CAUDAD TO CRANIAL VERSUS CRANIAL TO CAUDAD CT SCANNING OF THE THORAX: A COMPARISON OF TWO PROTOCOLS

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By

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ABSTRACT

Purpose: The current study compares artifact (motion at the lung bases and beam hardening from the superior vena cava and subclavian vein), clarity of vessels (hilar vessels, great vessels and aorta) and clarity of the nodal systems (stations 2R,2L,4R,5,6 and hilar) in the caudad to cranial and cranial to caudad direction when CT scanning the thorax. The purpose was to determine if one direction was associated with less artifact.

Methods: 100 consecutive consenting patients were randomized into either cranial to caudad or caudad to cranial CT scanning of the thorax using block randomization. The images were interpreted independently by two radiologists who were blind to the direction for the scan. Images were analyzed using a 5 point Likert scale for artifact (motion, superior vena cava, subclavian vein), clarity of the vasculature structures (hilar vessels, great vessels, aorta),clarity of the nodal stations (2R, 2L, 4R, 5,6,hilar) and overall impression. Each scan was assessed on two separate occasions by the radiologists. Inter and intra observer correlations were measured with the Spearman Rank Coefficient. The Wilcoxin Rank Sum test was used to compare the direction of scanning.

Results: Intra-observer correlations were strong ranging form 0.616-0.902 for Radiologist 1 and 0.537-0.902 for Radiologist 2. The inter-observer correlations were also good with Spearman Rank Coefficients values ranging from 0.102-0.793. The caudad to cranial direction of CT scanning was significantly better than cranial to caudad direction with respect to total artifact (motion + superior vena cava+ subclavian vein), however, there was no statistically detectable difference in motion artifact. Clarity of the vasculature was deemed better by one radiologist in the caudad to cranial direction but not the other. Lymph node clarity in the upper thorax was felt to be better visualized with caudad to cranial scans versus cranial to caudad imaging, however, hilar lymph nodes and lymph nodes in the lower mediastinum showed not statistical difference. The quality of the overall images was significantly better.

Conclusion: The caudad to cranial direction of CT scanning is significantly better with less beam hardening artifact and improved image quality, allowing better assessment of the great vessels and select nodal stations.

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Table 25: Wilcoxin Rank Sum results for total values comparing directional CT scanning (n=100) for cranial to caudad (down) and caudad to cranial (up) CT scans.

OBJECTIVE

The objective of the current study was to develop, validate and use a rating scale to compare directional CT scanning of the thorax. Specifically, the scale would be utilized to determine whether artifact (motion at the lung bases and beam hardening from the superior vena cava and subclavian vein), clarity of the vessels (hilar vessels, great vessels, and aorta) and clarity of the nodal systems (stations 2R, 2L, 4R, 5 and 6) is reduced with caudad to cranial CT scanning of the thorax compared to cranial to caudad scanning.

No previous research has addressed the importance of the direction of CT scanning, particularly CT scanning of the thorax. In addition, no previous research has produced a validated rating scale to assess the quality of CT images. Therefore, an extensive literature search was performed. The medical, psychological and business literature addressing the types of rating scales, their development, the advantages of Likert and Visual Analogue scales and their utilization was reviewed. This information was then used to determine which type of scale would best address the issue of directional CT scanning.

Once the developed rating scale was validated, it was then used to compare the direction of CT scanning of the thorax in 100 patients who were randomly assigned to either cranial to caudad (n=50) or caudad to cranial (n=50) CT scanning of the thorax

