop from epithelial cells, they are all classified as carcinomas. There are two major types: non-small cell lung cancer (NSCLC) and small cell lung cancer (SCLC), with differences associated with cell size, presentation, cause, growth patterns, metastatic potential, treatment strategies, and prognosis. Other less common primary cancers found within the lungs include pleural mesotheliomas, carcinoid tumours and fibrosarcomas. Regardless of tumour size, lung cancer can metastasize early in development due to high vascularization and a rich supply of lymphatic structures within the lung. The most common sites of metastasis are the chest lymph nodes, bone, brain, adrenal glands and the liver.

NSCLC accounts for ~80 – 85% of lung cancers and is further separated into three categories: adenocarcinoma (40%), squamous cell carcinoma (25 – 30%), and large cell undifferentiated carcinoma (10 – 15%). Adenocarcinoma is the most common form of lung cancer in non-smokers and those under 50 years of age. It is glandular in appearance and is most often found in the outer regions of the lungs. Squamous cell carcinoma is strongly associated with cigarette smoking and usually presents in central regions of the lung as it tends to originate in the larger airways. Finally, large cell carcinoma is the rarest form of NSCLC and has the least favorable prognosis. Cells are generally large and highly undifferentiated, with tumours occurring in any part of the lung.

SCLC accounts for the remaining ~15 – 20% of lung cancers and consists of abnormally small epithelial cells (sometimes referred to as “oat-cell” carcinoma due to its appearance). There is a strong relationship between SCLC and smoking. In its typical presentation, SCLC has a higher mitotic rater and metastasizes more quickly than NSCLC.
The most usual presentation of NSCLC is in the form of a lung nodule, with morphological features of the nodule useful in determining the abnormality is benign or malignant. These include: size, shape, contour and presence of calcification and/or fat. The size of a nodule is not a sufficient indicator of malignancy, although the likelihood of malignancy increases with volume.\(^{10}\) The composition (e.g., calcium, fat, etc.) is helpful in distinguishing benign and malignant nodules. Calcification is extremely useful in assisting cancer diagnosis and, depending on the pattern of calcium deposits, is a strong indicator of benignancy. Diffuse solid, central, popcorn and laminar calcifications are indicative of benign tumors. Fat infused within a nodule is characteristic of hamartomas (a benign malformation resembling a neoplasm).

**1.3.4 Lung Cancer Diagnosis and Staging**

Lung cancer is typically asymptomatic in the early stages of development, because normal lungs have a significant functional reserve capacity and few nerves. This large reserve allows tumours to grow for a considerable time before function is compromised or development of a central obstruction / pleural disease. At later stages, those afflicted with lung cancer exhibit symptoms that include: persistent cough or a change in existing cough (e.g., in patients with emphysema or other respiratory ailments); hemoptysis (coughing up blood); dyspnea (difficulty breathing); dysphagia (difficulty swallowing); chest pain or shoulder pain; swelling of the neck or face (indicative of cancer spread); fatigue; and weight loss.

Staging of lung cancer follows the “TNM” system of tumour staging. The “T” descriptor indicates the extent of the primary tumour, “N” the extent of lymph node involvement, and “M” the presence of metastases. Table 1.1 summarizes the staging system.
<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumour cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of tumour</td>
</tr>
<tr>
<td>T1</td>
<td>Tumour ≤ 3 cm in largest dimension, no main bronchus invasion</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour &gt; 3 cm in largest dimension, main bronchus or visceral pleura involvement</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour of any size involving: chest wall, diaphragm, parietal pericardium</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour of any size involving: mediastinum, heart great vessels, trachea, esophagus, vertebral bodies</td>
</tr>
</tbody>
</table>

| NX    | Lymph nodes cannot be assessed |
| N0    | No regional lymph involvement |
| N1    | Metastasis to ipsilateral peribronchial, intrapulmonary, or hilar nodes |
| N2    | Metastasis to ipsilateral mediastinal, or subcarinal nodes |
| N3    | Metastasis to contralateral mediastinal or hilar nodes, or any supraclavicular nodes |

| MX    | Distant metastases cannot be assessed |
| M0    | No distant metastases |
| M1    | Distant metastases confirmed |

Table 1.1. Summary of lung cancer TNM staging system

TNM staging is commonly grouped into subsets with similar survival and treatment prospects. These are categorized into four stages, denoted I, II, III, and IV with substages therein as described in Table 1.2.

<table>
<thead>
<tr>
<th>Stage</th>
<th>TMN Subset</th>
<th>5-Year Survival</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>T1N0M0, T2N0M0</td>
<td>38 – 61%</td>
</tr>
<tr>
<td>II</td>
<td>T1N1M0, T2N1M0, T3N0M0</td>
<td>24 – 34%</td>
</tr>
<tr>
<td></td>
<td>T3N1M0, T1N2M0, T2N2M0, T3N2M0</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>T4N0M0, T4N1M0, T4N2M0, T1N3M0, T2N3M0, T3N3M0, T4N3M0</td>
<td>5 – 3%</td>
</tr>
<tr>
<td>IV</td>
<td>Any T, Any N, M1</td>
<td>1%</td>
</tr>
</tbody>
</table>

Table 1.2. Summary of lung cancer staging system and the associated five-year survival.

Over 78% of newly diagnosed lung cancer is locally advanced, with more than 50% of patients presenting with distant metastases. As shown in Table 1.2, lung cancer survival is very low for advanced stage disease. The key to survival, therefore, is early detection. Approximately 60% of people with lung cancer die within 1 year of diagnosis, with 70 – 80% of the remaining
succumbing within 2 years. Approximately 50% of deaths occur before the age of 70, with an average loss of life expectancy of 22 years. This highlights the importance of early detection and classification of lung disease, particularly in at-risk populations.

Potential methods of lung cancer detection include cytological assays and image-based examination, each ultimately subject to confirmation by biopsy. Sputum cytology has proven ineffective in detecting disease at a sufficiently early stage to affect survival. Image-based examination presents the most important method for lung cancer detection in current clinical practice – either in screening of asymptomatic, at-risk populations or in baseline examinations (i.e., initial diagnostic testing for suspected disease) performed for other reasons. As discussed below, the need for an imaging modality with high sensitivity and specificity in the detection and diagnosis of lung cancer is clear.

2. Imaging of the Chest

The chest presents a challenging anatomical site for medical imaging due in part to the broad range of material types, including air, lungs, solid organs, and bony structures. While such a diversity of materials can present high image contrast (e.g., in x-ray radiography), it also necessitates a wide dynamic range in the imaging technology and may seriously diminish applicability (e.g., in ultrasound and magnetic resonance imaging). Furthermore, the range in anatomical size varies dramatically across the patient population, with chest thickness ranging 18 – 28 cm among non-obese adults. Furthermore, the anatomy is dynamic, with voluntary and involuntary motion on the timescale of seconds (e.g., respiratory motion) and milliseconds (cardiac motion). The most common modalities are summarized in Table 1.3.

Of these modalities, chest imaging is currently dominated by x-ray radiography and CT. The reasonable contrast (1 – 2%) associated with the x-ray attenuation coefficient of features
within the lung (bronchial structures, vasculature and nodules) combined with the high spatial resolution of these modalities have made x-ray imaging the most commonly performed chest imaging examination, particularly for baseline imaging, screening, and diagnosis tasks. X-ray fluoroscopy is a common means of interventional guidance. Tomosynthesis is an old technique that is gaining clinical importance due to the development of new detectors and 3D reconstruction techniques, providing volume images reconstructed from multiple x-ray projections. Functional imaging modalities such as PET and SPECT provide useful means of disease classification and staging as well as identification of distant metastases. Ultrasound and MR are currently not as prevalent for thoracic imaging. Apart from considerations of cost and availability, MR imaging suffers from low signal-to-noise ratio (SNR) in the chest due to a relatively low proton density in lung tissue. MR image acquisition times are also fairly long (several minutes), making it susceptible to motion artifacts. Ultrasound, although inexpensive, suffers from high (nearly complete) reflectivity at interfaces between soft tissue and air or bones, all but negating its role in lung imaging by means of an external transducer. Current research addressing these technical obstacles may lead to thoracic applications for MR (e.g., hyperpolarized $^3$He and $^{129}$Xe) or US in the future.
<table>
<thead>
<tr>
<th>Modality</th>
<th>Dimensionality</th>
<th>Ionizing Radiation</th>
<th>Utility / Thoracic Applications:</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-Ray Radiography</td>
<td>Projection (x,y)</td>
<td>Y</td>
<td>Lung abnormalities, bone fractures, foreign body detection, breathing/nasogastric tube placement</td>
</tr>
<tr>
<td>X-Ray Fluoroscopy</td>
<td>Projection (x,y) + Dynamic (t)</td>
<td>Y</td>
<td>Interventional (angiography, orthopedic surgery, catheter placement, upper gastrointestinal)</td>
</tr>
<tr>
<td>Tomosynthesis</td>
<td>Volumetric (x,y,z)</td>
<td>Y</td>
<td>Lung abnormalities, bone fractures, foreign body detection</td>
</tr>
<tr>
<td>Computed Tomography (CT)</td>
<td>Volumetric (x,y,z) + Dynamic (t)</td>
<td>Y</td>
<td>Lung abnormalities, pulmonary embolism, angiography, chronic interstitial processes</td>
</tr>
<tr>
<td>Nuclear Medicine (PET, SPECT)</td>
<td>Volumetric (x,y,z)</td>
<td>Y</td>
<td>Chest oncology (diagnosis, staging, treatment planning), cardiac applications, vascular disease</td>
</tr>
<tr>
<td>Ultrasound (US)</td>
<td>Volumetric (x,y,z) + Dynamic (t)</td>
<td>N</td>
<td>Cardiac applications, vascular disease, demarcation of pleura effusion</td>
</tr>
<tr>
<td>Magnetic Resonance Imaging (MR)</td>
<td>Volumetric (x,y,z) + Dynamic (t)</td>
<td>N</td>
<td>Cardiac applications, mediastinal/spinal and pleural abnormalities</td>
</tr>
</tbody>
</table>

Table 1.3. Summary of imaging modalities.

Clinical chest imaging can be generally characterized in terms of seven broad applications summarized in Table 1.4, each of which has unique imaging requirements dictated by the clinical task. Such requirements range from the fast, inexpensive, low-dose, and readily available nature of baseline exams for suspected abnormalities, to the more demanding image quality and functional requirements associated with diagnostic workup and staging. A complete diagnostic evaluation of lung cancer often involves multiple modalities – e.g., detection of suspicious disease in a baseline radiograph, confirmation by CT, biopsy guided by fluoroscopy and CT, and staging by PET. Therapy planning, guidance, and evaluation could similarly involve multiple modalities – e.g., CT for radiation therapy dose calculations, fluoroscopic guidance, and response assessment by PET. Even the most basic medical procedures often require imaging to ensure proper execution – e.g., a bedside radiograph acquired to verify placement of a nasogastric (NG) or breathing tube.
<table>
<thead>
<tr>
<th>Application:</th>
<th>Description:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline Imaging (initial test)</td>
<td>Initial diagnostic examination, (e.g., chest radiograph for persistent cough and dyspnea).</td>
</tr>
<tr>
<td>Temporal Following of Suspected Disease</td>
<td>Abnormality found in high-risk patient without clear indication of disease. Diagnostic examination repeated at future time to monitor changes (e.g., small lung nodule found in a smoker)</td>
</tr>
<tr>
<td>Screening</td>
<td>Imaging a high-risk population to identify disease at early, curable stage (e.g., mammographic screening in women over 50).</td>
</tr>
<tr>
<td>Diagnostic Workup / Staging</td>
<td>Diagnosis of disease confirmed, identifying extent and spread of disease (e.g., tuberculosis infection) or identifying cancer stage to direct treatment.</td>
</tr>
<tr>
<td>Therapy Planning</td>
<td>Imaging to define disease location and assist in the evaluation of treatment options (e.g., CT/MR for lung cancer boundaries and proximity to sensitive structures)</td>
</tr>
<tr>
<td>Therapy Guidance</td>
<td>Imaging used to guide disease treatment. (e.g., CT-guided fine-needle aspiration chest biopsy, placement of an intravascular stent, image-guided radiation therapy)</td>
</tr>
<tr>
<td>Therapy Response Assessment</td>
<td>Monitoring disease changes following therapy (e.g., tumour size following radiation therapy, confirmation of complete surgical resection)</td>
</tr>
</tbody>
</table>

**Table 1.4.** Broad categories of chest imaging applications.

2.1. Chest Radiography (CXR)

X-ray projection radiography is the predominant diagnostic chest imaging modality. It is inexpensive, quick, and logistically simple, and the resulting 2D images present fairly modest computer storage requirements. Radiographic image processing and display can be fairly sophisticated to ensure good visualization across a wide dynamic range.\(^{25}\) Radiographs exhibit high spatial resolution (typically \(~0.1\) mm) and are largely free of artifacts. Images are acquired at fairly low radiation dose, with an entrance surface dose of 0.1 – 0.2 mGy (\(~0.02\) mSv) depending on patient size (equivalent to approximately 3 – 4 weeks of natural background radiation).\(^{26}\) CXR is the most common medical imaging examination in Canada, and accounts for nearly half of all exams performed worldwide.\(^{27}\) It is almost always the initial diagnostic procedure for patients with a suspected thoracic abnormality (e.g., in diagnosis of adenopathy,
pleural effusion, pneumonia and bone abnormalities), and in many cases, is the only diagnostic test performed.

The primary limitation of CXR lies in the 2D nature of the modality itself – i.e., the projection of a 3D object (the patient) into a 2D image. Firstly, the contrast of a structure in the 2D projection is significantly less than the actual difference in x-ray attenuation coefficients in the 3D object. That is, the difference between line integrals through an object characterized by various attenuation coefficients is less than the difference in the coefficients themselves. Secondly, the superposition of 3D structures into a 2D image can result in obscuration of the structure of interest (e.g., a lung nodule) by overlying structures (e.g., the ribs), referred to as “anatomical clutter” or “anatomical noise”. Such has been identified as a major limiting factor in the detection of subtle lung disease.28

Over 110 years have passed since the discovery of the x-ray and its application in medical imaging. Chest radiography has evolved considerably over the last century, with the most significant advances represented by the development of: i.) efficient phosphors (e.g., Gd$_2$O$_2$S:Tb) for film-screen systems in the 1960s and 1970s; ii.) high-performance storage phosphor (computed radiography, CR) systems in the 1980s and 1990s; and iii.) large-area digital (flat-panel detector, FPD) systems in the 1990s and 2000s.29,30

2.1.1 Film-Screen Radiography

The earliest widespread radiographic imaging systems (still prevalent today) are based on silver halide film – usually in combination with a phosphor screen. While film can be exposed directly to x-rays, due to a small interaction efficiency, an intensifying phosphor screen is almost always used. X-rays interact with the phosphor (on one or both sides of the film), and a fraction of the absorbed energy is radiated as optical photons that in turn interact with silver grains in the film. Upon chemical processing, the silver halide ions convert to metallic silver, changing the
transparency of the film in (log) proportion to the x-ray exposure. Viewed on a light box, darker areas (higher optical density) therefore correspond to areas of reduced x-ray attenuation in the object.

The numerous practical and performance benefits of film-screen systems include high spatial resolution, low cost, ease of use, and dependability; however, it suffers from drawbacks that limit its use in modern CXR. The narrow latitude (limited sensitivity range) limits the use of film to a small range of exposure levels and constrains the dynamic range. Furthermore, screen-film systems must be simultaneously optimized as the medium for both image capture and display. Film-screen signal response is nonlinear, and the analog, non-real-time nature of film does not allow for extension to more advanced applications.

2.1.2 Computed Radiography

Digital x-ray detection systems were introduced in the early 1980s. Digital detectors separate image acquisition and display, and offer a linear response over a large exposure range. Increased sensitivity and reduced image noise offer improved image quality and/or reduced patient dose. The digital nature of images also allows the development of new image processing and display techniques, minimize the logistics of film processors and film libraries, facilitate the development of computer-assisted detection techniques, and allow for teleradiology. Referred to as computed radiography (CR), the first widespread digital detector systems were based on reusable, photostimulable storage phosphors, such as BaFBr, Ba₂B₂O₉Br and Y₂SiO₅. X-rays interacting with the phosphor raise atoms to a metastable, excited state. The distribution of excited atoms constitutes a latent image that is read and digitized using a dedicated reading device. The image reader uses a scanning laser to de-excite phosphor atoms, stimulating the release of optical photons that are recorded by a sensor for each position on the phosphor plate. Figure 1.2(a) illustrates a CR chest radiograph. CR has become a widespread technology over the
last two decades,\textsuperscript{32} sharing many of the practical advantages of film (e.g., ease of use, minimal cost, portability, and applicability to bedside procedures) but with the advantages of inherently digital acquisition.

\textbf{Figure 1.2.} (a) Example CR radiograph of the chest at (125 kVp, 3.6 mAs, posterior-anterior view). (b) Example DR radiograph of the chest (120 kVp, 3.2 mAs, same patient).

\textbf{2.1.3 Flat-Panel Detector Radiography}

Radiographic detectors based upon hydrogenated amorphous silicon (a-Si:H) thin-film electronics, called flat-panel detectors (FPDs), provide high-quality radiographs in real-time (i.e., immediate availability of the image without the need for an image reader). There are two main types of FPDs, classified as either direct- or indirect-detection, with each becoming clinically available over the last ~5 – 10 years.\textsuperscript{30} Direct detectors use a photoconductive material layer (such as a-Se or PbI\textsubscript{2}) to convert x-ray energy directly to electron-hole pairs. An electric field (~1 – 5 V/\textmu m) applied across the photoconductor directs charge to pixel electrodes.\textsuperscript{33} Indirect detectors convert x-rays to optical photons via a phosphor screen (commonly CsI:Tl or Gd\textsubscript{2}O\textsubscript{2}S:Tb), which are converted to electron-hole pairs by photodiodes.\textsuperscript{30} In each case, the stored charge is read out using an active matrix of a-Si:H thin-film transistors or diodes at each
Digital x-ray images acquired with a FPD are denoted as digital radiographs (DR), illustrated in Fig. 1.2(b).

The key advantages of FPDs over other radiographic detectors are increased detection efficiency (giving higher image quality and/or reduced patient dose) and real-time acquisition (with frame rates up to 30 frames per second). These characteristics extend the potential scope of applications of FPDs to fluoroscopy, cone-beam CT, and other advanced applications including tomosynthesis and high-performance dual-energy imaging.

2.2. Tomosynthesis

Digital tomosynthesis is a relatively new imaging modality in which a small number of projection radiographs acquired at multiple views surrounding an object are used to reconstruct a 3D image. Similar in principle to limited-angle tomography, the x-ray tube and associated detector (typically a FPD) move synchronously on opposite sides of the patient either linearly or in a circular arc. Tomosynthesis provides a number of sectional images (e.g., coronal slices) at varying depth in the object, improving the visibility of structures within a given slice and reducing obscuration (“anatomical noise”) associated with out-of-plane structures. In-plane spatial resolution is high (approximately equivalent to that of the 2D radiographs), whereas depth-resolution is fairly limited (~1 cm, depending on the source-detector orbit). Potential advantages relative to radiography include 3D visualization and increased conspicuity of subtle lung disease by virtue of reduced out-of-plane clutter. The radiation dose is ~0.1 mSv, higher than that of a posterior-anterior (PA) radiograph, but roughly equal to that of a lateral (LAT) radiograph. Systems for chest tomosynthesis became clinically available in 2006, with early clinical trials imminent at the time of writing.
2.3. Computed Tomography

X-ray computed tomography (CT) was the first 3D medical imaging modality, developed independently in the early 1970s by Hounsfield and Cormack. CT was made possible though advances in computers and digital signal processing and provides fully 3D images through the acquisition of multiple projections acquired in complete rotations around an object. Example axial slices from CT images of the chest are shown in Fig. 1.3.