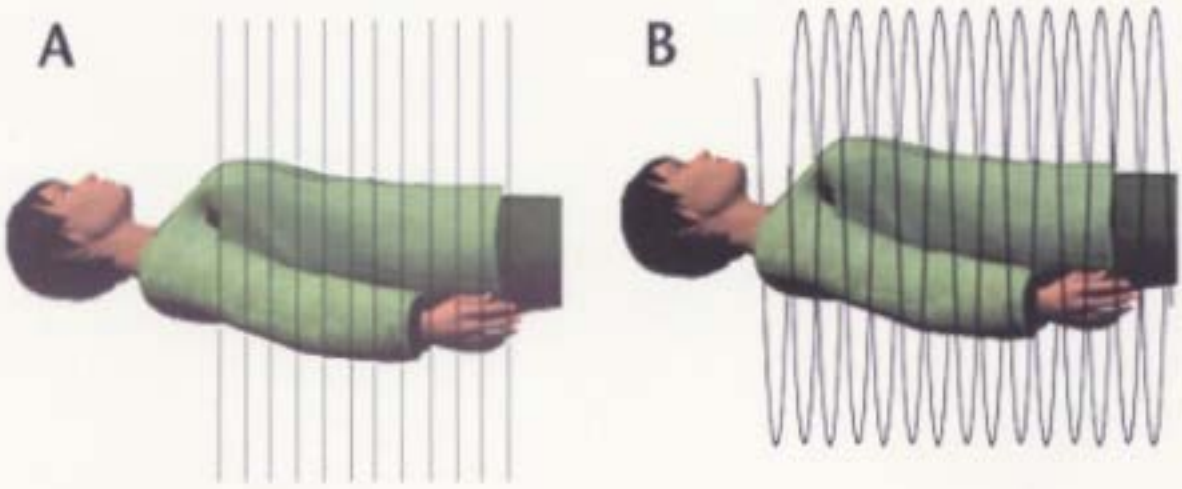
INTRODUCTION

1. Computed Tomography (CT)

1.1 Helical versus Conventional CT Scanning

The introduction of helical CT technology in the early 1990's had a significant impact on diagnostic imaging, particularly imaging of the thorax, abdomen and pelvis. Helical CT scanning surpassed its predecessor by using slip ring coupling between the rotating and the stationary portion of the gantry. In conventional CT, discontinuous cross section scans were acquired, with each rotation producing a separate set of data and images. The new slip ring technology enabled continuous table and patient translation and continuous rotation of the CT gantry which is constantly producing data (1, 2, 3, and 4). This coupling enabled the x-ray beam to trace a helical spiral path around the patient resulting in the acquisition of uninterrupted volumetric data and elimination of inter-scan delay. In other words, conventional CT required a stop-start maneuver to acquire a single slice, whereas helical CT used much faster and nonstop technology to acquire multiple transverse slices and volumetric results. Helical CT scanning enabled scanners with a single detector to acquire images through an area of interest in less than 20 seconds compared to over two minutes for non-helical scanners (1) (see Figure 1)

Figure 1: Scan principles of conventional (A) and spiral CT (B). In conventional CT the x-ray tube focal spot loci form a series of circles with each circle defining a plane. In helical CT the x-ray tube focal spot is a helix. Used with permission from www.imaging.cancer.gov



1.2 Helical CT Scanning of the Thorax

The delay between scans with conventional CT required the patient to take a breath-hold between each consecutive scan. This resulted in an arbitrary division between axial slices. Patient movement and inconsistency in the depth of breath-hold between scans lead to inaccuracy and the possibility of omission of anatomy or subtle abnormalities. In thoracic imaging the major advantage of spiral CT has been the ability to scan the entire thorax with a single breath-hold, eliminating inter-scan delay. This eliminates respiratory mis-registration and slice to slice variation inherent in conventional CT scanning. The scanning time is significantly shortened and rapid acquisition affords other advantages including greater flexibility in the administration of intravenous contrast and the timing of the scan relative to the injection. In addition, the capacity to perform axial slices at small increments enables three dimensional

reconstruction in post processing. Continuous data collection and the elimination of respiratory mis-registration means spiral CT can detect small pulmonary nodules not shown by conventional CT (5). Spiral CT has been shown to be superior to conventional CT in the detection of pulmonary nodules. Remy-Jardin et. al demonstrated that the mean number of nodules detected in 39 patients was significantly higher with spiral versus conventional CT, as were the number of nodules less than 5mm in diameter per patient (6). In addition, the increased scanning speed means less patient time and discomfort on the CT table and increased efficiency for the diagnostic imaging department (7,8,9).

1.2.1 *Indications for Thoracic CT*

CT is often more accessible than other modalities and is capable of imaging the entire body including solid and hollow viscera. Despite rapidly developing diagnostic imaging technology especially in MRI and PET scanning, CT continues to be the modality of choice for work-up of pulmonary neoplasms, both at initial presentation and for follow-up to therapy (surgery, radiation or chemotherapy) to determine primary tumor regression or progression and to assess for metastasis MRI and PET are more focused in their application. The majority of these cases would be for bronchogenic carcinoma; however other more rare pulmonary malignancies and nonmalignant entities are also visualized on CT. In addition, pathology involving the pulmonary interstitium (e.g. pulmonary fibrosis), mediastinum (e.g. thymic tumors), thoracic vasculature (e.g. angiosarcoma), lymph nodes (e.g. lymphoma), chest wall (e.g. lymphoma) and bone (e.g. sarcomas) are also demonstrated on thoracic CT. CT has also become the modality of choice for the diagnosis of pulmonary embolus in many diagnostic centers.

1.2.2 *Breath Hold Duration*

Scan coverage in the long axis is often limited by the patient's ability to sustain a breath-hold. For the majority of thoracic helical CT scans the typical breath-hold is 30 seconds. Larger patients or those with hyper-inflated lungs may require a 40 second breath-hold to cover the entire thorax. Hospitalized patients or those with cardiac, pulmonary, or co-morbid illnesses are generally limited to 18-32 second breath-holds. The advantage of a longer breath-hold or scan duration is that anatomical coverage can be increased at the same table speed or the z-axis resolution can be increased and coverage maintained by decreasing the table speed. Longer scan duration however requires more contrast medium and there may be decreased tube output and increased noise (fluctuation in image intensity or CT number in a uniform region of interest at the same input exposure).

Patient cooperation is critical for obtaining an optimal CT scan of the chest. If the patient cannot maintain the breath-hold for the entire duration of the scan they are instructed to slowly exhale and breathe normally (10). This results in motion artifact or blurring of the images performed during the end of the scan. Although most diagnostic imaging departments have standard protocols for CT scanning many parameters are tailored to the patient based on the clinical presentation. Having the patient hyperventilate and practice a breath-hold prior to the diagnostic scan can increase the patient compliance (11).

1.2.3 *Patient Positioning*

CT of the thorax is most often performed with the patient in the supine position. Beam hardening artifact can result from the osseous shoulders and upper extremity and therefore the patient's arms are placed above their head when possible (to be discussed in section 1.6.2). There is relative poor inflation and preferential blood flow to the dependent portion of lung. Therefore, on a supine image the posterior lung is often of higher attenuation relative to the anterior pulmonary parenchyma (12). This physiological effect is reversed when the patient is imaged in the prone position and if there is a question of posterior atelectasis or interstitial lung disease then the patient may be imaged in both positions (13).

1.2.4 *Field of View*

The field of view (FOV) is defined as the anatomy or portion of the body included on the axial images. Any size field of view has a fixed number of pixels, usually 512 X512. If the field of view is made larger then the pixel size increases and the spatial resolution decreases. Alternatively, if the FOV is made smaller then the pixel size is decreased and the spatial resolution improves. Therefore there is a tradeoff between the anatomy which can be included on an axial image and the image detail. In order to limit radiation dose and obtain the best resolution, exams should be adjusted to include only the anatomy being scanned. In thoracic CT this generally includes the thoracic cavity and chest wall, including the ribs. If there is a question regarding the shoulders, skin surface, or subcutaneous structures then the FOV is adjusted to encompass theses areas. A smaller FOV may be necessary if a particular anatomic region is of concern such as the aorta. In high-resolution lung imaging the FOV is restricted to the lungs in order to improve spatial resolution.