CT has undergone countless developments over the last three decades, evolving from early systems that acquired a single axial slice per source-detector rotation to the latest slip-ring, helical, multi-detector systems capable of scanning the entire thorax in a few seconds. The resulting 3D images can be viewed in axial, coronal or sagittal planes, depending on the diagnostic task. CT exhibits nearly isotropic spatial resolution, high contrast resolution, and is not hindered by anatomical superposition (anatomical noise). It is of widespread use in diagnostic imaging of most pulmonary abnormalities. Drawbacks associated with CT (compared to radiography) include increased capital cost, radiation dose, lower patient throughput, and increased data storage and visualization requirements. While the sensitivity of lung nodule detection is high, the specificity of lung nodule characterization is low, with false-positive rates as high as 90% in lung screening applications.
Figure 1.3. Axial chest CT images. Images are of the same patient: (a) Diagnostic CT (140 mA). (b) Low-dose CT (30 mA).

The radiation dose associated with CT is relatively high, with doses of ~5 – 10 mSv\(^3\) representing a factor of 250 – 500 increase compared to radiography. Such has motivated a considerable amount of research in recent years, including dose minimization in pediatric CT and the development of low-dose techniques in thoracic CT. Low-dose CT of the chest [LDCT, illustrated in Fig. 1.5(b)] can reduce the effective patient dose to approximately 1 – 2 mSv per exam while maintaining a high sensitivity for the detection of subtle structures.\(^{19}\)

2.4. Remaining Challenges in Lung Cancer Imaging

Considering the spectrum of thoracic imaging modalities, there remains a need for a high throughout, inexpensive, high sensitivity, high specificity, low-dose modality to serve as an alternative to CXR and/or as an adjuvant to LDCT in the detection and classification of lung cancer.

Decades of clinical practice has placed chest radiography at the front line against lung cancer. Conventional chest radiography, however, has proven inadequate in the detection of
early-stage disease, missing 50% of nodules measuring 10 mm or less.\textsuperscript{35} The lack of sensitivity is attributed in large part to the superposition of anatomical structures in the projection image\textsuperscript{28} – i.e., the obscuration of subtle soft-tissue nodules by overlying “anatomical noise” such as the ribs and clavicles. LDCT offers a dramatic improvement in diagnostic sensitivity;\textsuperscript{36} however, increased cost, radiation dose, and a lack of diagnostic specificity (limited in part by the lack of fine material characterization),\textsuperscript{37-39} present significant challenges.

Because early detection is central to lung cancer survival, screening of at-risk populations represents an important area of investigation. In the early 1970s, two large randomly controlled trials, the Mayo Lung Project (MLP) and the Czechoslovakian Study (CS) compared lung cancer screening by chest radiography and sputum cytology with an unscreened (or minimally screened) control group. Over 15,000 male, high-risk subjects were administered in the two trials, where the screened group underwent routine CXR once every 4 – 6 months, compared to a control group for which annual screening was recommended (MLP) or absent altogether (CS).\textsuperscript{40} The results of the trials were similar, demonstrating a significant increase in cancer incidence (22\% and 47\%, respectively), with a larger proportion of early-stage, resectable disease identified in the experimental (screening) groups.\textsuperscript{40} Although these results showed a strong increase in cancer survival with screening, there was no statistically significant difference in overall mortality between the screening and control groups.\textsuperscript{8,40} The results from the two trials were not without criticism. The MLP, for example, exhibited poor compliance with the scheduled screening (75\% in the screening group), contamination of the control group by non-study examinations (i.e., absence of an unscreened arm), unreliable outcome measures associated with a study designed to detect a 50\% decrease in mortality,\textsuperscript{8,40} and short follow-up time (3 years).

Recently, the advent of LDCT has renewed interest in lung cancer screening. Early results from the Early Lung Cancer Action Project (ELCAP) and the Mayo Clinic / National
Cancer Institute Trial have been mixed. As in the CXR screening trials, an increase in survival is observed with lung cancer screening, yet without conclusive evidence that mortality can be improved. Shortcomings with LDCT are also of concern, notably the potential for a large proportion of false-positive findings, overdiagnosis bias, and cost-effectiveness. Despite these shortcomings, the National Lung Cancer Screening Trial (NLST) is underway, enrolling over 50,000 current and former smokers in an attempt to identify a 20% reduction in mortality for screened individuals followed for 5 years.

With CXR still stationed at the front line of chest imaging, the need for a better “first read” is clear. As mentioned above, a significant number of lung cancers are detected incidentally in the course of other radiographic examinations. An improvement to both the sensitivity and specificity of chest radiography could potentially lead to more conclusive detection and diagnosis at earlier stages of disease. Discovering malignant disease at an earlier stage – either incidentally or in the process of screening – offers the potential for improved lung cancer survival. Moreover, identifying benign abnormalities (e.g., benign nodules, granulomas and calcified lesions) upon “first read” could reduce radiation dose associated with follow-up exams, obviate unnecessary biopsy intervention, and minimize financial and emotional cost.

3. Dual-Energy Imaging

With the advent of digital detectors, advanced approaches to thoracic x-ray imaging have become possible. Among these is dual-energy (DE) imaging. First proposed as early as 1953, DE imaging can potentially address the two major challenges that limit the detection and classification of pulmonary disease by CXR: i.) the loss in nodule sensitivity due to presence of overlying structure, (“anatomical noise”); and ii.) the difficulty in visualizing and characterizing fine material content (e.g., calcification). Through the decomposition of the image
into distinct material bases (e.g., soft-tissue and bone), DE imaging has been shown to offer a potentially promising alternative or adjuvant to accurate, early-stage detection of lung disease. This technique decomposes a pair of images acquired at different x-ray energies into component images by means of the energy-dependent differences in the material attenuation coefficient – e.g., in the context of chest imaging, soft-tissue (mean atomic number, $Z_{\text{soft mean}} \sim 7$) and bone/calcification ($Z_{\text{bone mean}} \sim 20$).

DE imaging involves the acquisition of projections acquired at two different beam energies ("peak kilovoltage," commonly termed kVp), one at a low-kVp ($kVp^L$, typically 60 – 90 kVp) and another at a high-kVp ($kVp^H$, typically 120 – 150 kVp). These two images are combined in such a way that a given material component is extinguished in the resulting image. For example, extinguishing bone yields an image of soft-tissue, and vice versa. Figure 1.7 illustrates example low-kVp, high-kVp, DE soft-tissue, and DE bone images.
Figure 1.4. Dual-energy imaging. (a) Low-kVp and (b) high-kVp images are decomposed into (c) soft-tissue and (d) bone images.
3.1. Physics of Dual-Energy Imaging

As mentioned above, DE imaging decomposes an image into component bases by exploiting the difference in energy dependence of photoelectric and Compton interactions for materials of different atomic number. The photoelectric effect is highly dependent on photon energy ($E$), and atomic number ($Z_{\text{eff}}$), with cross-section determined by the $3^{\text{rd}}$ and $4^{\text{th}}$ power, respectively:

$$\sigma_{\text{PE}} \propto \frac{\rho(Z_{\text{eff}})^3}{E^3} \quad (1.1)$$

where $\rho$ is the material density. Compton scatter, on the other hand, is more weakly dependent on both:

$$\sigma_{\text{Compton}} \propto \frac{\rho(Z_{\text{eff}})}{A \cdot E} \quad (1.2)$$

where $A$ denotes the material atomic mass. With regard to material bases of interest in chest imaging, calcified structures (higher $Z_{\text{eff}}$) attenuate with stronger energy dependence than soft tissues, with a sharp decrease in attenuation as the beam energy increases. Thus, an image acquired at low-kVp exhibits higher bone contrast than in a high-kVp image, whereas the soft-tissue contrast between the two images is relatively similar.

Two well-established techniques that exploit these underlying dependencies to create a DE image are weighted log-subtraction and basis decomposition. Comparative studies suggest no significant difference in image quality between the two techniques. The work described throughout this thesis employed weighted log-subtraction due to its ease of implementation and applicability to linear systems modeling (cascaded systems analysis, CSA). The decomposition of DE soft-tissue and bone images ($I_{\text{soft}}^{DE}$ and $I_{\text{bone}}^{DE}$, respectively) can be understood by
considering the Beer-Lambert law, describing x-ray attenuation through a object consisting of various materials:

$$I = I_o e^{-(\mu(E)_{1} + \mu(E)_{2} + ...)}$$  \hspace{1cm} (1.3)$$

where $I_o$ is the incident x-ray fluence, $I$ is the transmitted fluence, $\mu$ is the material attenuation coefficient, and $t$ is the material thickness.

Considering two materials of interest (soft-tissue and bone) and ignoring x-ray scatter and hardening of the x-ray spectrum, the high- and low-kVp images are correspondingly:

$$I^H = I_o^H e^{-\left(\mu^H_{soft}\cdot t_{soft} + \mu^H_{bone}\cdot t_{bone}\right)}$$ \hspace{1cm} (1.4)$$

$$I^L = I_o^L e^{-\left(\mu^L_{soft}\cdot t_{soft} + \mu^L_{bone}\cdot t_{bone}\right)}$$  \hspace{1cm} (1.5)$$

where subscripts denote different material components, and superscripts denote the high- or low-energy beam. To decompose the soft-tissue image ($I^B_{soft}$) and representing the image after extinguishing of bone), we consider a subtraction of the high-kVp and low-kVp log images, weighted by a factor denoted $w_s$:

$$\ln(I^D_{soft}) = \ln\left(I_o^H e^{-\left(\mu^H_{soft}\cdot t_{soft} + \mu^H_{bone}\cdot t_{bone}\right)}\right) - w_s \ln\left(I_o^L e^{-\left(\mu^L_{soft}\cdot t_{soft} + \mu^L_{bone}\cdot t_{bone}\right)}\right)$$

$$= \ln(I_o^H) + \ln\left(e^{-\left(\mu^H_{soft}\cdot t_{soft} + \mu^H_{bone}\cdot t_{bone}\right)}\right) - w_s \ln(I_o^L) - w_s \ln\left(e^{-\left(\mu^L_{soft}\cdot t_{soft} + \mu^L_{bone}\cdot t_{bone}\right)}\right)$$ \hspace{1cm} (1.6)$$

where $k$ is a constant. Close examination of this equation shows that terms related to bone can be canceled by selection of the weighting parameter as the ratio of bone attenuation coefficients, between high- and low-kVp, specifically:

$$w_s = \frac{\mu^H_{bone}}{\mu^L_{bone}}$$  \hspace{1cm} (1.7)$$

Substituting Eq. 1.7 into Eq. 1.6 gives:
\[
\ln(I_{\text{soft}}^{DE}) = k - (\mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}}) \frac{\mu_{\text{bone}}^H}{\mu_{\text{bone}}^L} \left( \frac{\mu_{\text{soft}}^L}{\mu_{\text{soft}}^L} t_{\text{soft}} + \mu_{\text{bone}}^L t_{\text{bone}} \right)
\]

\[
= k - (\mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}}) - \left( \frac{\mu_{\text{bone}}^H}{\mu_{\text{bone}}^L} \frac{\mu_{\text{soft}}^L}{\mu_{\text{soft}}^L} \right) t_{\text{soft}} + \mu_{\text{bone}}^L \left( \mu_{\text{soft}}^L t_{\text{soft}} + \mu_{\text{bone}}^L t_{\text{bone}} \right)
\]

\[
= k - t_{\text{soft}} \left( \mu_{\text{soft}}^H - \frac{\mu_{\text{bone}}^H}{\mu_{\text{bone}}^L} \mu_{\text{soft}}^L \right) + w_{b} \mu_{\text{bone}}^L
\]

which is an image consisting solely of soft-tissue.

The same process can be applied for decomposition of the bone image \(I_{\text{bone}}^{DE}\) with the weighting parameter selected to cancel soft tissue. To wit:

\[
\ln(I_{\text{bone}}^{DE}) = \ln \left( I_{\text{o}}^H e^{-\left( \mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}} \right)} \right) - w_{b} \ln \left( I_{\text{o}}^L e^{-\left( \mu_{\text{soft}}^L t_{\text{soft}} + \mu_{\text{bone}}^L t_{\text{bone}} \right)} \right)
\]

\[
= k - \left( \mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}} \right) - w_{b} \left( \mu_{\text{soft}}^L t_{\text{soft}} + \mu_{\text{bone}}^L t_{\text{bone}} \right) \tag{1.9}
\]

Selecting the cancellation parameter to negate terms associated with soft tissues:

\[
w_{b} = \frac{\mu_{\text{soft}}^H}{\mu_{\text{soft}}^L} \tag{1.10}
\]

yields the DE bone image:

\[
\ln(I_{\text{bone}}^{DE}) = k - \left( \mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}} \right) \frac{\mu_{\text{soft}}^H}{\mu_{\text{soft}}^L} \left( \frac{\mu_{\text{soft}}^L}{\mu_{\text{soft}}^L} t_{\text{soft}} + \mu_{\text{bone}}^L t_{\text{bone}} \right)
\]

\[
= k - \left( \mu_{\text{soft}}^H t_{\text{soft}} + \mu_{\text{bone}}^H t_{\text{bone}} \right) - \left( \mu_{\text{soft}}^H t_{\text{soft}} + \frac{\mu_{\text{bone}}^H}{\mu_{\text{bone}}^L} \mu_{\text{soft}}^L \right) \tag{1.11}
\]

\[
= k - t_{\text{bone}} \left( \mu_{\text{bone}}^H - \frac{\mu_{\text{soft}}^H}{\mu_{\text{soft}}^L} \mu_{\text{bone}}^L \right) - w_{b} \mu_{\text{bone}}^L
\]

Disregarding the constant offset in each case, we have for the DE soft-tissue and bone images:

\[
\ln(I_{\text{soft}}^{DE}) = \ln(I^H) - w_{s} \ln(I^L) \tag{1.12a}
\]

\[
\ln(I_{\text{bone}}^{DE}) = -\ln(I^H) + w_{b} \ln(I^L) \tag{1.12b}
\]
The weighting parameters, \( w_s \) and \( w_b \), can be selected in a number of ways. They may be selected theoretically from the ratio attenuation coefficient at low- and high-kVp (Eq. 1.7, 1.10), experimentally (iteratively selected to cancel a given material), or qualitatively by an observer. Variation in the parameter from the theoretically expected value may be attributed to x-ray scatter and beam hardening that are not accounted for the Beer-Lambert expression (Eq. 1.3).

### 3.2. Evolution of Dual-Energy Imaging

DE imaging of the chest was first investigated in the 1980s, based on CR technology.\textsuperscript{42} Referred to as the “single-shot” method, low- and high-energy images are acquired using a single x-ray exposure, in which two CR detectors are separated by a copper plate (~1 – 2 mm). The low-energy image is recorded by the front storage phosphor and has characteristics somewhat similar to a conventional PA radiograph. The rear phosphor records an image formed at higher average x-ray energy, since the fluence creating the image is that transmitted through the interspersing copper plate. Although initial clinical performance was promising,\textsuperscript{43-45} numerous technical limitations restricted clinical deployment. The primary disadvantage of the single-shot technique is increased noise resulting from the loss of x-ray quanta in the copper intersperser, resulting in a correspondingly noisy high-energy image. This results in a severe decrease in detective quantum efficiency (DQE).\textsuperscript{46} Single-shot DE imaging also necessitates increase patient dose requirements, because higher tube output is needed to ensure sufficient exposure to the rear detector. Also, the energy separation between low- and high-energy images is minimal, with improved energy separation coming at the cost of efficiency (a thicker intersperser). The notable advantage of the single-shot technique is that the images are acquired simultaneously and are correspondingly free anatomical misregistration (motion) artifacts.
The advent of FPDs in the late 1990s offered a promising technology for DE imaging, with high DQE and real-time readout offering the potential for DE imaging at unprecedented levels of imaging performance. DE imaging with an FPD uses a single detector with two exposures acquired at separate kVp. Termed “double-shot” imaging, the low-energy image is acquired at a low kVp (typically, 60 – 90 kVp) and the high-energy image at a high kVp (e.g., 120 – 150 kVp). The performance of FPD-based DE imaging is considerably higher than the single-shot technique, due in part to the improved DQE of the FPD itself (compared to a storage phosphor), but also the lack of a metal intersperser (no loss of x-ray quanta), the increased spectral separation through independent selection of low- and high-kVp, and the application of differential added filtration between the low- and high-kVp beams (e.g., using a filter wheel). Additional advantages of the “double-shot” technique include the capability to vary the proportion of patient dose between low- and high-kVp images (shown in Chapter III to be an important technique factor subject to optimization) and the potential for advanced DE imaging applications, including real-time fluoroscopy.

The chief disadvantage of double-shot (compared to single-shot) DE imaging is the temporal separation between projections. The time required for kVp switching and FPD readout are the primary contributors to such delay, ranging from hundreds of milliseconds to several seconds, depending on system configuration. The finite time interval can result in anatomical misregistration between low- and high-kVp projections, giving rise to motion artifacts in the DE images. Such artifacts notably occur as edges at the lung periphery, ribs, great vessels, bronchial structures, and the heart.
3.3 Applications of Dual-Energy Imaging

Chest imaging was one of the initial and most widely investigated applications of DE imaging, where anatomical clutter (ribs) is a major impediment to soft-tissue (nodule) detectability, and extinguishing of bone could significant boost soft-tissue conspicuity. Conventionally, DE imaging has been limited in widespread clinical application by suboptimal implementation, a relatively high radiation dose, and the lack of a high-performance detector. The availability of FPDs offering real-time digital readout and performance consistent with the demands of chest radiography, however, promises to remove conventional limitations, permitting high-performance DE imaging at total dose equivalent to that of a single chest radiograph.

The potential clinical advantages of DE chest imaging are twofold. It can potentially improve the sensitivity of conventional chest radiography with equivalent or improved specificity, allowing for a better “first read” and facilitating earlier, more accurate detection of disease. Recognizing the important, emerging role of LDCT in the early detection of lung cancer, the increased specificity associated with DE imaging creates the potential for adjuvant DE + LDCT, a combined modality reading offering high sensitivity and specificity in early-stage lung cancer detection.

Interest in DE imaging has surged significantly over the last ~5 years, bolstered by the availability of high-performance FPDs, recognition of anatomical clutter as the main limiting factor in lung nodule detectability, and the capability for more streamlined and optimized clinical implementations. Such raises the need to identify optimal DE image acquisition techniques and to address and minimize limitations in the context of this new detector technology. Further, such renewed interest in DE imaging using FPDs extends beyond chest imaging. For example, cardiovascular imaging of calcifications and atherosclerotic disease is an active area of research.
are applications in musculoskeletal imaging (e.g., differentiation of fractures and bony metastases), real-time interventional imaging (DE fluoroscopy), and DE computed tomography.

4. Overview of Thesis

This thesis describes original research in three important areas aiming to maximize the performance of DE imaging in the detection and classification of lung cancer. These include:

**Aim 1.** Design and implementation of a high-performance DE imaging system;

**Aim 2.** Optimization of DE image acquisition techniques; and

**Aim 3.** Creation of a cardiac gating system to minimize cardiac motion artifacts.

Chapter II describes the development of a novel DE imaging system, focusing on aspects of system design required for high-performance DE imaging, including the selection of differential added x-ray filtration implemented by means of a filter wheel. The work was published in a conference proceedings [Proc. SPIE Physics of Medical Imaging 6510: Pages 651006-1-651006-12 (2007)] and in the Medical Physics Journal [34(10): Pages 3904-3915 (2007)]. The chapter also introduces metrics of imaging performance and dosimetry used throughout the thesis.