1.3 Technical Considerations in CT

Helical CT scanning requires both the radiologist and the technologist to be cognizant of certain technical choices or parameters including collimation, table speed, total scan time, pitch, and rate and volume of intravenous contrast administration. These parameters are guided by the volume of anatomy being imaged, limitations of the CT scanning machine, the ability of the patient to remain on the CT scanning table and the size of the abnormality being investigated.

1.3. 1 Collimation and Pitch

As with conventional CT scanning, one must first determine the slice thickness which is dependant on the organ of interest and the diagnostic goal of the scan. The parameters useful in optimizing high resolution CT technology for thoracic imaging have been described (14,15). A high resolution view of the lung obtains a single axial image through a very thin section of pulmonary parenchyma utilizing a single rotation of the gantry. Thin samples of lung parenchyma at varying intervals are obtained, typically every 1-2 cm producing high resolution images of detailed lung parenchyma at regular intervals. Axial sections of parenchyma are omitted in the interest of fine detail. Both conventional and spiral CT scans image a volume of parenchyma typically 5-10 mm thick and in doing so result in some degree of volume averaging in each axial image. Although, the images are not as detailed, theoretically the entire thoracic cavity is imaged. With both conventional and spiral CT the radiologist and technologist must determine the collimation or slice thickness.

The parameter unique to spiral CT is pitch. Pitch is defined as table speed (mm/sec) divided by slice collimation (mm) multiplied by the gantry rotation period (sec). In other words, the rate of coverage over the long axis of the patient is directly related to table speed (16,17).

At a pitch of 1, the patient is translated 1 collimation width per 360 gantry rotation (750-1000 milliseconds); at a pitch of 2 the patient is translated 2 collimation widths during a 360 gantry rotation. Image noise, which is measured as the standard deviation of pixel values in a homogeneous region of interest is not affected by an increase in pitch (18,19). This is because the same number of photons reach the detector regardless of the scan pitch. Collimation however affects helical CT quality by narrowing the section sensitivity profile and improving spatial resolution. Increased resolution however occurs at the expense of decreased number of photons reaching the detector and therefore increase in image noise (20).

1.3.2 Table Travel Distance

Prior to performing a CT scan, an accurate determination of the volume of anatomy necessary to cover during the scan must be determined. A scout image scanogram or tomogram consists of a computed radiograph which is reconstructed from numerous contiguous images with the x-ray tube held in a stationary position. In CT scanning of the thorax, the chest from apex to the lung base including the costo-phrenic angles is imaged. This almost always includes the upper abdomen. The cranial to caudal extent of the CT region of interest (table travel distance) is determined to comfortably include the anatomy of interest within the helical scan volume.

1.3.3 Helical Acquisition

Once the volume of interest from the localizing scanogram and the tolerable scan duration/breath-hold has been determined, the table speed is determined by:

$$\text{Table speed} = \frac{\text{required scan length (mm)}}{\text{Total breath hold (sec)}}$$

The collimation is then selected based on the table speed. A narrow collimation results in increased spatial resolution and detection of more subtle abnormalities however this may increase noise. As described previously, increase in pitch will increase coverage at the expense of resolution. Increasing the pitch from 1 to 2 broadens the results in section thickness by approximately 30% (21,22). Using a pitch of more than 1 however enables a narrower collimation and the anatomy can be covered in the same amount of time

Although an increase in scan pitch at the same collimation width would not affect the image noise, the corresponding decrease in collimation would result in increased noise. The thorax has the highest intrinsic contrast of any body part. The pulmonary vessels and ribs are very different densities from the adjacent lung parenchyma and in most adults the lymph nodes and mediastinal vasculature are surrounded by fat such that they are easily demarcated. Because of this high inherent contrast an increase in noise is often tolerable with a thoracic CT as compared to a routine abdominal CT. In abdominal and pelvic CT the detection of subtle, low contrast lesions especially in solid viscera is more limited by poor resolution and increased noise. Based on this reasoning the collimation is usually selected as the minimal value that allows the helical scan pitch to be less than or equal to 2.