Chapter III describes the optimization of DE image acquisition technique parameters for DE soft-tissue and bone-only decompositions. Experiments were performed to identify optimal kVp pair and allocation of dose between projections, with the results guiding the specification of a clinical technique chart suitable for patient studies. This work was published in two articles in the Medical Physics Journal, [34(10): Pages 3904-3915 (2007)] and [35(2): (2008)].

Chapter IV describes the design, implementation, and evaluation of a cardiac gating system developed to trigger low- and high-kVp exposures at a specified cardiac phase to minimize anatomical misregistration due to heart motion. This gating system utilizes a fingertip
pulse oximeter to trigger x-ray projections within diastole, the quiescent phase of the heart cycle. The system is based on a model for calculating systole and diastole intervals and was evaluated using patient data acquired in an early clinical trial. This work has been submitted for publication in the Medical Physics Journal (pending revision, January 2008).

The final chapter summarizes the significance of the work and describes the translation of the work to clinical trials in which the optimal image acquisition techniques and cardiac gating system are tested in patients. Future directions of the research from both technical and clinical perspectives are discussed.
Chapter II: Development of a High-Performance Dual-Energy Imaging System
1. Introduction

The development and characterization of an imaging system requires quantitative assessment of imaging performance metrics, technique parameters, and a means to describe and determine radiation dose. This chapter defines the basic metrics of radiation dosimetry and imaging performance used throughout the remainder of the thesis. Following definition of these metrics, the design and implementation of a high-performance DE imaging prototype suitable for clinical trials is reported.

2. Metrics of Dosimetry and Imaging Performance

2.1. Imparted Energy ($\varepsilon$) and Entrance Surface Dose (ESD)

Radiation dose was characterized in terms of the imparted energy:

$$\varepsilon = \int_{0}^{E_{\text{max}}} q_{E}(E) \cdot \eta(E; t) dE$$  \hspace{1cm} (2.1)

where $\varepsilon$ has units of $\mu$J/cm$^2$, $q_{E}(E)$ is the incident x-ray energy fluence (keV/cm$^2$), and $\eta(E; t)$ is the fraction of energy absorbed as a function of x-ray energy, $E$, and patient (water) thickness, $t$.\textsuperscript{55} Throughout this work, spectra were calculated using the SPEKTR\textsuperscript{56} implementation of the TASMIP algorithm.\textsuperscript{57} The absorbed energy fraction was based on Monte Carlo calculations of Boone, computed as a function of x-ray energy and (water) thickness\textsuperscript{55} and accounting for the principal x-ray interactions (coherent scatter, photoelectric effect, and Compton scatter) at diagnostic imaging energies (5 – 140 keV). For example, the absorbed fraction, $\eta(E)$, for three values of water thickness is displayed in Fig. 2.1(a), along with the associated energy imparted as a function of tube potential [Fig. 2.1(b)].

For conventional DR chest imaging, the imparted energy was determined from Eq. (2.1) for typical clinical techniques\textsuperscript{58} (kVp, mAs, and filtration), various body habitus (e.g., chest
thickness ranging 18 – 30 cm), and typical source-to-patient distance (equal to the source-to-detector distance, SDD ~ 170 cm, minus the chest thickness). For example, for an average chest thickness\(^5^9\) (24 cm), the imparted energy was computed to be 0.91 \(\mu\)J/cm\(^2\), which is consistent with the mean DR imaging dose reported in the Nationwide Evaluation of X-ray Trends (NEXT) Survey of 2001.\(^5^8\) In comparison to alternative detector technologies, the dose for a DR image is slightly lower than for computed radiography (CR) or film-screen (400 speed). The imparted energy can be converted directly to absorbed dose (mGy) and effective dose (mSv). Considering a volume of water simulating the patient thickness (30×30×10 cm\(^3\)), the absorbed dose for an average patient can be computed as \(D_{\text{abs}} = (0.91 \ \mu\text{J/cm}^2) \times (30 \times 30 \ \text{cm}^2) / (1 \ \text{g/cm}^3) / (30 \times 30 \times 10 \ \text{cm}^3) = 0.091 \ \text{mGy}\), and the effective dose as \(D_{\text{eff}} = D_{\text{abs}} \times (0.12) = 0.011 \ \text{mSv}\) (where 0.12 is the absolute to effective dose conversion factor for lung).\(^2^9\)

Throughout this work, unless stated otherwise, the total imparted energy for a DE acquisition (\(\varepsilon^{\text{Total}} = \varepsilon^{L} + \varepsilon^{H}\)) was equal to that of a single DR radiograph (within ± 5%) for the same chest thickness. For example, for an average chest thickness (24 cm), \(\varepsilon^{\text{Total}} = 0.91 \ \mu\text{J/cm}^2\), with the dose divided (“allocated”) between the low- and high-energy projections as described in the following section. Note that fixing the total DE imaging dose to that of a DR radiograph represents a conservative operating point for the studies described in this work (since DR dose is lower than that of other radiographic technologies – viz., CR and film-screen).
Figure 2.1. (a) Absorbed fraction as a function of photon energy for three equivalent chest thicknesses (18, 24, and 30 cm). (b) Imparted energy per unit mAs as a function of kVp, with beam filtration typical of clinical DR (3.5 mm Al + 0.2 mm Cu).

The entrance surface dose (ESD) provides an alternative dose metric that is often reported in the literature, because it is more directly measurable. To ensure consistency with values reported in the NEXT Survey\textsuperscript{58}, the ESD was computed for DR and DE imaging techniques as:

\[
ESD = \left[ \int_0^{E_{\text{max}}} \frac{q_\phi(E)}{q/X(E)} dE \right] \cdot \frac{\text{BSF} \cdot f_{\text{water}}}{\text{water}}
\]

where ESD has units of mGy, \(q_\phi(E)\) is the incident x-ray spectrum, \(q/X(E)\) is the fluence per unit exposure\textsuperscript{60}, and \(E_{\text{max}}\) is the maximum energy of the x-ray spectrum. The f-factor \((f_{\text{water}})\) and backscatter fraction \((\text{BSF})\) were taken from Hubbell\textsuperscript{61} and Johns et al.,\textsuperscript{62} respectively, averaged over the incident x-ray spectrum. The dependence of ESD on kVp and chest thickness typical in DR is illustrated in Fig 2.2.
2.2. Dose Allocation

An important technique factor in DE imaging is the proportion of total dose imparted by the low- and high-kVp projections, referred to as dose allocation. For a fixed total imparted energy, $\varepsilon^{\text{Total}}$, the dose allocation, $A_\varepsilon$, is defined as the fraction of dose imparted by the low-energy projection:

$$A_\varepsilon = \frac{\varepsilon^L}{\varepsilon^L + \varepsilon^H}$$  \hspace{1cm} (2.3)

where $\varepsilon^L$ and $\varepsilon^H$ are the energies imparted in low- and high-kVp projections, respectively. Dose allocation ranges from 0 (all dose allocated to the high-kVp projection) to 1 (all dose allocated to the low-kVp projection).

2.3. Dual-Energy Image Contrast, Signal, and Noise

A simple metric used below to characterize DE imaging performance in the visualization of a given structure (e.g., soft-tissue or bone) relative to the background is the signal-difference-to-noise ratio (SDNR$^{\text{DE}}$). The SDNR is a “large-area transfer characteristic,” meaning that it relates to the detectability of structures whose size (e.g., ~1 cm) is much greater than the
characteristic resolution length of the imaging system (e.g., <1 mm). While more sophisticated, spatial-frequency-dependent metrics – such as noise-equivalent quanta (NEQ) – are certainly valuable in the measurement and modeling of imaging performance, their application in DE imaging is a subject of ongoing research, and analysis of the basic signal and noise characteristics is a valuable initial approach. In sections below, theoretical and experimental descriptions of DE image signal and noise are described. Theoretical descriptions are used primarily for the identification of optimal differential added filtration (Section 3.4). Experimental descriptions form the basis of the technique optimization studies (Chapter III).

### 2.3.1 DE Material Contrast

The intrinsic contrast (C\textsuperscript{DE}) of two structures in a DE image may be calculated in terms of the effective attenuation coefficients at a given low- and high-energy pair. For example, the contrast between a nodule and background lung is calculated from the difference in attenuation coefficients at low- and high-kVp:

\[
C^{DE} = \left( \mu^H_{\text{nodule}} - \mu^H_{\text{lung}} \right) - \frac{\mu^H_{\text{bone}}}{\mu^L_{\text{bone}} \left( \mu^L_{\text{nodule}} - \mu^L_{\text{lung}} \right)} \left[ \mu^L_{\text{nodule}} - \mu^L_{\text{lung}} \right] d_{\text{nodule}}
\]  \hspace{1cm} (2.4)

where \(d_{\text{nodule}}\) is the thickness of the nodule, and \(\mu\) is the effective attenuation coefficient for nodule, lung, or bone.

In general, the effective attenuation coefficient is:

\[
\mu_{\text{eff}} = \frac{1}{t} \left[ \int_0^{E_{\text{mu}}} e^{-\mu(E)t} q_o(E)dE \right] - \left[ \int_0^{\infty} q_o(E)dE \right]
\]  \hspace{1cm} (2.5)

where \(t\) is the thickness object (e.g., nodule, bone, etc.), and \(q_o\) is the x-ray spectrum following transmission through the patient (to account for beam hardening).

Equation (2.4) indicates that increasing the spectral separation improves nodule contrast, accomplished by hardening the high-kVp beam or softening the low-kVp beam (e.g., with a K-
edge filter). For example, $C^{DE}$ calculated as a function of filter thickness added to the high-kVp beam is displayed in Fig. 2.3. As shown in Fig. 2.3 (a), addition of Cu ($Z_{filter} = 29$) to the high-kVp beam significantly improves nodule contrast. Fig. 2.3(b) illustrates the point further, plotting $C^{DE}$ as a function of filter thickness for material types ranging $Z_{filter} = 1 – 92$ and showing a significant boost in DE image contrast as the spectral separation increases. Contrast is seen to improve for $Z_{filter} \sim 45 – 65$ and $Z_{filter} > 85$, selections that considerably harden the high-kVp beam. A sharp reduction in contrast is observed for filter materials in the range $Z_{filter} \sim 70 – 79$, as a result of filter K-edge absorption that effectively “softens” the x-ray beam relative to other filters, reducing the mean energy and thus the spectral separation. The effects are investigated in greater detail in relation to selection of added filtration in the DE imaging prototype (Section 3.4), below.

![Figure 2.3](image)

**Figure 2.3.** (a) Effect of added copper filtration ($Z_{filter} = 29$) of the high-kVp beam. DE contrast between a simulated lung nodule and background is shown as a function of filter thickness. (b) Effect of added filtration on contrast between a simulated lung nodule and background in DE images. Calculations are shown as a function of high-kVp filter material ($Z_{filter}$) and thickness ($s_{filter}$). kVp-pair and kVp$^L$ filtration was fixed at [70/130] kVp and 2.5 mm Al, respectively.

### 2.3.2 DE Image Signal

The relative signal difference between an object of interest (e.g., nodule or bone) and background in a DE image was investigated through theoretical and experimental studies. For
theoretical calculations, cascaded systems analysis (CSA) was used to provide an analytical description of signal propagation and has been applied successfully to several imaging systems.\textsuperscript{66-73} The detector signal for both low- or high-energy images was computed through varied filter materials and decomposed using Eq. 1.12.

The tissue cancellation parameter, \( w_s \) or \( w_{bs} \), is theoretically described by the ratio of effective attenuation coefficients, as described in Chapter I. For theoretical calculations, the parameter yielding the DE soft-tissue image was computed using:

\[
\begin{align*}
\ln \frac{I_{\text{bone}}^L}{I_{\text{bone}}^H} &= \ln \left( \frac{I_{\text{bone}}^H}{I_{\text{bone},0}^H} \right) \\
&= \ln \frac{I_{\text{bone}}^L / I_{\text{bone},0}^L}{I_{\text{bone}}^L / I_{\text{bone},0}^L} \\
&= \ln \frac{I_{\text{bone},0}^L}{I_{\text{bone},0}^L} \\
\end{align*}
\]

where \( I_{\text{bone},0} \) denotes the signal without bone attenuation.

The theoretical relative signal difference could then be computed using:

\[
\begin{align*}
SD_{\text{rel, theoretical}}^{\text{DE}} &= \frac{I_{\text{DE, object}} - I_{\text{DE, background}}}{\sqrt{2} \left( I_{\text{DE, object}} + I_{\text{DE, background}} \right)} \\
\end{align*}
\]

where \( I_{\text{DE, object}} \) and \( I_{\text{DE, background}} \) are the computed signal transmitted through an object (simulated nodule) and background (lung) of a DE image, respectively.

In experimental studies, the relative signal difference was measured as the difference in mean signal between two regions of interest (ROIs) of an image containing the two materials, normalized by the mean signal level:

\[
\begin{align*}
SD_{\text{rel, experimental}}^{\text{DE}} &= \frac{\overline{I_{\text{DE, object}}} - \overline{I_{\text{DE, background}}}}{\sqrt{2} \left( \overline{I_{\text{DE, object}}} + \overline{I_{\text{DE, background}}} \right)} \\
\end{align*}
\]

where \( \overline{I_{\text{DE, object}}} \) and \( \overline{I_{\text{DE, background}}} \) are the mean signal in the object and background regions of a DE image, respectively. Example regions of interest for measurement of mean signal (and noise) in soft-tissue and bone images are shown in Fig. 2.4.
Signal difference ($SD_{rel,\text{theoretical}}^{DE}$ and $SD_{rel,\text{experimental}}^{DE}$) was used as a measure of nodule contrast in both and theoretical calculations (below) and experimental studies (Chapter III).

### 2.3.3 DE Image Noise

Theoretically, DE image noise was computed from the noise-power spectrum (NPS) in low- and high-kVp projections, combined to yield the dual-energy relative NPS. The NPS is a measure of the noise transfer properties of a system, and was computed using CSA, including effects such as K-fluorescence, scintillator blur, noise aliasing, and electronic noise. For example, the NPS of the DE soft-tissue image is given by:

$$NPS_{rel}^{DE} = NPS_{rel}^H + w_s^2 NPS_{rel}^L$$

(2.9)

where the subscript “rel” indicates relative NPS (i.e., the absolute NPS divided by the square of the mean signal).

The pixel variance was computed by integrating the NPS over the Nyquist region of the 2D Fourier domain, yielding the relative DE pixel noise:

$$\sigma_{rel,\text{theoretical}}^{DE} = \sqrt{\left(\sigma_{rel}^H\right)^2 + w_s^2 \left(\sigma_{rel}^L\right)^2}$$

(2.10)

where $(\sigma_{rel}^H)^2$ and $(\sigma_{rel}^L)^2$ are the relative variances in high- and low-kVp images, respectively.
Experimentally, the noise in DE images was measured in terms of the variation in pixel values in regions of the nodule and background, with relative noise given by the mean standard deviation divided by the mean signal:

$$\sigma_{DE, \text{rel, experimental}} = \frac{\sigma_{DE, \text{object}}^2 + \sigma_{DE, \text{background}}^2}{I_{DE, \text{object}} + I_{DE, \text{background}}}$$

(2.11)

where $\sigma_{DE, \text{object}}$ and $\sigma_{DE, \text{background}}$ are the standard deviations in signal in the nodule and background regions. Regions of interest for measurement of the pixel noise are as in Fig. 2.4 above.

### 2.3.4 DE Image Signal-Difference-to-Noise Ratio (SDNR)

Theoretically, the SDNR$^{DE}$ was calculated as the ratio of relative signal difference and noise as computed by cascaded systems analysis [Eqs. (2.7) and (2.10)]:

$$SDNR_{DE, \text{theoretical}}^{DE} = \frac{SD_{rel, \text{theoretical}}^{DE}}{\sigma_{rel, \text{theoretical}}^{DE}}$$

(2.12)

Experimentally, the SDNR was measured in DE images of a chest phantom as the ratio of relative signal difference and noise [Eqs. (2.8) and (2.11), respectively] as measured in ROIs illustrated in Fig. 2.4

$$SDNR_{DE, \text{experimental}}^{DE} = \frac{SD_{rel, \text{experimental}}^{DE}}{\sigma_{rel, \text{experimental}}^{DE}}$$

(2.13)

### 3. Dual-Energy Imaging Prototype

#### 3.1 The Chest Imaging Platform (RVG-5100)

A DE imaging system has recently been developed in our laboratory$^{53,74}$ and translated to patient imaging trials designed to test the sensitivity and specificity of lung nodule diagnosis. The system is illustrated in Fig. 2.5. Based on a Kodak RVG-5100 digital radiography chest stand (Carestream Health Inc., Rochester, NY), the system includes a high-frequency, 3-phase
generator (Indico 100, CPI, Georgetown, Ontario), a 400 kHU x-ray tube (Varian Rad-60, Salt Lake City, UT), and a 10:1 antiscatter Bucky grid (Advanced Instrument Development Inc., Melrose Park, NJ).

The DE system has been implemented within a digital x-ray imaging suite in the Medical Imaging Day Unit at the Toronto General Hospital (Toronto, ON, Canada). A detailed schematic of the system is shown in Fig. 2.6. An acquisition workstation controls every aspect of the system, including generator technique settings, filter selection, detector acquisition parameters, digital image readout, preliminary image display, and data transfer to a central picture archiving and communication system (PACS) and diagnostic workstation. Communication with the generator and timing/distribution unit (TDU) occurs through RS-232 ports, the filter wheel is driven via a controller area network (CAN) bus, and communication with the FPD is via RS-232 and fiber-optic connections.

**Figure 2.5.** Research prototype for DE chest imaging. The system is based on a radiographic chest stand (Kodak RVG 5100, Carestream, Inc. Rochester NY), modified to perform cardiac-gated DE imaging.
Figure 2.6. Detailed schematic illustrating the research prototype and describing specific cable communications between components. Also shown are the dedicated workstations associated with the system (Sec. 3.4 – 3.5), including the diagnostic workstation (image review), acquisition workstation (image acquisition), and cardiac monitoring workstation (monitoring signals related to the cardiac trigger described in Chapter IV).

A number of modifications to the RVG-5100 platform were undertaken to achieve high-performance DE imaging. The main modifications are described below, including: replacement of the CR cassette with a flat-panel detector; a collimator incorporating a computer-controlled filter wheel for differential low- and high-kVp filtration; a simple cardiac gating system based on a fingertip pulse oximeter; and dedicated workstations for DE image acquisition, decomposition, and display.

3.2 The Detector (Pixium-4600)

The detector stand was equipped with a high-performance flat-panel detector, FPD (Trixell Pixium-4600, Moirans, France). The Pixium-4600 is a large-area (~43×43 cm²) indirect-detection (250 mg/cm² CsI:Tl) detector composed of 3121×3121 pixels at 143 µm pitch. The pixel fill-factor is 0.68, with each pixel incorporating an a-Si:H photodiode plus double-diode pixel readout architecture. Pixel signal is digitized to 14 bits. Prior to implementation on the
RVG-5100 platform, the FPD was characterized in laboratory studies of pixel- and Fourier-based characterization, showing linear response across dose for all kVp, ~4025 electrons of electronics noise, and a zero-frequency DQE of ~0.6 at 80 kVp. The Pixium-4600 exhibits a variable delay upon image request (250 – 385 ms between an image request and the detector-ready state) and an image readout time of ~5 seconds. A detailed description of detector timing is reported in Chapter IV. Future versions of the detector, offering equivalent imaging performance but improved timing characteristics, are anticipated.