A summary of the helical prescription is:

Scan length (mm) + scan duration (sec) Table speed (mm/sec) Collimation (mm)

Routine helical imaging of the thorax is usually performed with pitch values between 1-1.5, utilizing a collimation range of 7-10 mm and a table speed of 8-15 mm per second (1,2,3).

1.4 CT Numbers and Window levels

During image reconstruction, a CT numerical value is assigned to each voxel or volume of CT information according to the degree of x-ray attenuation in that voxel. For each pixel, the CT computer determines a relative linear attenuation coefficient, u, and then normalizes this number to the reference material, water (23). To obtain numerical values of convenient size for interpretation the CT number is defined as:

$$CT=1000 \times (u-u_{water}/u_{water})$$

The unit for CT attenuation is a Hounsfield unit (HU). The numbers are set on a scale with 1000 representing the attenuation of air and 0 the attenuation of water. There is no upper limit to the scale. Bone has HU ranging from 1400 to 600, soft tissues 240 to -160, lung 100 to -1300, and air less than -1000 (24).

The human eye can distinguish only 40-100 levels of grey depending on the viewing conditions, while the complete diagnostic range of CT numbers are in excess of 4000 HU (24). The discrimination between structures with small differences in CT numbers would not be possible.

Therefore just a portion of the CT scale is displayed. This number of windows is defined by its width which reflects image contrast and by its level or center, which determines image brightness. Reducing the window width increases image contrast and lowering the window level darkens the image. If contrast material is utilized the values change slightly. Optimal window width and levels include:

Table 1: Optimal Window Width and Length/Center for Various Anatomy (24)

	Width	Length/Center
Lung	1500	-650
Soft Tissues, non contrast	400	40
Soft tissues with contrast	400	70
Liver non contrast	200	40
Liver with contrast	300	60-100
Bone	400	70

Post processing analysis and manipulation of a CT image often involves measurement of lengths and angles and the analysis of CT numbers within a selected region of interest (ROI). This is particularly important in determining whether a lesion or mass contains fluid and/or soft tissue, or detecting the presence of free air (25). If a window is set too wide image contrast is reduced and low contrast lesions particularly in solid organs such as the liver or pancreas go undetected.

Too narrow a window setting can significantly increase image noise and decrease grey scale differentiation.

The thorax contains a wide variety of tissue densities, including inflated lung, blood vessels, lymph nodes, osseous structures and fat. Due to the wide range of densities they cannot all be displayed on a single image and different window widths and lengths must be used to visualize the lung architecture, mediastinal soft tissues, bone and chest wall. Most radiologists use at least two settings for interpretation of a thoracic CT, one for optimal visualization of the lung parenchyma and another for the soft tissues of the mediastinum and chest wall. A third set of window settings can be displayed if fine osseous detail is required. Because of the high inherent contrast in thoracic CT narrow window settings are rarely used.

1.5 Contrast material

1.5. 1 Why is Contrast material Necessary

The degree of attenuation of an x-ray beam depends on multiple factors, particularly the thickness of the substance imaged, its density and the number of protons in the nucleus of the element (atomic number) (25). Organs are a complex mixture of elements and the attenuation of tissue is determined by the average of the atomic numbers of all the atoms involved.

When there is a natural contrast between two adjacent structures such as the solid muscles of the heart and the adjacent inflated lung the outlines of the structures can be visualized. Similarly, if there is a significant difference between the average atomic number of two adjacent structures

such as soft tissues which have a low atomic number and bone which has a higher atomic number due to the calcium content then the outlines of the anatomy can be seen by natural contrast.

However, if two organs or adjacent structures are of similar densities and average atomic number then there is little natural contrast and it will be difficult on CT to distinguish anatomical borders. Therefore, it is often not possible to differentiate blood vessels or the internal structure of a solid organ without artificially altering the density or attenuation with intravenous contrast. Similarly, the lumen of the esophagus cannot be delineated without giving oral contrast.