### 3.3 Collimator and Filter Wheel

A collimator assembly (Ralco R302 ACS/A, Biassono, Italy) incorporating a computer-controlled filter wheel was incorporated on the RVG-5100 platform. The filter wheel provides four positions for varying the added filtration in the low- and high-kVp beams. The transition time between filter wheel positions is ~1.5 seconds, less than the current inter-exposure readout time supported by the FPD.

The four filter wheel positions are summarized in Table 2.1. The added filtration in positions 1 and 2 (the low- and high-kVp positions, respectively) were guided by results described in Section 3.4, below. Filter wheel Positions 3 and 4 are used for conventional DR acquisition and monthly quality assurance, respectively.

<table>
<thead>
<tr>
<th>Filter Wheel Position</th>
<th>Used for:</th>
<th>Added Filtration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Low-kVp Projection</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>High-kVp Projection</td>
<td>2 mm Al + 0.6 mm Ag</td>
</tr>
<tr>
<td>3</td>
<td>DR Projection</td>
<td>1 mm Al + 0.2 mm Cu</td>
</tr>
<tr>
<td>4</td>
<td>Testing / QA</td>
<td>2 mm Al</td>
</tr>
</tbody>
</table>

**Table 2.1.** Filter wheel added filtration. Inherent filtration of the x-ray tube and collimator amounts to 2.5 mm Al.
3.4 Differential Added Filtration

One of the main benefits of double-shot DE imaging is the potential for increased energy separation between low- and high-kVp projections. This can be achieved through the optimization of differential filtration between beams as well as though careful selection of low- and high-kVp pair (Chapter III). The selection of x-ray filtration for high-performance DE imaging has been investigated previously, most notably in the context of mammography \(^{76-79}\) and to a lesser extent, single-shot DE imaging of the chest. \(^{80}\) Such work provides a valuable basis for investigation of optimal image acquisition techniques in the current context of double-shot imaging. This work extends previous work by optimizing DE filtration specifically for FPD-based systems.

The effect of differential added filtration between low- and high-kVp projections was examined as a function of the material type (atomic number, \(Z_{\text{filter}}\)) and thickness (coverage, \(s_{\text{filter}}\), given by the product of thickness and density) of added filtration. Performance was evaluated in terms of DE image contrast, SDNR\(^{\text{DE}}\), as well as patient dose and tube loading characteristics. The imaging task was the detection of a 0.95 cm diameter lung nodule, with corresponding optimization of the soft-tissue DE image.

Calculations were performed based on Eq. 2.14 on the basis of a hypothetical chest model composed of 10 cm water and 10 cm inflated lung. \(^{61}\) Ribs were modeled as 5 mm cortical bone, and pulmonary nodules as 9.5 mm polyethylene. \(^{61}\) For each filter selection, the exposure at the detector was fixed at 1 mR, and patient dose was calculated in terms of the imparted energy. As typical of clinical practice, therefore, \(\varepsilon^{\text{Total}}\) was allowed to vary in these calculations such that the detector exposure was 1 mR.

The dependence of DE imaging parameters and performance metrics on beam filtration is illustrated in Fig. 2.7. In each case, calculations are shown as a function of high-kVp filter
material type ($Z_{\text{filter}}$) and thickness ($s_{\text{filter}}$), with the low-kVp beam fixed at 70 kVp (+2.5 mm Al inherent filtration) and a high-kVp of 130 kVp. Previous studies\textsuperscript{74} indicate that effects of the low-kVp filter (e.g., softening the beam with a ~0.1 – 0.2 mm Ce) are fairly small due to subsequent hardening of the beam by the patient. The results below focus on the high-kVp filter, with a fixed low-kVp filter of 2.5 mm Al.

Figure 2.7(a) shows the reduction in tissue weighting parameter, $w_s$ ($Z_{\text{filter}}$, $s_{\text{filter}}$), as filter thickness and atomic number increase (up to $Z_{\text{filter}}$ ~ 65), corresponding to reduced bone contrast for harder beams. The increase in $w_s$ in the region $Z_{\text{filter}} = 65 – 80$ is due to the filter K-edge falling close to the mean energy of the high-kVp beam, effectively softening the beam. A sharp decrease in $w_s$ occurs as the K-edge increases at higher atomic numbers, $Z_{\text{filter}} > 80$.

**Figure 2.7.** Effect of added filtration on DE imaging performance. Calculations are shown as a function of high-kVp filter material ($Z_{\text{filter}}$) and thickness ($s_{\text{filter}}$). (a) Tissue weighting parameter, $w_s$, for decomposition of a soft-tissue only image. (b) DE image signal difference (nodule contrast) computed as in Eq. (2.7). (c) DE image signal-difference to noise ratio, $\text{SDNR}^{\text{DE}}$. (d) Tube mAs required to deliver an exposure of 1 mR to the detector (in the high-kVp projection). Note the logarithmic scale. (e) Imparted energy. (f) $\text{SDNR}^{\text{DE}}$ per unit patient dose (imparted energy). All results are for an average patient thickness.”
The effect of filtration on SD\textsuperscript{DE} is shown in Fig. 2.7(b). The overall dependence of nodule signal difference on high-kVp filter selection is similar to the results shown in 2.5(b). A harder beam results in increased spectral separation, giving increased DE signal difference at $Z_{\text{filter}} \sim 42$ – 63 and $Z_{\text{filter}} > 84$ at thicknesses greater than 1.5 g/cm\textsuperscript{2}. The K-edge effect at $Z_{\text{filter}} = 65 – 80$ significantly reduces SD\textsuperscript{DE} at all thicknesses due to softening of the high-kVp beam.

While a harder high-kVp beam increases nodule contrast, the tradeoff in image noise and SDNR\textsuperscript{DE} is illustrated in Fig. 2.7(c), suggesting optimal filtration in the region $Z_{\text{filter}} = 25 – 50$ (depending on filter thickness), and a second region of even higher SDNR\textsuperscript{DE} above $Z_{\text{filter}} > 77$.

The filters thus implied were considered in relation to tube loading and patient dose as in Figs. 2.7(d-e). Figure 2.7(d) shows the mAs required to deliver 1 mR to the detector as a function of high-kVp filtration, implying an enormous heat load for thick, high-Z filters. Such loading effectively rules out the upper-right quadrant of ($Z_{\text{filter}}$, $s_{\text{filter}}$), for which mAs\textsuperscript{H} $\sim 100$ mAs. The patient dose (impacted energy) for the high-kVp beam is shown in Fig. 2.7(e), showing increased dose for softer beams and suggesting a region in the range $Z_{\text{filter}} \sim 30 – 65$ consistent with lower patient dose. Because the calculations were performed with a fixed detector exposure of 1 mR, the patient dose varies significantly over the range of ($Z_{\text{filter}}$, $s_{\text{filter}}$) investigated.

The SDNR\textsuperscript{DE} per unit dose (impacted energy) is shown in Fig. 2.7(f). Similar to Fig. 2.7(c), the results illustrate the degradation in performance at low atomic number ($Z_{\text{filter}} < 20$), the influence of the K-edge ($Z_{\text{filter}} = 65 – 80$), and the enhancement at very high atomic number ($Z_{\text{filter}} > 80$). The effects within the optimal range $Z_{\text{filter}} \sim 25 – 50$ implied by Fig. 2.7(c) exhibit a shift toward higher filter thickness [due to reduced patient dose, as in Fig. 2.7(e)]. Such is consistent with the generally recognized notion that increasing filter thickness improves SNR per unit dose, but at the cost of tube loading [Fig. 2.7(d)].
A practical, optimal filter selection must therefore account for the tradeoffs among SDNR$_{DE}$, tube loading, and patient dose. For example, considering SDNR$_{DE}$ [Fig. 2.7(c)], an optimal filter selection of $Z_{filter} = 47$ (Ag) $s_{filter} = 0.5$ g/cm$^2$ (0.48 mm) is implied, and such is consistent with reasonable tube output [mAs$^H = 17$ mAs in Fig. 2.7(d)]. Considering SDNR$_{DE}$ per unit dose, on the other hand [Fig. 2.7(f)], the optimal filter thickness increases to 0.85 g/cm$^2$ (0.81 mm Ag) with an increased high-kV tube output of 35 mAs. A reasonable compromise among competing factors of SDNR$_{DE}$, tube output, and dose, for example, is 0.63 g/cm$^2$ (0.6 mm) Ag, corresponding to an acceptable tube output (mAs$^H = 25$ mAs) without significant tradeoff in SDNR$_{DE}$ or SDNR$_{DE}$/$\varepsilon_{Total}$. Such is reflected in the filter selections implemented on the clinical prototype, summarized in Table 2.1.

The results of Fig. 2.7 imply a fairly broad range of filter materials that, given an appropriate thickness, represent equivalently “optimal” filter selections. To illustrate this point, the peak SDNR$_{DE}$ from Fig. 2.7(c) and the associated filter thickness are shown in Fig. 2.8. A plateau in $Z_{DE, peakSDNR_{filter}} = 25 – 50$, suggesting a fairly broad range of choices for high-kVp filtration. The increase in SDNR$_{peak}$ at $Z_{filter} \sim 80$ was ruled out due to unacceptably high tube loading. For filters in the range $Z_{filter} \sim 45 – 52$, optimal filtration is achieved with filter thickness less than $\sim 1$ mm, aiding practical implementation. Reasonable filter selections include $\sim 2.1$ mm Cu ($Z_{filter} = 29$), $\sim 1.2$ mm Zr ($Z_{filter} = 40$), $\sim 0.7$ mm Mo ($Z_{filter} = 42$), $\sim 0.4$ mm Pd ($Z_{filter} = 46$), and $\sim 0.5$ mm Ag ($Z_{filter} = 47$).
As mentioned above, the reduction in mean beam energy in the range $Z_{\text{filter}} \sim 65 – 80$ [shown in Fig. 2.7(b-c)] is attributed to K-edge absorption. Such an effect in the high-kVp beam results in increased spectral overlap, thereby reducing DE image contrast. When applied to the low-kVp beam, K-shell filters can potentially increase the spectral separation (thereby increasing $SD^{DE}$) through this same effect. However, subsequent beam-hardening by the patient was found to significantly reduce the potential benefit of K-edge filtering of the low-kVp beam.\textsuperscript{74}

3.5 Cardiac-Gating System

To minimize misregistration associated with cardiac motion between low- and high-kVp projections, a cardiac gating system was implemented to trigger x-ray exposure within the quiescent phase of the heart cycle.\textsuperscript{53,74} Based on a fingertip pulse oximeter, the system offers a fast, logistically convenient means of reducing the cardiac motion artifact. In addition to the oximeter instrumentation itself, the imaging platform incorporates timing based on a model of heart-rate-dependent diastole and systole periods.
Communication between the oximeter and acquisition workstation occurs through serial RS-232 connection, transmitting data at 75 frames per second, with each frame consisting of a 5-byte packet. Software designed by collaborators at Carestream Health Inc. was developed to interface the oximeter data with image acquisition workstation based on specifications described in the cardiac gating model.

A cardiac monitoring workstation (IBM PC, IBM, Armonk, NY; 2.2 GHz, 1 GB physical memory) was implemented to record timing data from the patient and x-ray generator, allowing post-acquisition analysis of trigger accuracy. The monitoring workstation passively records data from the oximeter through an onboard data acquisition card (PCI-6036E, National Instruments, Austin, TX). In addition to the cardiac signal, data from digital pin-outs on the generator and timing/distribution unit are also obtained by the acquisition card, and record the time of x-ray exposure. Synchronous reporting of both oximeter and generator/tube information allow for quantitative evaluation of the cardiac gating system. The development, implementation, and evaluation of cardiac-gated acquisition are described fully in Chapter IV.

### 3.6 Acquisition and Display Workstations

Lastly, two dedicated workstations were implemented in the DE imaging prototype. The first is the acquisition workstation (Dell Precision 650, 2×2.66 GHz Xeon CPU, 2GB physical memory), with software developed for cardiac-gated DE image acquisition (Carestream Health, Rochester, NY). A second workstation [Dell Precision 650, 3.0 GHz, 2.0 GB physical memory)] as implemented in a radiology reading room for DE image decomposition and display. Novel aspects of DE image decomposition under investigation in other work include: automatic, spatially-varying determination of tissue cancellation parameters; deformable registration of low- and high-energy projections;\textsuperscript{81} and implementation of generalized noise reduction techniques.\textsuperscript{82}
The diagnostic workstation incorporates two medical imaging displays [1536×2048, diagnostic-quality, 8-bit grayscale displays (AXIS III, National Display Systems, Morgan Hill, CA)] suitable for human observer performance studies.\(^\text{83}\)

**Figure 2.9.** (a) Screenshot of acquisition software for the DE imaging prototype. (b) Photograph of diagnostic workstation incorporating two medical imaging displays.

**4. Conclusions**

A high-performance DE imaging system for the detection and classification of early-stage lung cancer is under development. Several modifications were made to a commercially available chest imaging platform to maximize DE imaging performance. Major modifications include: incorporation of a high-performance FPD, a collimator with computer-controlled filter wheel for differential-added filtration, a cardiac gating system, and integration with advanced DE image processing, decomposition, and display tools.

One of the important technique factors in DE imaging was investigated in detail above – viz., selection of optimal x-ray filtration. Optimal filter material types and thickness were identified that balance the tradeoffs between contrast and noise, presenting techniques that are achievable at acceptable tube loading and patient dose. A range of high-kVp filters providing comparable imaging performance is suggested – e.g., as shown in Figs. 2.7 and 2.8, metals in the range \(Z_{\text{filter}} \sim 40 – 47\) with thickness less than 1 mm.
Chapter III: Dual-Energy Imaging Technique Optimization
1. Introduction

Optimization of acquisition technique parameters is an important aspect in developing a new imaging system suitable for clinical studies. Two essential technique parameters for double-shot DE imaging are the kVp-pair (denoted \([kVp^L / kVp^H]\)) and dose allocation \((A_\varepsilon)\). A thorough experimental study using a custom-built chest phantom was performed to optimize these parameters, with the objective of maximizing the visibility of lung nodules in DE soft-tissue images and/or the visibility of bone in DE bone-only images. A range of \(kVp^L\) (60 – 90 kVp), \(kVp^H\) (120 – 150 kVp), and \(A_\varepsilon\) (0 – 1) was investigated, with total radiation dose equivalent to that of a single chest radiograph in all cases (e.g., \(\varepsilon = 0.91 \mu J/cm^2\) for an average-sized patient). Also investigated was the effect of total dose on image quality and dose allocation. Other system parameters were not varied in this work (i.e., they were fixed based on the results from prior experimentation), including: added filtration (differential filtration fixed as in Table 2.1, Chapter II), the anti-scatter Bucky grid (a 10:1 grid as mentioned in Chapter II), and the system geometry (e.g., patient-detector gap), etc.

Several previous studies have investigated DE technique optimization in the context of mammography\(^{76-79}\) and single-shot DE imaging of the chest.\(^{80}\) Optimization of double-shot DE chest imaging with a FPD provides a valuable basis for implementing such systems in clinical use. Taken together, the theoretical optimization of filter in Chapter II and the experimental optimization of kVp and dose allocation, below, constitute a fairly complete characterization of technique factors, suitable for definition of an optimal “technique chart” for use in clinical studies.
2. Materials and Methods

2.1. Imaging Phantom

Optimal acquisition techniques, including kVp-pair and dose allocation, were investigated experimentally using a chest phantom modeled after the ANSI patient-equivalent phantom,\textsuperscript{84} as illustrated in Fig. 3.1(a). The phantom is a highly idealized “slab” representation of a human chest, containing materials simulating soft-tissue and bone and with thickness variable through the addition or removal of slabs. Lung nodules (9.5 mm right-circular cylinders) were simulated using materials ranging from micro-bubble-infused polyurethane (-500 HU) to nylon (~+75 HU). Ribs were simulated by Al slats (3 and 6 mm thick). The correspondence between phantom thickness and patient thickness was established by measuring the transmitted exposure (i.e., the exposure at the surface of the anti-scatter grid) for “thin,” “average,” and “thick” DR technique stations, varying the thickness of acrylic such that the transmitted exposure was ~1 mR in each case. The phantom (acrylic) thicknesses corresponding to “thin” (18 cm), “average” (24 cm), and “thick” (30 cm) patient thicknesses were 7.5, 10, and 12 cm acrylic, respectively. As the lung field is the main area of interest when imaging for the detection of solitary lung nodules, the phantom thickness corresponds to this region. Therefore, the phantom thickness (e.g., 7.5 – 12 cm acrylic) corresponds to the effective thickness in the region of the lung for a given patient thickness (e.g., 18 – 30 cm chest) as measured from the xiphoid process to the thoracic vertebra (~T8).
Figure 3.1. (a) Schematic illustration of the chest “slab” phantom containing simulated lung nodules (9.5 mm diameter right-circular cylinders) and simulated ribs (3 and 6 mm thick Al slats). Chest thickness is variable through the addition or removal of additional acrylic slabs. (b-e) Example low-kVp, high-kVp, and DE soft-tissue and bone images of a simulated lung nodule (polyethylene) obscured by a 3 mm thick rib (Al). ROIs for analysis of SDNR$^{DE}$ are as shown in Chapter II, Fig. 2.4.

2.2. DR Technique Factors and Dose

DR technique factors for “thin,” “average,” and “thick” patient sizes were obtained from a review of the literature and clinical technique charts at in the Department of Medical Imaging, Toronto General Hospital (Toronto, ON Canada). The resulting kVp and mAs are shown in Table 3.1, along with the transmitted exposure measured behind the corresponding thickness of acrylic ($X_{\text{Detector}}$) and total imparted energy ($\varepsilon_{\text{Total}}$). Other factors relating to x-ray scatter and glare were held fixed at nominal selections for the prototype system – e.g., use of a 10:1 bucky grid, and a fixed geometry (~10 cm object-detector air gap).
### Table 3.1. Summary of DR technique factors for thin, average and thick patient sizes.

<table>
<thead>
<tr>
<th></th>
<th>Thin</th>
<th>Average</th>
<th>Thick</th>
</tr>
</thead>
<tbody>
<tr>
<td>( t_{\text{chest}} )</td>
<td>18 cm</td>
<td>24 cm</td>
<td>30 cm</td>
</tr>
<tr>
<td>( t_{\text{acrylic}} )</td>
<td>7.5 cm</td>
<td>10 cm</td>
<td>12 cm</td>
</tr>
<tr>
<td>kVp</td>
<td>120 kVp</td>
<td>120 kVp</td>
<td>120 kVp</td>
</tr>
<tr>
<td>Added Filtration</td>
<td>1mm Al + 0.2 mm Cu</td>
<td>1mm Al + 0.2 mm Cu</td>
<td>1mm Al + 0.2 mm Cu</td>
</tr>
<tr>
<td>mAs</td>
<td>2.0 mAs</td>
<td>3.2 mAs</td>
<td>6.4 mAs</td>
</tr>
<tr>
<td>( X_{\text{Detector}} )</td>
<td>(1.10 ± 0.004) mR</td>
<td>(1.14 ± 0.005) mR</td>
<td>(1.34 ± 0.003) mR</td>
</tr>
<tr>
<td>( \varepsilon^{\text{Total}} )</td>
<td>0.44 ( \mu )J/cm(^2)</td>
<td>0.91 ( \mu )J/cm(^2)</td>
<td>2.08 ( \mu )J/cm(^2)</td>
</tr>
<tr>
<td>ESD</td>
<td>0.066 mGy</td>
<td>0.11 mGy</td>
<td>0.21 mGy</td>
</tr>
</tbody>
</table>

#### 2.3. Dose Allocation and kVp Pair

Measurements of SDNR\(^{\text{DE}}\) were performed using the phantom of Fig. 3.1 across a range of low-kVp (60 – 90 kVp), high-kVp (120 – 150 kVp), dose allocation (\( A_{\varepsilon} = 0 – 1 \)), and patient dose (\( \varepsilon^{\text{Total}} = 0.20 – 1.73 \ \mu \)J/cm\(^2\)). To acquire DE images at various low-kVp, high-kVp, and allocation but at the same total dose, imparted energies were computed at all available kVp and mAs stations permitted by the x-ray generator. For each patient thickness and kVp pair, combinations of \( \varepsilon^{L}(\text{mAs}) \) and \( \varepsilon^{H}(\text{mAs}) \) were identified that yielded a given total dose, \( \varepsilon^{\text{Total}} \), within ±5%. For example, at a kVp-pair of [70/130] kVp, mAs settings of [3.2/16] mAs give \( \varepsilon^{\text{Total}} = 0.88 \ \mu \)J/cm\(^2\) with an allocation of \( A_{\varepsilon} = 0.29 \), whereas mAs settings of [10/2] mAs deliver the same total dose (\( \varepsilon^{\text{Total}} = 0.90 \ \mu \)J/cm\(^2\)), but with allocation of \( A_{\varepsilon} = 0.91 \). In this manner, ~10 stations were identified for each patient thickness, kVp pair, and total dose that resulted in allocation across the desired range, \( A_{\varepsilon} \sim 0.1 – 0.9 \).
2.4. Soft-Tissue Image

SDNR⁰ was evaluated in soft-tissue DE images of the phantom, with the bone cancellation parameter (wₛ) determined automatically to minimize the signal difference between regions of simulated rib and background, ensuring optimal bone cancellation in the DE soft-tissue images. As illustrated in Chapter II, Fig. 2.4(a), seven ROIs (41×41 pixels) were identified, one within the polyethylene nodule (yielding \( I_{\text{nodule}}^{\text{DE}} \)) and six in the adjacent background (yielding \( I_{\text{background}}^{\text{DE}} \)). Signal difference, noise, and SDNR were computed as in Eqs. (2.8), (2.11), and (2.13), respectively. The mean and standard deviation in each measurement were determined from ten repeat image acquisitions.

Measurements were performed for a total of sixteen kVp-pairs and three phantom thicknesses. In addition, for the average phantom thickness, measurements were performed as a function of imparted energy – viz., 11 dose levels ranging from about one-fifth to twice that of a conventional DR chest exam (0.20 – 1.73 µJ/cm²) at [70/130] kVp. Slight variations in the dose (constant to within ±5% for fixed patient thickness and kVp-pair) were corrected by normalizing the measured noise by the square root of the ratio of calculated and target level of \( \varepsilon^{\text{Total}} \).

2.5. Bone-Only Image

SDNR⁰ was also evaluated in the complementary DE bone image. Like the soft-tissue image, the tissue weighting parameter (wₜ) was automatically selected, though in this case to minimize the nodule contrast with respect to background (bone) using the same seven ROIs in Fig. 2.4(a). The SDNR in the resulting DE bone images was then computed using the ROIs shown in Fig. 2.4(b), six within the bone (\( I_{\text{bone}}^{\text{DE}} \)), and six in the nearby acrylic background (\( I_{\text{background}}^{\text{DE}} \)). Again, the mean and standard deviation in each measurement were determined from
ten repeat image acquisitions with measurements repeated for all kVp-pairs. For this study, one phantom thickness (average) was investigated. As in the soft-tissue studies, above, measurements were also performed as a function of total imparted energy at a fixed [70/130] kVp.

2.6. Curve-Fitting

Curves of SDNR\textsuperscript{DE} versus dose allocation (for a given kVp pair and \(\varepsilon^{Total}\)) were fit using a 3-parameter empirical function. Curve fits were intended to guide the reader’s eye in the results below and to identify optimal dose allocation, denoted \(A^*_\varepsilon\), as indicated by the maximum of the curve. Fits were found to give a better representation of the data under a change of variables, where a modified independent variable, \(A'\varepsilon\), was defined as \(A'\varepsilon = A\varepsilon / (1 – A\varepsilon)\). Nonlinear fitting using the Levenberg-Marquardt method was used to minimize the \(\chi^2\)-value between fitted data and measurement.

2.7. Anthropomorphic Phantom

An anthropomorphic chest phantom (Model 55-8PL, Radiology Support Services, Long Beach, CA) was imaged as a function of dose allocation to illustrate the effect of allocation on image quality. For the soft-tissue image, images were acquired at [70/130] kVp with varied allocation (\(A\varepsilon = 0.06, 0.30, 0.63, \) and 0.91). For bone-only decomposition, images were acquired at [60/130], at \(A\varepsilon = 0.06, 0.29, 0.45, 0.72, \) and 0.91. As in the experiments described above, the total dose delivered to the phantom was fixed, and only the dose allocation was varied. The phantom was imaged at techniques corresponding to an average patient, and images were interpreted by an expert chest radiologist on a diagnostic workstation. The tissue weighting parameter (\(w_s\) and \(w_b\)) were chosen qualitatively in each case.
3. Results

3.1. Optimization of the DE Soft-Tissue Image

3.1.1 Optimal kVp and Dose Allocation

Varying the proportion of dose between low- and high-kVp images had a substantial effect on SDNR\textsuperscript{DE}. Figures 3.2(a-c) show SDNR\textsuperscript{DE} for soft-tissue images as a function of $A_\varepsilon$ at a fixed high-kVp (130 kVp) for three phantom thicknesses. The four curves in each figure correspond to low-kVp of 60, 70, 80 and 90 kVp, respectively, each corresponding to the same total dose level ($\pm$5\%). For each curve, the peak SDNR\textsuperscript{DE} is found at an allocation of $\sim$0.3, suggesting optimal image quality when one-third of the total dose is imparted by the low-kVp beam. A significant increase in SDNR\textsuperscript{DE} is observed with increasing spectral separation (i.e., reduced low-kVp).

![Figure 3.2](image)

**Figure 3.2.** SDNR\textsuperscript{DE} measured as a function of dose allocation for (a) thin, (b) average, and (c) thick phantom thicknesses. The results plotted here correspond to a fixed high-kVp (130 kVp), with the low-energy technique varied from 60 – 90 kVp. Curve fits are as described in the text. For each patient thickness, an optimal allocation of $A^\star_{\varepsilon_{\text{soft}}}$ $\sim$ 0.3 is suggested.

These results are qualitatively illustrated in Fig. 3.3, showing DE images of a simulated (polyethylene) nodule acquired at optimal allocation (with the optimum denoted by the “*” in denoted $A^\star_{\varepsilon_{\text{soft}}}$) for each of the twelve curves shown in Fig. 3.3. For a given phantom thickness, nodule contrast is seen to improve with reduced low-kVp. The reduction in nodule contrast for
thicker phantoms is attributed to x-ray scatter, offset somewhat by a reduction in noise (an increase in total dose) such that \( \text{SDNR}^{\text{DE}} \) is similar for each phantom thickness.

**Figure 3.3.** DE soft-tissue images of a polyethylene lung nodule. Images were acquired at a fixed \( kVp^H = 130 \text{ kVp} \) and various \( kVp^L \) for three phantom thicknesses. All images were acquired at optimal allocation for the given kVp pair. Nodule contrast is highest at lower kVp (60 kVp) and for the thin phantom. Reduced contrast and \( \text{SDNR}^{\text{DE}} \) in thicker phantoms is offset in part by increased dose (reduced noise).

Measurements as in Fig. 3.3 were repeated for all 16 kVp pairs, summarized in Fig. 3.4, where each parameter plotted corresponds to the peak \( \text{SDNR}^{\text{DE}} \) (i.e., optimal allocation). As shown in Fig. 3.4 (a), the weighting parameter giving optimal bone cancellation decreases with increasing high-kVp (reduced bone contrast). Figure 3.4 (b) illustrates the trend toward lower low- and high-kVp, suggesting maximum DE soft-tissue signal difference at [60/120] kVp. The results suggest a tradeoff between spectral separation (i.e., increased contrast for lower low-kVp) and x-ray scatter (i.e., reduced nodule contrast at higher high-kVp). As shown in Fig. 3.4 (c), image noise was highest at 90 kVp [likely due to decreased quantum detection efficiency (QDE)]. Taken together, the effects of kVp selection on nodule contrast and noise are shown in
Fig. 3.4(d), where SDNR$^{DE}$ is found to be highest at [60/120] kVp, reduces sharply with increasing low-kVp (reduced spectral separation), and reduces slightly with increasing high-kVp (increased x-ray scatter).

Finally, as shown in Fig. 3.4(e), the selection of kVp-pair was found to have a small effect on the optimal dose allocation, with $A_{e} \sim 0.3$ presenting a smooth optimum across all conditions. Although the trends are comparable to the experimental error, higher allocation was required for reduced low- and high-kVp, suggesting: i) adequate transmission through the patient required a larger proportion of dose at the lower low-kVp; and ii) increasing the high-kVp necessitates lower allocation to reduce quantum noise associated with reduced QDE at higher kVp. When low-kVp increases from 80 to 90 kVp, $A_{e}$ increases indicating tradeoff between imparted energy, transmitted exposure, and quantum noise. In particular, the increased noise at 90 kVp combined with the larger weighting parameter suggest an increase in the dose allocation.

![Graphs showing various parameters for optimal kVp pairs](image)

**Figure 3.4.** Optimal kVp pairs for soft-tissue images. (a) Tissue weighting parameter, $w_{s}$, for optimal bone cancellation. (b) Relative signal difference (contrast), (c) image noise, (d) peak SDNR$^{DE}$, and (e) optimal dose allocation in the resulting soft-tissue DE images. All results are shown for the average patient thickness.
3.1.2 Dose Allocation and Total Dose

For a fixed kVp-pair and patient thickness, the behavior of $w_s$, $SD^{DE}$, $\sigma^{DE}$, $SDNR^{DE}$, peak $SDNR^{DE}$, and optimal dose allocation was investigated as a function of the total imparted energy. $SDNR^{DE}$ measured as a function of $A_\varepsilon$ for imparted energy ranging from approximately one-fifth to double that of a conventional DR radiograph are shown in Fig. 3.5(a). DE images of the polyethylene nodule acquired at optimal allocation are shown in Fig. 3.5(b). The tissue weighting parameter and signal difference did not appreciably vary with dose, although image noise decreased in proportion to the inverse square-root of dose as expected, resulting in the square-root dependence shown in Fig. 3.5(c). Reduction of $\sigma^{DE}_{rel}$ was the driving factor for the increase of peak $SDNR^{DE}$. The optimal dose allocation decreased slightly with dose as shown in Fig. 3.5(d).

![Figure 3.5](image)

**Figure 3.5.** Effect of dose on DE imaging performance. (a) DE image SDNR measured as a function of dose allocation for four total dose levels ($\varepsilon_1 = 0.20$, $\varepsilon_2 = 0.45$, $\varepsilon_3 = 0.86$, and $\varepsilon_4 = 1.73 \mu J/cm^2$). (b) DE images of a polyethylene nodule acquired at conditions corresponding to $SDNR^{DE}_{peak}$ for $\varepsilon_1$, $\varepsilon_2$, $\varepsilon_3$ and $\varepsilon_4$. (c) Peak $SDNR^{DE}$ as a function of total imparted energy, plotted in comparison to a square-root fit. (d) Optimal dose allocation measured as a function of total imparted energy, with a linear fit superimposed and suggesting a slight decrease with higher total dose. All results were acquired at [70/130] kVp.
3.1.3. Anthropomorphic Phantom

Figure 3.6 illustrates the effect of dose allocation on DE image quality. In each case, a magnified view of the right lung of an anthropomorphic phantom is shown for DE soft-tissue images acquired across a broad range in dose allocation. The results are generally consistent with Fig. 3.2(b), suggesting strong degradation in image quality at extreme values of allocation (e.g., $A_e = 0.06$ and $A_e = 0.91$), with a fairly weak dependence in the range $A_e \sim 0.2 - 0.6$. Interpretation by an expert thoracic radiologist indicates that the visibility of spherical nodules in the lung is highest for the case $A_e = 0.30$, slightly reduced at $A_e = 0.63$, and significantly degraded at allocation extremes.

**Figure 3.6.** DE soft-tissue images of an anthropomorphic phantom acquired at four levels of dose allocation. Images were acquired at [70/130] kVp and at equivalent total dose (~0.9 $\mu$J/cm$^2$, corresponding to the energy imparted for an average patient). Optimal image quality is obtained at $A_e = 0.30$. A noticeable increase in image noise is evident at very low ($A_e = 0.06$) and very high ($A_e = 0.91$) allocation.
3.2. Optimization of the DE Bone Image

3.2.1 Optimal kVp and Dose Allocation

Figure 3.7(a-d) illustrates the effect of kVp-pair and dose allocation on the SDNR\textsuperscript{DE} in DE bone images. For these studies, patient size was fixed at the average phantom thickness (10 cm acrylic). Each plot represents a fixed high-kVp, with the four curves corresponding to the four selections of low-kVp (60 – 90 kVp). As with the DE soft-tissue image (Fig. 3.2), dose allocation was observed to have a strong effect on image quality in bone decompositions. Similar effects also include the significant improvement in SDNR\textsuperscript{DE} at increased spectral separation and the reduction of image quality at extreme values of allocation. The dependence of SDNR\textsuperscript{DE} on $A_e$ is shifted toward higher allocation, with optima in the range about $A_e \sim 0.5$.

![Figure 3.7](image)

**Figure 3.7.** Dual-energy image SDNR for bone-only images measured as a function kVp-pair. The results plotted here correspond to a) 120 kVp, b) 130 kVp, c) 140 kVp, d) 150 kVp, with the low-energy technique varied within each figure from 60-90 kVp. Curve fits are as described in the text. For each patient thickness, an optimal allocation of $A_e \sim 0.5$ is suggested.
DE bone images illustrating peak SDNR\textsuperscript{DE} for each kVp pair is shown in Fig 3.8. For each kVp-pair, the nodule has been optimally cancelled. For a given low-kVp, nodule contrast is highest at a $kVp^H = 120$ kVp. A strong dependence of SDNR\textsuperscript{DE} on low-kVp is seen, with a weaker dependence on high-kVp.

\begin{figure}[h]
\centering
\includegraphics[width=0.8\textwidth]{figure3.8.png}
\caption{DE bone images demonstrating perfect cancellation of a polyethylene lung nodule. Images were acquired at 16 kVp-pair for the average phantom thickness. Nodule contrast is highest at [60/120] kVp and a reduction in contrast was observed at increased low- or high-kVp selection. SDNR\textsuperscript{DE} remain stable across $kVp^H$ as the reduction in contrast is offset by a reduction in image noise.}
\end{figure}

The signal and noise characteristics of DE bone images across the 16 kVp pairs are summarized in Fig. 3.9, where, as in Fig. 3.8, each parameter plotted corresponds to the peak SDNR\textsuperscript{DE} (i.e., optimal allocation). Figs 3.9(a), 3.9 (b) and 3.9 (c) illustrate results similar to those observed in the soft-tissue image analysis. The weighting parameter giving optimal nodule cancellation ($w_b$) decreases with increasing high-kVp. Although contrast is maximized at the lowest $kVp^L$ and $kVp^H$, noise is minimized at the lowest $kVp^L$ and the highest $kVp^H$. The results of kVp selection on SDNR\textsuperscript{DE} are summarized in Fig. 3.9 (d), where imaging performance is
found to have negligible dependence on kVp\textsuperscript{H}, within experimental error. The optimal pair lies at [60/130] kVp, with only a slight improvement compared to [60/150]. The benefit of reduced kVp\textsuperscript{L} remains at all values of kVp\textsuperscript{H}.

Optimal dose allocation, A\textsuperscript{* bone}, varied little with selection of kVp-pair, with optima at ~0.5 (approximately equal dose imparted by the low- and high-kVp beam). As observed with the soft-tissue image described in section 3.4(e), lower values of kVp\textsuperscript{L} and kVp\textsuperscript{H} required reduced A\textsuperscript{* bone} with subtle dependence on kVp pair owing to the tradeoffs in contrast and noise (i.e., spectral separation and DQE).

![Figure 3.9](image)

**Figure 3.9.** Optimal kVp pairs for bone decompositions. (a) Tissue weighting parameter, w\textsubscript{b}, for optimal bone cancellation. (b) Relative signal difference (contrast), (c) image noise, (d) peak SDNR\textsuperscript{DE}, and (e) optimal dose allocation. All results are shown for the average patient thickness.

### 3.2.2 Dose Allocation and Total Dose

The dependence of DE bone image SDNR\textsuperscript{DE} on total imparted energy is summarized in Fig. 3.10. The patient thickness and kVp-pair were fixed at average and [70/130] kVp, respectively. SDNR\textsuperscript{DE} was measured as a function of dose allocation at 11 total dose levels,
exhibiting optima about $A_{e}^*_{\text{bone}} \sim 0.5$. DE bone images acquired at optimal allocation corresponding to the peaks of curves in Fig 3.10(a), are shown in Fig 3.10 (b). Image noise decreased in proportion to the inverse square-root of dose as expected, resulting in the square-root dependence in $\text{SDNR}_{\text{peak}}^{DE}$ shown in Fig. 3.10(c). Optimal dose allocation decreased slightly with an increase in total imparted energy (Fig 3.10(d)).

**Figure 3.10.** Effect of dose on bone-only DE imaging performance. All images acquired at a fixed [70/130] kVp. (a) $\text{SDNR}_{\text{DE}}^{DE}$ measured as a function of dose allocation for four total dose levels ($\varepsilon_1 = 0.203$, $\varepsilon_2 = 0.453$, $\varepsilon_3 = 0.864$, and $\varepsilon_4 = 1.725 \, \mu\text{J/cm}^2$). (b) DE images of a polyethylene nodule acquired at conditions corresponding to $\text{SDNR}_{\text{peak}}^{DE}$ for dose level. (c) Peak $\text{SDNR}_{\text{DE}}^{DE}$ (acquired at $A_{e}^*_{\text{bone}}$) as a function of total imparted energy, plotted in comparison to a square-root fit. (d) Optimal dose allocation measured as a function of total imparted energy.

### 3.2.3 Anthropomorphic Phantom

The effect of dose allocation on DE bone image quality is shown in Fig 3.11. Using the same region of interest as in Fig 3.6 (a magnified view of the right lung), a strong effect is observed as the allocation varies, qualitatively consistent with Fig. 3.7. Image quality is only subtly affected across the range $A_{e} = 0.29 – 0.72$, with a significant increase in image noise at
extreme values ($A_e = 0.06$ and $A_e = 0.91$). The image acquired at optimal allocation, $A_e = 0.45$, shows slightly improved noise characteristics compared to $A_e = 0.29$ and $A_e = 0.72$.

Figure 3.11. DE bone-only images of an anthropomorphic phantom acquired at four levels of dose allocation. As in Fig. 3.6, images were acquired at [60/130] kVp and at equivalent total dose (~0.9 µJ/cm$^2$, corresponding to the energy imparted for an average patient). Similar image quality is obtained between $A_e = 0.30$ and $A_e = 0.72$, with only subtle improvements in noise and contrast at $A_e = 0.45$. A noticeable increase in image noise is evident at very low ($A_e = 0.06$) and very high ($A_e = 0.91$) allocation.

3.3. Dual-Energy Imaging Technique Chart

The optimal DE imaging techniques identified above guided the formation of a clinical technique chart for use in patient studies. In the creation of the chart, the main imaging task was the detection of pulmonary nodules; thus, the optima draw directly on the conclusions from the soft-tissue decomposition.

Interestingly, the optimal technique parameters for soft-tissue optimization show very little dependence on patient thickness. Table 3.2 summarizes the optimal techniques along with energy imparted and entrance surface dose for three patient thicknesses.
The optimal dose allocation for the soft-tissue images ($A_{\varepsilon}^{\text{soft}}$) was used in development of the technique chart. Depending on the clinical application, the slightly competing optima between soft-tissue and bone decomposition should be considered in terms of multi-task optimization, with $A_{\varepsilon}^{*} \sim 0.38$ a reasonable choice for the situation in which the soft-tissue and bone-only images are equally important.

<table>
<thead>
<tr>
<th>Patient Thickness</th>
<th>Thin (18 cm chest)</th>
<th>Average (24 cm chest)</th>
<th>Thick (30 cm chest)</th>
</tr>
</thead>
<tbody>
<tr>
<td>kVp</td>
<td>60</td>
<td>60</td>
<td>60</td>
</tr>
<tr>
<td>mAs</td>
<td>3.2</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>$\varepsilon$ (µJ/cm²)</td>
<td>0.131</td>
<td>0.246</td>
<td>0.543</td>
</tr>
<tr>
<td>ESD (mGy)</td>
<td>0.032</td>
<td>0.052</td>
<td>0.106</td>
</tr>
<tr>
<td>$A_{\varepsilon}^{\text{soft}}$</td>
<td>–</td>
<td>0.31</td>
<td>0.28</td>
</tr>
</tbody>
</table>

Table 3.2. Dual-energy imaging technique chart describing optimal acquisition techniques for three patient thicknesses.

4. Conclusions

The optimal kVp pair in DE imaging has been shown to be task dependent, with optima ranging from [60/120] to [80/110] kVp. The results above indicate an optimal soft-tissue imaging performance at a kVp pair of [60/120] kVp for all patient thicknesses investigated and with total dose equivalent to that of a single chest radiograph. Likewise, the bone-only image has an optimal kVp pair of [60/130] kVp. In both types of decomposition, low-kVp exhibited a stronger effect on SDNR$_{DE}$, with 60 kVp providing improved nodule contrast and higher detector efficiency. The effect of high-kVp was less significant, suggesting competing effects among energy separation (contrast), image noise, and x-ray scatter in relation to soft-tissue or bone...
visibility. The optimal kVp for the bone-only image demonstrated a slight discrepancy from the [60/120] kVp optimum measured for soft-tissue decomposition, but was within experimental error considering the weak dependence on kVpH. The results are furthermore consistent with previous studies of human observer performance in DE imaging, where improved bone-only image quality was identified at slightly higher kVpH than for the soft-tissue image.

As expected, for the soft-tissue image weighting parameter, ws, was observed to be dependent on phantom thickness – slightly larger for thinner phantoms. This effect was accounted for in the experimental studies by selecting ws independently in each DE image to automatically minimize the signal difference (contrast) between simulated bone and soft-tissue background. The soft-tissue DE images therefore exhibit optimal bone cancellation (i.e., ws selection) in all cases.

The optimal dose allocation for this soft-tissue imaging task was found to be fairly constant (A∗soft ≈ 0.3) for all kVp-pair and patient thicknesses investigated. The majority of patient dose is allotted to the high-kVp image to reduce noise associated with the high-kVp image. Conversely, for bone visualization, optimal dose allocation was also constant, in this case (A∗bone ≈ 0.45), suggesting approximately equal dose imparted from both low- and high-kVp beams. Here, the increased contrast from the low-kVp projection makes up for the increase in noise from the high-kVp image.

The optimization of acquisition technique parameters detailed above ensure high DE imaging performance for the system under development. The technique chart has directed the implementation of the prototype in patient trials currently underway.
Chapter IV: A Cardiac Gating System for Dual-Energy Imaging
1. Introduction

Double-shot DE imaging provides a number of advantages over single-shot, including improved soft-tissue contrast and DQE.\textsuperscript{46,47} The primary disadvantage of double-shot image acquisition is the finite time interval separating the low- and high-kVp projections during which anatomical motion can occur, resulting in motion artifacts. Respiratory motion is minimized by patient breath-hold; however, cardiac motion necessitates the use of a prospective gating system to trigger x-ray exposures at a specified phase of the heart cycle. The two exposures need not be acquired within the same heartbeat (i.e., they may be acquired on subsequent cycles), but each exposure must be acquired at the same phase of the cardiac cycle – e.g., both exposures acquired within diastole, the quiescent phase.

The electrocardiogram (ECG) provides a means for cardiac gating that is fairly widespread in medical imaging – e.g., in cardiac CT\textsuperscript{86-89} and MR.\textsuperscript{90,91} By measuring electrical activity of the heart, an ECG can provide a real-time surrogate for cardiac motion. It is fast and reliable and can easily distinguish heart phase – including sub-phases within diastole and systole. The electrocardiogram is a fairly standard heart monitoring device for clinical use and is available at reasonable prices with small form factors. For chest radiography, however, ECG presents a variety of logistical disadvantages. For such high-throughput imaging procedures, the setup time for attaching 3 or more leads to the patient, verifying adequate conductivity and the need for additional disposables diminishes workflow and can increase costs. Furthermore, ECG components can obstruct the visibility of anatomy in a projection image if placed on the chest, and although the leads can be placed elsewhere (e.g., the forearm), setup and disposables remain as logistical drawbacks.
Pulse oximetry provides a potentially useful alternative to ECG. By measuring pulsatile characteristics in peripheral arteries\textsuperscript{92,93}, an estimate of heart motion can be obtained by characterizing the “plethysmogram” with respect to an ECG and accounting for the delay associated with physical propagation of blood to peripheral arteries. As described below, a fingertip pulse oximeter was employed in this work to provide a surrogate measurement of cardiac phase. The purpose of the work described below was to devise a system capable of triggering exposures during the diastole “window” (but not necessarily at a specific diastolic sub-phase) to reduce cardiac motion artifacts. While inter-patient variations in pulse propagation delay may limit the use of a pulse oximeter as a precise phase surrogate, this work investigates the extent to which an oximeter can be used as a simple trigger that reproducibly triggers exposures within diastole (i.e., within a \(\sim 300\text{-}700\text{ ms}\) period during which cardiac motion is minimal). The simple probe provides advantages in cost and workflow compared to an ECG and does not obstruct radiographic images. Such an oximeter could furthermore be incorporated directly within the handles on the imaging system, as common in exercise equipment.

The modeling, implementation, and performance of an oximeter-based cardiac gating system is reported. Building on the development of a cardiac-gated DE imaging prototype developed in our laboratory\textsuperscript{53,74}, we describe the temporal characteristics of each system component, including those due to the trigger system (i.e., physiological processes and oximeter processing) and the imaging system (i.e., the generator, x-ray tube, anti-scatter grid, and flat-panel detector, FPD). A system model that accounts for the heart-rate dependent duration of the diastolic period is used to compute timing schemes that trigger x-ray exposure within diastole. The performance of the triggering system is evaluated through analysis of cardiac-gated acquisition in 37 patient images acquired with the prototype. DE images decomposed from projections separated in time by \(\sim 2\text{-}8\) cardiac cycles are evaluated with and without gating to
analyze the magnitude of cardiac motion artifacts and the potential for accurate gating to improve visualization of pulmonary structures. Note that the gating system developed in this work could be usefully applied to other double-exposure radiography systems with either reduced inter-exposure time\textsuperscript{47,48,94} or increased inter-exposure time.\textsuperscript{95} Each type of system is, in fact, prone to cardiac motion artifact, and a system of gating exposures to diastole would be of value. For example, Xu et al.\textsuperscript{94} has developed a system for imaging coronary artery calcium with a ~35 ms inter-exposure time, and Sabol et al.\textsuperscript{48} reported on a chest imaging system with an inter-exposure time of ~200 ms, both noting the potential for cardiac motion artifacts. The prototype imaging platform implemented in this work has an inter-exposure time an order of magnitude greater than the systems mentioned above (several seconds), but this limitation does not affect the performance of the gating system. Each x-ray exposure is individually triggered coincident with diastole, independent of the subsequent or previous exposure. Thus, the triggering system could be implemented in systems with the capability to acquire projections in close succession (i.e., within the same diastole period). Without a gating system, such systems are susceptible to acquisition of one or both images during systole, as triggering would be performed randomly, with subsequently increased cardiac motion artifact. Similarly for very long inter-exposure time intervals (weeks or months), as in temporal subtraction radiography,\textsuperscript{95} although gross patient motion is by far the dominant source of artifact, for which deformable registration is the best defense, a cardiac gating method could help to minimize cardiac deformation between the two projections. Therefore, the cardiac gating system reported below is of potential value to a broad range of double-exposure imaging applications, including very fast dual-energy cardiac\textsuperscript{94} and chest\textsuperscript{48} imaging (for which the gating system triggers exposures within the same diastole), slower dual-energy chest imaging (such as the prototype considered below, for which the gating system triggers exposures within diastole on subsequent heartbeats), and
very slow double-exposure techniques (such as temporal subtraction imaging, for which the gating system acquires both exposures within diastole and helps to reduce the effect of internal organ deformation). The cardiac-gated DE imaging system is currently being investigated in a research cohort of 200 patients, providing an important basis for performance characterization (Fig. 4.1).

![Photograph of the DE chest imaging research prototype. The patient is setup in PA position in front of the detector stand (containing the FPD and anti-scatter Bucky grid). Clipped to left forefinger is the pulse oximeter.](image)

**Figure. 4.1.** Photograph of the DE chest imaging research prototype. The patient is setup in PA position in front of the detector stand (containing the FPD and anti-scatter Bucky grid). Clipped to left forefinger is the pulse oximeter.

### 2. Materials and Methods

#### 2.1. The Cardiac Cycle

The cardiac cycle involves two distinct mechanical periods: systole and diastole. Systole is the phase of the heart cycle involving sudden mechanical contraction of the ventricles, whereas diastole is the quiescent phase during which blood flows passively from the atria to the ventricles. Referring to the ECG of Fig. 4.2, systole is defined as the Q-T interval, whereas diastole is the T-Q interval. The proportion of time that the heart spends in each phase depends on heart rate (HR). Typically, diastole occupies ~60 – 70% of the heart period [e.g., 0.6 s at HR = 67 bpm], compared to ~30 – 40% (~0.3 s) for systole. At lower HR, a proportionally
large amount of time is spent in diastole, and as HR increases, the diastolic period reduces considerably, while the duration spent in systole (~0.3 s) is only slightly affected. As shown below, knowledge of the patient HR and position within the cycle allows the time and duration of systolic and diastolic phases to be determined.

2.2. Cardiac Gating with a Pulse Oximeter

A fingertip pulse oximeter typically has two clinical purposes. The first is to identify blood oxygen levels and detect hypoxemia. A second is to monitor changes in blood volume and pulse propagation as characterized in a plethysmogram, which is derived from the measurement of a pulsatile signal in arterial blood coupled with the absence of motion in venous structures and surrounding tissue. Pulse oximeters can provide a digital trigger occurring at any characteristic point in the plethysmogram waveform. For example, as shown in Fig. 2, the fingertip pulse oximeter employed in this work (Ipod, Nonin Inc., Minneapolis MN) incorporates digital processing directly on the fingertip probe to provide a digital trigger associated with the rising edge the plethysmogram. Thus, the oximeter output – either the digital trigger or the plethysmogram itself – provides a surrogate for cardiac activity. However, there are temporal delays associated with the oximeter digital processing that need to be accounted and – more importantly – with intra- and inter-patient variability in pulse propagation time, including HR, level of breath inspiration, and blood pressure. As described below, dependence on HR was accounted by way of a cardiac timing model. To reduce variability associated with breath inspiration, patients were instructed and trained to hold their breath at a comfortable level of inspiration for 3 – 5 seconds prior to the first exposure, holding a comfortable level of inhale for ~10 sec. This allowed for stabilization of the oximeter pulse at a reasonably fixed level of inspiration. Finally, variation in pulse propagation time associated with blood pressure presents a
limiting factor, and as described below, such variation was accounted in terms of a range in temporal delay incorporated in the cardiac timing model. While such is shown to allow triggering of exposures during the diastole window, this limits the extent to which the system can be expected to trigger at precise phase time-point.

In the DE imaging prototype, the patient is setup in PA position with the pulse oximeter clipped to the left index finger. Plethysmogram and HR measurements are acquired in real-time. The imaging system is initialized, and the patient is instructed to undertake a comfortably inspired breath-hold. Upon the first oximeter trigger pulse following the technologist’s exposure request (button press), the HR is recorded and the timing for actual x-ray exposure is computed in a manner that accounts for various system and implemented delays, described below. The x-ray exposure thus occurs synchronous to diastole. The timing characteristics are recorded by means of an auxiliary monitoring workstation for retrospective analysis of timing accuracy for each patient.

**Figure 4.2.** Timing diagram displaying the electrocardiogram (ECG) trace, associated plethysmogram, and digital trigger. Regions of systole, (Q-T interval), diastole, (T-Q interval), and heart period are shown. Measurements of the delay between the R-wave and midpoint of plethysmogram as well as between the R-wave and digital trigger are indicated.
2.2.1 Characterization of System Delays

There are several potential temporal delays associated with the cardiac-gated DE imaging system, including intra-exposure delays (i.e., those occurring between the heartbeat that induces a digital trigger and the end of the corresponding x-ray exposure) and inter-exposure delays (i.e., those occurring after the first x-ray exposure but before the request for the second.) The cardiac gating system described in this work is dependent on intra-exposure delays, since the high- and low-kVp images are acquired independently as triggered by separate heartbeats. Systems for which both images are acquired within a single heart cycle necessarily consider both intra- and inter-exposure delays.

Measurement of Pulse Propagation Delay

The first delay contributing to the intra-exposure delay is the time required for blood propagation from the left ventricle to the fingertip (left index finger). A distance-normalized value of 303 ms in humans\(^9\) (pulse transit velocity = 3.3 m/s) is a representative mean, with variability dependent on factors including cardiovascular health and blood pressure. A second delay is due to digital signal processing within the pulse oximeter itself. This delay, in addition to the pulse propagation delay, offsets the plethysmographic indicator of systole from the true mechanical event. Although the magnitude and variability of the digital processing delay for the device employed were proprietary, the combined delay due to pulse propagation and processing (termed the “trigger delay”) was analyzed by measuring the plethysmogram relative to ECG (taken as truth). Specifically, the delay between the peak of the QRS complex (the R-wave, an indicator close to systole initiation) and the rising edge (50% peak value) of the plethysmogram was measured. Studies measuring the delay were performed in a subgroup of nine volunteers varying in age (34 – 49) and lifestyle (1 smoker / 8 nonsmokers), with each volunteer monitored using a 3-lead ECG on the chest and the pulse oximeter clipped to their left index finger. Data
were collected under conditions that mimicked the actual DE imaging procedure – viz., standing position, relaxed, arms placed at the hips, and a comfortably inspired 10 second breath-hold. For each volunteer, measurements were repeated 5 – 8 times to evaluate the mean trigger delay as well as intra- and inter-patient variability. Volunteer heart rate was monitored during the test.

Measurements of pulse propagation delay were incorporated in the gating system for use in a 200 patient research cohort, currently underway.

<table>
<thead>
<tr>
<th>Study Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Patients ($N_{\text{patients}}$)</td>
<td>111</td>
</tr>
<tr>
<td>Male / Female</td>
<td>75 / 56</td>
</tr>
<tr>
<td>Age (Mean)</td>
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</tr>
<tr>
<td>Age (Range)</td>
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<td>Chest Thickness (Mean)</td>
<td>23.7 cm</td>
</tr>
<tr>
<td>Time Between Exposures (Mean)</td>
<td>8.09 sec</td>
</tr>
<tr>
<td>Diastole Triggers ($N_{\text{diastole}}$)</td>
<td>94</td>
</tr>
<tr>
<td>Systole Triggers ($N_{\text{systole}}$)</td>
<td>17</td>
</tr>
</tbody>
</table>

Table 4.1. Summary of patient study parameters.

As summarized in Table 4.1, the cases in the current study ($N_{\text{patients}} = 111$) were drawn from a patient imaging trial in progress (from which 131 cases were available at the time of the study, with 20 cases excluded for reasons not related to the triggering system). The cohort exhibited a slight preponderance of male subjects, with an average age across all patients of 64.9 years. The average HR during image acquisition was 77.0 bpm. Patients exhibiting abnormally high heart rate (>115 bpm) were not accrued into the study (with the exception of one exam in which the HR fluctuated from 112 bpm to 125 bpm during image acquisition). Cases exhibiting both exposures within diastole (diastole-diastole triggers, $N_{\text{diastole}}$) were all from the protocol group for which the cardiac trigger was used. Cases exhibiting at least one exposure in systole (N_{systole}) were drawn from either a protocol subgroup for which the trigger was not used or from
the main group for which a timing error [as in Fig. 4.5(a), below] caused an erroneous trigger during systole.

**Measurement of Imaging System Delays**

The DE image acquisition workstation and software also contribute potential intra- and inter-exposure delays. Similarly, the generator (Indico 100, CPI, Georgetown, Ontario) and x-ray tube (Varian Rad-60, Salt Lake City, UT) potentially contribute to the inter-exposure delay. For the prototype, the time for generator and tube preparation takes place between images (in parallel with other delays), poses no bottleneck, and was therefore neglected. Likewise, a collimator (Ralco R302 ACS/A, Biassono, Italy) incorporating a filter wheel was implemented to provide differential filtration between high- and low-kVp projections and potentially contributes to inter-exposure delay as the wheel switches from one position to another. Because this delay occurs in parallel with other inter-exposure delays, it was not a consideration in the current work. Also imparting a potential intra-exposure delay is the anti-scatter Bucky grid (Advanced Instrument Development Inc., Melrose Park, NJ). This delay occurs before x-ray exposure as the system verifies that the grid is in motion. In the current work, it was included within the FPD delay, described below.

The FPD (Pixium-4600, Trixell, Morains, France) imparts distinct intra- and inter-exposure delays. The intra-exposure component is due to the detector initialization and readout refresh processes. The FPD delay encompasses the time from a frame request to the detector-ready state. The FPD incorporated in the DE imaging prototype exhibits a variable delay dependent on the time within the refresh cycle the frame request occurs. This delay was measured using digital pinout signals detailing the time of initialization and exposure. The second delay associated with the FPD is the time involved in detector readout. This panel-
specific delay is significant and is the primary factor in determining the time between projections. This delay was also measured using digital pinout provided by the detector.

From the intra-exposure delays described above, it is possible to group and categorize as either “trigger delays” or “imager delays.” The former are associated with physiological pulse propagation and pulse oximeter digital trigger processing, which combine to give a variable delay, denoted $t_{\text{trigger}}$, with superscripts “mean,” “range,” “min,” and “max” to describe the associated characteristic of the distribution – e.g., $t_{\text{trigger}}^{\text{min}}$ and $t_{\text{trigger}}^{\text{max}}$ are the lower and upper bounds of the trigger delay, respectively. The second category of intra-exposure delay are those occurring after the digital trigger, and are the contribution of a number of parallel delays including those of the acquisition software, anti-scatter grid, and FPD. Denoted $t_{\text{imager}}$, the delay is dominated in the current prototype by that of the FPD and exhibits variability associated with detector refresh as described above. We similarly characterize $t_{\text{imager}}$ as a distribution characterized by superscripts “mean,” “range,” “min,” and “max” – e.g., a minimum delay, $t_{\text{imager}}^{\text{min}}$, and a range of $t_{\text{imager}}^{\text{range}}$.

### 2.2.2 Cardiac Triggering

The purpose of the cardiac-gating system is to synchronize x-ray exposures with the diastolic period. For patients with sufficiently low HR, the duration of the cardiac cycle is long enough to accommodate the intra-exposure system delays, allowing x-ray exposure to occur within the same heart cycle as the digital trigger despite all sources of timing variability. At higher HR, the mean, range, and/or maximum of system delays are too long to guarantee exposure within the same heartbeat. In this case, the exposure must be postponed to the subsequent heart cycle – and into the subsequent diastolic period – by means of an implemented delay, denoted $t_{\text{imp}}$. These considerations suggest two distinct timing regimes, dependent on patient HR. The first regime is that below a threshold heart rate ($HR_{\text{thresh}}$) for which the
implemented delay is zero ($t_{imp} = 0$), and the exposure occurs immediately following the digital trigger. The threshold is computed as:

$$HR_{\text{thresh}} = \frac{60 \min}{t_{\text{trigger}}^{\max} + t_{\text{imager}}^{\max} + t_{\text{buffer}}}$$

(4.1)

where $t_{\text{buffer}}$ is a fixed parameter that accounts for the finite x-ray exposure time, as well as acting as a buffer to account for errors within estimates of the measured temporal delays. The threshold is thus determined by the largest values of the trigger and imager delays — i.e., $t_{\text{trigger}}^{\max} = t_{\text{trigger}}^{\min} + t_{\text{trigger}}^{\text{range}}$, and $t_{\text{imager}}^{\max} = t_{\text{imager}}^{\min} + t_{\text{imager}}^{\text{range}}$.

For patient HR greater than the threshold, the implemented delay is nonzero and postpones x-ray exposure to the center of the subsequent diastole. The required implemented delay is:

$$t_{\text{imp}}(HR) = t_{HR}(HR) - t_{\text{trigger}}^{\min} + t_{\text{systole}}(HR) - t_{\text{imager}}^{\min} + \frac{1}{2} t_{\text{diastole}}(HR) - t_{\text{trigger}}^{\text{range}} - t_{\text{imager}}^{\text{range}}$$

(4.2)

where $t_{HR}(HR)$, $t_{\text{systole}}(HR)$, and $t_{\text{diastole}}(HR)$ are the heart period, systole duration, and diastole duration, respectively, each a function HR. The implemented delay postpones x-ray exposure beyond the period of ventricular filling (the current diastole), past ventricular contraction (the next systole), and into the following diastole region. Note that $t_{\text{imp}}$ incorporates the minimum trigger and imager delays to ensure a delay of sufficient length to avoid the systolic period.

Due to the two independent sources of timing variability and the reliance of $t_{\text{imp}}$ on minimum delay values, $t_{\text{trigger}}^{\min}$ and $t_{\text{imager}}^{\min}$, there is a maximum HR that the model can support. Above this maximum HR, $t_{\text{imp}}$ would delay the exposure so long as to fall beyond the subsequent heart cycle (i.e., into the heart cycle twice removed from the trigger that initiated the exposure). The maximum HR is determined by the inequality:

$$t_{\text{trigger}}^{\max} + t_{\text{imager}}^{\max} + t_{\text{imp}}(HR) \leq 2[t_{\text{systole}}(HR) + t_{\text{diastole}}(HR)]$$

(4.3)
specifying the upper bound in HR for triggering on the same or immediately subsequent heart cycle.

The pulse propagation delay was used as an indicator of ventricular systole in order to trigger x-ray exposures within diastole. Specifically, the model computes the “implemented delay” ($t_{imp}$) required such that the x-ray exposure is coincident with the center of diastole. In itself, this provides considerable temporal flexibility (tolerance), since the diastole period is relatively large, ranging from ~300 ms (HR = 115 bpm) to ~700 ms (HR = 60 bpm). Variability in the pulse propagation delay due to patient-specific physiological processes is accounted for by describing $t_{trigger}$ using a range, described by upper and lower bounds ($t_{imag}^{\text{max}}$ and $t_{imag}^{\text{min}}$). Thus, the cardiac trigger model accommodates any value of $t_{trigger}$ that falls within the range of measured temporal delays (Section 2.2.1). This allows for an effective “widow” that ensures proper triggering of the x-ray exposure during diastole.

2.3. Trigger and Exposure Monitoring

2.3.1 Monitoring System

An auxiliary workstation (IBM PC, IBM, Armonk, NY; 2.2 GHz, 1 GB physical memory) was implemented on the clinical prototype to monitor and evaluate system performance. It was connected in parallel to both the acquisition PC and pulse oximeter using an onboard data acquisition card (PCI-6036E, National Instruments, Austin, TX). By means of a custom software oscilloscope developed in Matlab (The Mathworks, Natick, MA), the monitoring system records the actual time of x-ray exposure, the total imager delay, the patient plethysmogram, and heart rate (as measured by the pulse oximeter, denoted $HR_{ox}$). These measurements allow quantitative evaluation of the coincidence of x-ray exposure relative to the modeled target diastole window.
2.3.2 Robust Estimation of Patient HR

Pulse oximeters are usually intended to provide a simple measure of heart rate and need to be robust against missed heartbeats (sampling errors), patient motion, intermittent contact, and other sources of false alarm or HR estimation errors in patient monitoring. To achieve a robust HR estimate, the oximeter initially implemented in the DE imaging prototype appears (based on analysis of plethysmograms and resulting HR estimates) to apply a running average in HR across ~10 beats. The resulting estimate, $HR_{ox}$, thus involves a fairly long lag and a degree of inaccuracy under conditions where the HR is changing rapidly. Such is the case under conditions of breath-hold, where patient HR is expected to change upon initiation of breath-hold\textsuperscript{1,86} – typically increasing briefly (~2 – 4 s) due to increased venous return, followed by a significant reduction in HR due to increased interthoracic pressure. Slowly (after ~6 – 8 s, depending on cardiovascular health), the HR increases and surpasses the resting HR until normal respiration resumes. Because calculation of the implemented delay is a function of HR [$t_{imp}(HR)$ in Eq. (4.2)], an accurate estimate of patient HR even in the context of such dynamics is essential to precise cardiac gating.

HR estimation schemes alternative to that intrinsic to the device (~10 cycles running average) were explored to determine a methodology that was both accurate (minimizing lag) and robust (minimizing artifacts due to erroneous sampling etc.). The instantaneous HR (calculated directly from the time between the current and previous cycles) provides the least lag (i.e., most accurate estimate in the presence of HR change) but is also the most susceptible to spurious error. Alternative smoothing windows were investigated to determine the accuracy and precision of triggering based on HR estimates calculated with smoothing windows of 0 (instantaneous), 1, 3, 5, 7, and 9 cycles. Retrospective analysis of timing data acquired with the monitoring system
(Sec. 3.2.1) for thirty-seven patients participating in the DE imaging trial provided the basis for evaluation.

2.4. Trigger Performance Evaluation

2.4.1 Timing Relative to Diastole Window

The performance of the cardiac trigger was evaluated in terms of the x-ray exposure time (“location”) with respect to the modeled diastole window as well as the magnitude of cardiac motion artifacts in DE images. For the former, data from the monitoring system provided retrospective analysis across the first 37 patients involved in the clinical trial. Timing plots identifying exposure location with respect to the target HR-dependent diastole window allowed quantitation of gating accuracy and precision.

2.4.2 Image-Based Measurement of Cardiac Artifact

Cardiac motion typically manifests in DE images as white or dark edges along the periphery of the image of the heart, as well as around the aortic arch and adjacent bronchioles and vasculature. To quantify the effectiveness of the gating system in reducing image artifacts, a human observer study was performed in which six observers (physicists) were independently presented 111 DE bone-only images in randomized order and asked to measure the size of the artifact using a custom Matlab measurement tool. Physicists were considered adequate observers for this test (as opposed to expert chest radiologists), because the imaging task was simple and required little clinical knowledge of anatomy, disease, or image interpretation. Following a training set of 5 – 9 images, observers were asked to measure the thickness of the largest visible artifact on the left edge of the heart. The study was conducted in a radiology reporting room with subdued lights. Tissue weighting factor ($w_b = 0.56$) and window-level settings (image mean ± 3
standard deviations) were fixed for all images, and observers were allowed to magnify the images as desired.

Patient images were categorized into two groups: 1.) 94 images with successful diastole-diastole triggers, and 2.) 17 images in which at least one of the two projections involved exposure during systole. The latter group exhibited fewer cases, because the patient imaging protocol was designed primarily to provide successfully gated image acquisition, aside from a small sub-group for which image acquisition was without the benefit of cardiac gating. To evaluate the statistical significance of the results, a one-sided, two-sample Student t-test was performed, assuming unequal variance between the two groups (heteroscedastic) and testing the hypothesis that the sample mean magnitude of the motion artifact was different in the two groups.

3. Results

3.1. System Delays and Cardiac Trigger Timing

The delays associated with the pulse oximeter are displayed in Fig. 2. The delay between R-wave and midpoint of the plethysmogram was measured to be \((347 \pm 26)\) ms, whereas the corresponding delay between R-wave and the digital-trigger was measured to be \(t_{\text{mean \ trigger}} = (457 \pm 25)\) ms. An offset of -50 ms correctly aligned the oximeter pulse-wave to the ECG phase of maximum mechanical motion, such that the upstroke of the plethysmogram pulse coincided with the ECG Q-wave.\(^{93,97}\) The parameters of interest, \(t_{\text{min \ trigger}}\) and \(t_{\text{max \ trigger}}\), correspond to the range of corrected mean volunteer delay measurements and were computed to be 382 ms and 458 ms, respectively. These delays were found to be stable across volunteer age and heart rate \((HR_{\text{volunteer}} = 74.8\) bpm). Thresholds were used to account for differences in physiological pulse propagation...
times between patients as well as spontaneous delay changes within the same patient. The larger of the two was the inter-subject delay, which defined $t^{\text{min}}_{\text{trigger}} = 382 \text{ ms}$ and $t^{\text{max}}_{\text{trigger}} = 458 \text{ ms}$, mentioned above. Although other factors influencing the pulse propagation delay were not directly monitored within these measurements, the intra-subject variability in $t_{\text{trigger}}$ ranged from 13 – 30 ms in the experimental cohort – well inside the width of the thresholds. Such was a result of replicating the clinical procedure during the delay measurements, effectively reducing changes in respiratory volume (breath-hold). Furthermore, such variabilities in the patient cohort were controlled somewhat in this study by exclusion of patients exhibiting cardiovascular and/or respiratory irregularity (e.g., cardiac arrhythmia or apnea).

Example implemented delay curves are shown in Figs. 4.3(a–c) for various settings of $t^{\text{min}}_{\text{imager}}$ and $t^{\text{range}}_{\text{imager}}$. The curves were computed using the two components of the trigger delay ($t^{\text{min}}_{\text{trigger}}$ and $t^{\text{max}}_{\text{trigger}}$), described above. The buffer period, $t_{\text{buffer}}$, was fixed at 75 ms, a value larger than any exposure time used in the imaging protocol. For each curve, the implemented delay is zero below $HR_{\text{thresh}}$, above which $t_{\text{imp}}$ increases to a value sufficient to delay exposure to the subsequent heartbeat and decreases gradually as $HR$ increases. The value of the threshold [Eq. (4.1)] is influenced by the sum of $t^{\text{min}}_{\text{imager}}$ and $t^{\text{range}}_{\text{imager}}$.

Figure 4.3(a) shows the implemented delay for a fixed delay range ($t^{\text{range}}_{\text{imager}} = 100 \text{ ms}$) and three hypothetical values of $t^{\text{min}}_{\text{imager}}$ (0, 200, and 400 ms). The $HR_{\text{thresh}}$ for these three examples are 95, 73 and 59 bpm, respectively. Only in the last example is the delay so long that a maximum HR is evident (~120 bpm), necessitating a delay to the third cardiac cycle. Figure 4.3(b) shows the implemented delay for a fixed minimum imager delay ($t^{\text{min}}_{\text{imager}} = 100 \text{ ms}$) and three hypothetical values of $t^{\text{range}}_{\text{imager}}$ (0, 100, and 200 ms). As the imager delay range is increased,
$HR_{thresh}$ decreases, with an associated increase in the length of the implemented delay. For these examples, $HR_{thresh} = 95, 82$ and $73$ bpm, respectively. Comparing Figs. 4.3(a) and 4.3(b), for the same maximum delay ($t_{\text{imagert}}^{\text{max}}$), increased variability calls for larger implemented delays to account for the chance that either extreme of the delay range will occur.

**Figure 4.3.** Implemented delay curves computed for various system delay parameters. Curves in (a) and (b) are for hypothetical configurations involving (a) fixed $t_{\text{imagert}}^{\text{range}} = 100$ ms with three values of $t_{\text{imagert}}^{\text{min}}$, and (b) fixed $t_{\text{imagert}}^{\text{min}} = 100$ ms with three values of $t_{\text{imagert}}^{\text{range}}$. Curves in (c) show $t_{\text{imp}}$ for the clinical prototype used in patient studies ($t_{\text{imagert}}^{\text{min}} = 250$ ms, $t_{\text{imagert}}^{\text{range}} = 135$ ms) along with an ideal imager with no measurable delays ($t_{\text{imagert}}^{\text{min}} = t_{\text{imagert}}^{\text{range}} = 0$ms).

For the prototype system configuration, the minimum delay from the imager was measured to be $t_{\text{imagert}}^{\text{min}} = 250$ ms, with a range of $t_{\text{imagert}}^{\text{range}} = 135$ ms, giving the implemented delay curve in Fig. 4.3(c). The threshold lies at a heart rate of 65 bpm. The upper limit for which the system can operate normally (i.e., exposure on the current or subsequent heart cycle) is 140 bpm. Also shown in Fig. 4.3(c) is the delay curve for the ideal system configuration absent of imager delays ($t_{\text{imagert}}^{\text{min}} = t_{\text{imagert}}^{\text{range}} = 0$ ms). For this hypothetical system, the heart rate threshold is 113 bpm, above which an implemented delay is required due to $t_{\text{trigger}}^{\text{min}}$ (and $t_{\text{trigger}}^{\text{range}}$) in combination with the shortened cardiac period.
3.2. Trigger Performance Evaluation

3.2.1 Timing Relative to Diastole Window

For each patient image acquisition, a timing diagram as seen in Fig. 4.4 was recorded by the monitoring system, showing the trigger pulses originating from the oximeter in relation to the modeled diastole region and duration of the x-ray pulse. Figure 4.4(a) shows an example acquisition for which the patient HR was less than $HR_{\text{thresh}}$. Hence, the x-ray exposure occurred within the same cardiac cycle as the trigger. An example with patient heart rate greater than the threshold is shown in Fig. 4.4(b), and the x-ray exposure correctly occurred within the diastole period of the subsequent cardiac cycle.

![Timing Diagram](image)

**Figure 4.4.** Timing diagrams displaying the digital trigger, the diastole region, and the time/duration of x-ray exposure as recorded by the monitoring system. (a) Timing for a patient with $HR < HR_{\text{thresh}}$, for which the exposure occurs within the same heart cycle (diastole region) as the digital trigger (arrow). (b) Timing for a patient with $HR \geq HR_{\text{thresh}}$. In the latter case, the heart period is too short to accommodate same-cycle acquisition, and the implemented delay forces exposure to the central region of subsequent diastole.

Figures 4.5(a-c) plot the time at which exposure occurred vs. the true patient HR (i.e., the instantaneous HR) for the first 37 patients imaged on the clinical research prototype. The implemented delays for the data in Fig. 4.5 are those for the clinical system as plotted in Fig. 4.3(c). The modeled diastole period is plotted as a function of HR as the region between symmetric grey bands above and below the x-axis. The space between the bands corresponds to
the diastole “window,” whereas the space outside the bands corresponds to systole. The width of the bands represents the variability in the trigger delay, and is equal to \( \Delta t_{\text{trigger}} \). Each band is separated into three curves corresponding to the diastole region specified by the corresponding minimum, mean, and maximum trigger delay. Successful diastolic triggering corresponds to exposures between the upper and lower bands. Exposures within the grey bands may or may not have been acquired in diastole, depending on variations in trigger delay. Exposures above or below the bands are failures – i.e., exposure during systole. Solid and open symbols correspond to low-kVp and high-kVp, respectively, with range bars representing duration of the x-ray pulse.

Figure 4.5. Incidence of x-ray exposure with respect to the diastole window as a function of patient HR. Data are for 37 patients participating in a DE imaging trial. (a) Triggering based on HR as reported by the oximeter gives reasonable accuracy, yet poor precision and several instances of unsuccessful gating due to errors in the HR estimate (\( HR_{\text{ox}} \), subject to temporal smoothing). Triggering based on (b) the instantaneous HR or (c) smoothing HR by 3 previous heart cycles shows considerable improvement in accuracy (100%) and precision.

Three methods of HR determination are also evaluated in Figs. 4.5(a-c). Figure 4.5(a) shows the coincidence of x-ray exposure and modeled diastole region for HR values reported by the pulse oximeter. Although trigger accuracy is reasonably high (success rate = 85%), the precision is fairly low, and a number of systolic triggers are evident. These timing errors are associated with deviation in \( HR_{\text{ox}} \) from the true value, due to oximeter smoothing in cases where the true HR was changing significantly at the time of exposure. This also explains the reduced
precision and accuracy in low-kVp exposures (which are delivered first) compared to those at high-kVp, due to the large initial drop in HR after breath hold.

The same data were re-evaluated using the same trigger and imager delays as Fig. 4.5(a), but with $t_{imp}$ computed from the instantaneous HR. Results are shown in Fig. 4.5(b), showing a significant increase in both accuracy (100%) and precision. Also visible in the distribution of data is the $HR_{thresh}$ occurring at 65 bpm. For exposures occurring slightly below the threshold, exposures tend to occur near the end of diastole (positive time points). At lower HR, exposures occur nearer the start of diastole (negative time points). This occurs because at $HR < HR_{thresh}$, the system trigger occurs immediately following the perfusion delay. As HR decreases, the duration of diastole increases, and thus the exposure occurs proportionally closer to the beginning of diastole.

The data were re-evaluated retrospectively with heart rates computed based on various smoothing windows to provide precision and accuracy comparable to that in Fig. 4.5(b), yet provide robustness to spurious HR measurements. Performance was comparable for smoothing windows of width 0 – 3 beats, beyond which accuracy steadily decreased to that shown in Fig. 4.5(a) for a window width of ~10 beats. As shown in Fig. 4.5(c), a smoothing window of 3 heart cycles was found to provide accuracy and precision comparable to that of instantaneous HR [Fig. 4.5(b)] – providing a measure of robustness against spurious HR measurements, intermittent oximeter contact, sampling errors, etc., while still accounting for rapid changes in HR.

### 3.2.2 Image-Based Measurement of Cardiac Artifact

Soft-tissue and bone-only DE images acquired with the clinical prototype are shown in Fig. 4.6. Images were cropped to (2000×2000) pixels with window and level independently adjusted to best illustrate the regions of the lungs. Subtle misalignment caused by patient motion
is evident, manifesting as artifacts at the diaphragm and ribs. Future research involves deformable registration of the low- and high-energy projections to mitigate such artifacts. Ungated images are shown in Figs. 4.6(a-b). In the soft-tissue image [Fig. 4.6(a)], the cardiac motion artifact is barely discernable. Misregistration is more evident in the bone-only image as dark bands located on both sides of the heart [Fig. 4.6(b)]. An example diastole gated DE image is shown in Fig. 4.6(c-d), for which there is little or no visible artifact in either the soft-tissue or bone-only images.

Figure 4.6. Dual-energy patient images. (a-b) Images acquired without cardiac gating. Cardiac motion artifacts are apparent on both sides of the heart (arrows), particularly in the bone-only image. (c-d) Image acquired with cardiac gating, demonstrating a marked reduction of heart misregistration and motion artifact.

Human observer measurements demonstrate a statistically significant reduction in the magnitude of the motion artifact. Figure 4.7(a) illustrates the location of six example observer measurements in a DE bone-only image acquired using the clinical prototype. The image illustrates the magnitude of cardiac motion artifact (typically 1 – 5 mm) and the degree of inter-
observer variability, mitigated by the large number of measurements. Images were divided into two categories – successful diastole-diastole triggers, and unsuccessful triggers in which at least one image was acquired during systole – and the resulting measurements were pooled across all observers, giving 666 total measurements. Upon revision of the placement of observer distance measurements, an additional 6 were removed from the pool due to an obvious misinterpretation of the artifact – giving a final total of 660 measurements. Histograms showing the pooled data for each group are shown in Fig. 4.7(b-c). The total number of measurements in the diastole group was $N_{\text{diastole}} = 558$, with $N_{\text{systole}} = 102$ for the systole group. Mean artifact size ($d_{\text{artifact}}$) for diastolic and systolic triggers was 2.80 mm and 3.83 mm, respectively. The Student t-test $p$-value computed on the pooled data was $p < 0.001$, demonstrating a statistically significant difference between the two sample means. These results reveal a marked reduction of the cardiac motion artifact with diastolic triggering of the gating system. The nonzero artifact encountered even with perfect diastolic triggering is indicative of other effects, notably misregistration due to gross patient motion (slouch, breath-hold release, etc.).
Figure 4.7. (a) Magnified region of a DE bone image in the region of the left lung acquired with systole triggering. The six black segments illustrate distance measurements made by each observer in this example image. (b) Histogram showing pooled observer measurements in cases with diastole triggering. (c) Histogram showing pooled measurements with unsuccessful (systole) triggering. The data show a statistically significant reduction in the magnitude of the cardiac motion artifact, from ~3.8 mm to ~2.8 mm (p-value < 0.001).

4. Discussion and Conclusions

Cardiac gating improves DE image quality by reducing heart motion between successive radiographs. By acquiring both radiographs during diastole, anatomical registration is improved, reducing artifacts due to misalignment. These motion artifacts diminish image quality by introducing black or white edges (depending on the direction of motion and the decomposition algorithm) surrounding the heart. The presence of such artifacts degrades image quality, can obscure underlying anatomy, and potentially distract a reader from a correct diagnosis. For a DE imaging system triggered randomly (i.e., without cardiac triggering), the probability that both exposures coincide with diastole can be computed based upon the fraction of time the heart spends within the phase at a given HR. The probability of correct diastolic triggering simply by
chance ranges from 52% (72% per projection) at low HR (40 bpm) down to 30% (55% per projection) at high HR (110 bpm). Imaging systems often utilize the ECG to perform either prospective or retrospective cardiac gating. Although the electrocardiogram can provide a nearly instantaneous depiction of heart phase, the limitation for high-throughput imaging procedures warrants consideration of alternative cardiac monitoring systems. A simple fingertip pulse oximeter combined with a cardiac triggering model can be used in such procedures to gate DE acquisition.

The prototype imaging system described in this work is not without its limitations, the foremost being the considerable time between exposures (~8 seconds) required by the current detector configuration (Trixell Pixium-4600). Such is being resolved through implementation of a faster FPD supporting sub-second double-exposure acquisition. Note that this limitation, however, does not significantly affect the functionality and performance of the cardiac gating system, which triggers x-ray exposures coincident with diastole regardless of the inter-exposure time. Thus, the gating system is potentially applicable to faster systems featuring faster double-exposure acquisition (e.g., ~35 ms inter-exposure time\textsuperscript{94}) or even slower double-exposure acquisition (e.g., temporal subtraction imaging\textsuperscript{95}).

A limitation of using a pulse oximeter as a cardiac monitoring device is the inter- and intra-patient variability in the pulse propagation delay. This variability is caused by extraneous factors aside from patient HR, including level of inspiration and blood pressure. To account for this variability, the cardiac model accounts for a significant range of propagation delays. The clinical procedure (e.g., standing, comfortable breath-hold, etc.) was consistently repeated for all subjects, helping to minimize variations associated with respiratory function / inspiration. Upper and lower bounds defining the tolerable range of propagation delays (including processing delays on the oximeter) were defined by $t_{\text{trigger}}^{\text{min}}$ and $t_{\text{trigger}}^{\text{max}}$. This accounted for both the differences in
physiological pulse propagation times between patients as well as potential spontaneous changes in the delay within the same patient. Thus, while the pulse oximeter does not provide a trigger specific to a phase time-point, when combined with a cardiac timing model that is tolerant of variability in pulse propagation time, it provides a simple measure of cardiac function sufficient for triggering during the diastole window.

Representing the cardiac cycle as a binary system is a very simple model for characterizing heart motion. Diastole could be more accurately separated into five sub-phases, including segments in which heart may undergo a fair degree of mechanical motion. In this work, the gating system was engineered to trigger x-ray exposures at mid-diastole, accepting small errors thereabout due to timing variability and counting any exposure falling within the diastole window as a success. Identifying these diastolic sub-regions would require detailed physiological information that may be difficult to extract from the plethysmogram. This introduces the question as to what amount of cardiac motion can be expected or tolerated. While the significant motion associated with ventricular ejection can be avoided, the heart is never idle.

Of course, gross patient motion can contribute significantly to motion artifacts. Anatomical misregistration of the clavicles (shoulder relaxation / slouch), ribs, and diaphragm (slow respiratory rebound during breath-hold) can cause large artifacts in DE images. Proper patient training prior to the examination helps minimize such factors considerably. Such effects are certainly evident with the current system implementation (which exhibits a large inter-exposure time) and will be reduced in future work that incorporates a faster FPD with sub-second inter-exposure time.

The performance of the cardiac gating system described in this work was evaluated in two independent studies. A quantitative analysis investigated the coincidence of the exposure time with respect to the diastole window in order to assess the implementation of the triggering
system with respect to the cardiac model. The result of this study was positive, demonstrating a trigger accuracy of 85% in the basic, initial implementation, improving to 100% accuracy through temporal smoothing of the heart-rate estimate (improved estimate of HR).

The second analysis investigated the magnitude of the cardiac artifact in DE bone images to evaluate the improvement in image quality offered by the gating system. The magnitude (i.e., size) of the artifact was measured independently in images acquired with diastole and systole triggering. The observer study verified that the gating system significantly reduced the size of the cardiac motion artifact ($p < 0.001$). Future work will examine the clinical significance of such image quality improvement in tests of diagnostic performance. Such will be investigated in a variety of human observer tests (e.g., preference tests, diagnostic satisfaction tests, and/or ROC) utilizing diastole- and systole-gated DE images with trained radiologists as expert observers.

While the triggering scheme detailed above was shown to successfully reduce artifacts associated with cardiac motion, it is interesting to note that edge artifacts are never completely obviated in DE imaging – even for perfect anatomical registration. This was evident by the non-zero artifact size measured in the properly gated images. One source of such edge artifacts is the decomposition itself: as recognized in the literature, various noise reduction algorithms that differentially filter the low- and high-kVp images can introduce edge artifacts in the resulting subtraction image. A similar effect arising purely from the physics of x-ray interaction is associated with the energy-dependent attenuation of various materials. For example, increased penetration for high-kVp beams can diminish the boundary of the heart compared to the associated low-kVp image, resulting in an apparent darkening of the cardiac periphery (in soft-tissue images) or brightening (in bone images).

In summary, a model for cardiac gating that accounts for various sources of trigger and imager delays has been reported and implemented in a DE imaging prototype. Using a simple
pulse oximeter as a surrogate for cardiac motion, the model forces x-ray exposures to occur synchronous to diastole. Characterization of serial and parallel delays in the imaging system is essential. A triggering scheme exhibiting two regimes results, wherein above a certain $HR_{\text{thresh}}$, x-ray exposures are delayed to the subsequent diastole. Accurate measurement of heart rate is required to prevent erroneous triggering, particularly during rapid changes in HR due to physiological effects, or errors involving the oximeter itself. Smoothing the heart rate over three cycles was found to provide a fairly robust assessment of HR. The model described in this work is a simple yet effective means to improve DE image quality by reducing cardiac motion artifacts. The ease of implementation and convenience of use in high-throughput imaging procedures present valuable logistical benefits.
Chapter V:  
Conclusions and Future Work
1. Significance of this Work

The research described in this dissertation was essential to the development and implementation of a new, high-performance DE imaging system for the detection of lung cancer. The development of the system itself facilitated the acquisition of high-quality DE images, and the investigation of optimal image acquisition techniques ensured maximum imaging performance at radiation dose equivalent to that of a conventional chest radiograph. The development of a cardiac-gating system based on a fingertip pulse oximeter provided a simple, logistically efficient, and effective means of reducing motion artifacts caused by heart motion between the low- and high-energy projections.

Conventionally, DE imaging has been somewhat constrained by the need for increased total imaging dose, but the optimal techniques investigated in Chapters II and III, including x-ray filtration, kVp-pair, and dose allocation, correspond to a total dose equivalent to that of a single DR chest radiograph (PA view). Such studies will facilitate deployment of DE imaging systems at clinically accepted dose levels. Furthermore, the insensitivity of certain optima (viz., kVp-pair and dose allocation) to patient thickness is desirable from the standpoint of simplified system implementation – i.e., once the optima are established, they are applicable to a fairly broad range of patient body types. This allowed the technique factors (mAs\(^H\) and mAs\(^L\)) to be simply interpolated for any patient thickness within the range of measurements – e.g., at 1 – 2 cm increments in the range 18 – 30 cm for the technique chart developed for clinical trials with this prototype.
2. Multimodality Imaging Trial

A preclinical study is underway, designed to investigate DE imaging performance in a cohort of 200 patients. The primary objectives of the study are: (i) to test the optimal image acquisition techniques described in Chapters II – IV, and (ii) to evaluate the diagnostic performance of DE imaging in comparison to conventional (CR and DR) radiography and low-dose CT. Volunteer patients are recruited by radiology fellows at the University Health Network (Toronto, ON) from a population undergoing lung biopsy. Eligibility requirements include: age (18 years or older), chest thickness less than or equal to 28 cm, ability to stand unassisted for the duration of the DE exam, ability to hold his/her breath for 10 seconds, and a basic understanding of English (to understand instructions given by the fellow and/or technologist). Exclusion requirements include: abnormal heart conditions (including arrhythmia) and pregnancy.

Eligible patients are enrolled under informed consent and randomly assigned to one of the five groups shown in Figure 5.1. In Group 1 (120 patients), the low- and high-energy projections are acquired using parameters (e.g., kVp pair and dose allocation) that previous investigation indicates to be optimal, specifically: (a) optimal differential filtration (0.6 mm Ag-added filtration in the high-kVp beam), (b) optimal kVp pair of [60/120] kVp, (c) cardiac-gated triggering, and (d) optimal dose allocation ($A_e \sim 0.3$). In Group 2 (20 patients), images are acquired at an alternative kVp (e.g., $kVp^H = 150$) to investigate the tradeoffs among spectral separation, contrast, and image noise. In Group 3 (20 patients), image acquisition is performed without cardiac-gated triggering. In Group 4 (20 patients) the dose allocation is $A_e \sim 0.55$. In Group 5, images are acquired such that total dose is approximately 1/10th that of the standard technique (to test the development of advanced noise reduction algorithms in DE imaging).
For each patient, a large set of diagnostic information and image data are abstracted into a database and appropriately anonymized such that no direct or indirect identifiers allow linking back to the original patient. Date of birth is maintained for purposes of age stratification in the results. As summarized in Table 5.1, a multi-modality dataset is collected for each patient.

<table>
<thead>
<tr>
<th>Modality</th>
<th>Acquisition Notes</th>
<th>Technology: Typical Technique</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopsy (Bx)</td>
<td>Manual percutaneous. Sectioning (4–5 µm) + microscopy.</td>
<td>Multi-slice CT with fluoroscopy: Core (preferred) or fine needle</td>
</tr>
<tr>
<td>Diagnostic CT (CT)</td>
<td>1–4 weeks prior to Bx.</td>
<td>Multi-slice CT scanner: 120 kVp / 200 mA / 5 mm slices at 2.5 mm overlap</td>
</tr>
<tr>
<td>Minimum Dose CT</td>
<td>In the interventional suite immediately following to Bx. For comparison with DE.</td>
<td>Multi-slice CT scanner: 120 kVp / 10 mA / 0.8 s / 5 mm slices at 2.5 mm overlap</td>
</tr>
<tr>
<td>(minDCT)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low-Dose CT (LDCT)</td>
<td>In the interventional suite immediately prior to Bx. To localize lesion.</td>
<td>Multi-slice CT scanner: 120 kVp / 30 mA / 0.8 s / 5 mm slices at 2.5 mm overlap</td>
</tr>
<tr>
<td>Computed Radiograph</td>
<td>In the CR room 1 hour after Bx. To check for subtle pneumothorax.</td>
<td>CR chest stand: 125 kVp / 2.5 mAs</td>
</tr>
<tr>
<td>(CR)</td>
<td></td>
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</tr>
<tr>
<td>Dual-Energy Images</td>
<td>In DE room prior to Bx.</td>
<td>Preclinical DE imaging system: High-kVp: 120 kVp / 25 mAs Low-kVp: 60 kVp / 5 mAs</td>
</tr>
<tr>
<td>(DE)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Digital Radiograph</td>
<td>In DE room prior to Bx.</td>
<td>Preclinical DE imaging system: 120 kVp / 3.2 mAs</td>
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<tr>
<td>(DR)</td>
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Table 5.1. The anonymized data set collected for each patient includes: pathology results from the biopsy, diagnostic CT images, minDCT images, LDCT images, conventional CR radiograph, DE projections, and a DR radiograph. Typical techniques are shown for a patient of average size (chest thickness ~24 cm).
Imaging performance in patient trials is assessed according to two main types of clinical evaluation. The first analyzes DE imaging performance among the various groups collected in the imaging trial – viz., (i) the effect of kVp on nodule conspicuity, (ii) the magnitude and effect of cardiac motion artifacts, (iii) the effect of alternative dose allocation on image noise, and (iv) the impact of reduced dose on image quality (and the associated performance of noise reduction algorithms). Images from Group 1 will be compared to images from Groups 2, 3, 4, and 5 in observer-based preference and diagnostic satisfaction tests. Further evaluation analyzes the diagnostic performance of DE imaging in the detection and characterization of lung nodules in comparison to conventional radiography (CR or DR) and low-dose CT. Results and conclusions from this trial will help to clearly identify the performance and role of DE imaging in chest radiology.

3. Future Directions

The work reported in this dissertation has identified optimal DE chest imaging techniques and has augmented the implementation of a system suitable for clinical trials; still, there are a number of questions that deserve additional investigation. Potential future directions of this work were separated below in terms of two categories: technical and clinical. Technical considerations relate to the physics and engineering of DE imaging, whereas clinical considerations relate to the role of DE imaging within the larger context of chest radiology.

3.1 Technical

From the perspective of imaging physics, the influence of x-ray scatter in low- and high-kVp projections on the resulting DE decomposition deserves further investigation. An improved theoretical and experimental understanding of such would provide valuable insight into
enhancing overall image quality, improving tissue cancellation, and may facilitate even further reductions in the patient dose. Scatter reduction, (or correction) could also have a profound effect on image quality and the sensitivity and specificity of long nodule detection.

The selection of optimal tissue cancellation parameters is also an interesting area of ongoing research. A scalar value of $w_s$ or $w_b$ is useful for the initial implementation and phantom studies to minimize bone or soft-tissue contrast within the lung field of DE decompositions. The human chest, however, is a complicated, heterogeneous structure, with complexities in the selection of tissue cancellation across the lung field. In particular, distal ribs are difficult to “cancel” by way of a single, scalar parameter. Also, due to their increased thickness, other areas of the chest (e.g., the mediastinum, shoulders, etc.) require weighting parameters that are different from that of the lung field. Research into methods for automatic selection of spatially varying cancellation parameters is an area of ongoing research.

Future work to improve this gating system would require an increase in the temporal accuracy of trigger location through sub-diastolic triggering. The current binary triggering system does not account for motion within the diastole (filling) phase, counting any exposure within the “diastole window” as successful. However, x-ray images acquired at the beginning and end of diastole exhibit a difference in ventricular volume. Although the phase yielding the majority of cardiac movement (systole) is avoided, acquiring both low- and high-kVp images in the same sub-phase of diastole could potentially improve registration further. To accommodate the temporal resolution requirements of this advanced triggering scheme, both a faster pulse oximeter (reduced processing time) and a faster FPD (reduced $t_{\text{image}}^{\text{min}}$, and $t_{\text{image}}^{\text{range}}$) would be necessary.
3.2 Clinical

It is important to consider how DE imaging systems such as the one described in this dissertation could be implemented clinically with respect to existing diagnostic examinations. The potential clinical implementations include: replacement of conventional DR imaging in baseline examinations (increasing the incidental detection of disease); a higher-performance modality for follow-up of suspicious symptoms or lesions; and implementation of DE imaging as part of the full arsenal of a diagnostic work-up of disease.

For imaging lung cancer, it remains to be seen where DE radiography fits with regard to low-dose CT. A boost in diagnostic sensitivity for the detection of lung nodules has been observed with respect to conventional radiography, yet such does not likely rival the extremely high sensitivity of LDCT. A potential increase in specificity may augment the importance of DE imaging for the detection of early-stage lung cancer as an adjuvant, dual-read LDCT + DE. The most likely role of DE imaging with respect to CT is as an alternative in rural and/or economically challenged areas or as an adjuvant to LDCT, giving higher combined sensitivity and specificity. In addition, DE radiography may provide a promising implementation in temporal post-curative follow-up, minimizing the use of CT in repeat yearly examinations monitoring successful treatment.

It is also important to consider how DE imaging could be implemented with respect to conventional PA and lateral (LAT) radiographic exams. It is unlikely that a PA DE image would replace the conventional two-view chest exam – e.g., to visualize the retro-hepatic lung. Moreover, the imaging performance and diagnostic value of a LAT DE image remains to be fully investigated. Hence, a likely short-term clinical implementation would involve a PA DE image, followed by a conventional LAT DR. However, to the extent that a truly equivalent DR image can be decomposed from the low- and high-kVp projections (e.g., by log-weighted addition),
both the PA and LAT views could be acquired as DE images. In such implementation, the PA and LAT views could be rendered at the clinician’s discretion as either an equivalent radiograph or a soft-tissue / bone-only decomposition. Such potential implementations should, of course, be considered with respect to further clinical research.

Furthermore, it is interesting to consider the extent to which DE imaging could provide a useful modality for the numerous functions and indications of general chest imaging – e.g., line placement, foreign objects, rib fractures/metastases. For these applications and others beyond thoracic imaging (e.g., musculoskeletal, cardiac and interventional imaging), the potential role of DE imaging depends on its performance in PA and LAT views, the capacity to decompose an equivalent DR image from the low- and high-energy projections, and the ability to provide a high degree of material discrimination. Such questions are the subject of future technical and clinical investigation.
References