A factor which can be manipulated is the average atomic number of a structure. By filling the lumen of a blood vessel with a non-toxic solution that contains a significant proportion of iodine the density of the hollow vessel can be increased and the lumen visualized.

Intravenous contrast material is used during a CT scan of the chest to distinguish between normal structures such as mediastinal blood vessels, and pathological processes such as soft tissue masses and aneurysms. In thoracic CT imaging mediastinal fat and inflated pulmonary parenchyma provide a natural contrast with adjacent solid structures. In thin patients with a paucity of mediastinal fat it may be difficult to distinguish lymph nodes from contiguous normal mediastinal structures such as the left atrium or esophagus without using intravenous contrast. If a patient has significant atelectasis or pleural effusions, the differentiation of pulmonary masses from adjacent fluid or collapsed lung may also be difficult (26,27). Intravenous contrast can be essential for the accurate differentiation of lymph nodes from normal mediastinal vasculature and

hilar anatomy and for demonstration of neoplasm's encasing or invading the mediastinal vessels. Also, most intra-vascular tumors such as angiosarcomas involving the vessel lumen are not perceptible without the use of IV contrast (28).

1.5.2 *Types of Intravenous Contrast Material*

All intravenous contrast material are based on the element iodine. No other element of a high atomic number has the same chemical characteristics that make iodine able to form soluble compounds with low toxicity and therefore suitable for radiography. Intravenous contrast material can be classified into ionic and non-ionic or alternatively into high-osmolar, low-osmolar and iso-osmolar (relative to blood).

The osmotic pressure or osmolality of a solution is a function of the concentration of particles within it. This concept has an important impact on the tolerance of contrast material, since the higher the osmotic pressure the poorer the tolerance (29). Ionic contrast material undergoes dissociation to form ions which increases the osmolality while non-ionic contrast material does not. The closer the osmolality of a radiographic contrast material is to plasma the better the general tolerance (30)

Osmolality is responsible for many of the clinical effects of contrast material including the sensation of heat and discomfort or even pain (31). Both the osmolality and viscosity of a contrast material are related to the concentration of iodine. The osmolality depends on the ratio of iodine atoms to osmotically active particles. Traditional high osmolality agents are ionized and extremely hypertonic to plasma (about 2000 mOsm/kg H2O). Diatrizoate is a tri-iodinated

benzoate and thus a ratio 1.5 agent, because the substance separates into two osmotically active particles for each three iodine atoms. "Low" osmolality agents (about 600 to 900 mOsm/kg H20) were introduced in the 1980s. These are nonionic monomers with three iodine atoms for each osmotically active particle or monoacidic dimers with six iodine atoms for each two osmotically active particles. The term low osmolar is a misnomer. They have a lower osmolality than conventional radiocontrast agents. However these agents are hyperosmolar relative to plasma More recently, multimertic iso-osmolar agents (osmolality 290 mMom/kg) have been introduced (32). The strength of a contrast agent is usually given as its concentration in iodine (mg/ml) which is noted after the brand name. At our institution we utilized both MD 60 (Mallinckrodt, Point Claire, PQ) and Isovue 300 (Bracho Diagnostics, Mississauga, Ont.). MD-60 (Diatrizoate Meglumine and Diatrizoate Sodium) is a high osmolar, ionic contrast agent. Isovue (Iopamidol injection) is a non-ionic low osmolar agent. Although some physicians advocate the exclusive use of non-ionic, low osmolality agents because of fewer adverse reactions, the higher cost of non-ionic agents prohibits their world wide use (33, 34). Non-ionic contrast cost up to 10 times more than high-osmolality ionic agents. Guidelines have been developed by the American College of Radiology for the use of low-osmolality, non-ionic agents (35).

1.5.3 *The Injection of Contrast material*

Most thoracic CT scans are performed utilizing a medially directed angiocatheter with a flexible cannula. The antecubital vein is the preferred route of contrast material injection as drainage is directly into the basilic system and superior vena cava which helps maintain the strength of the bolus. 20 gauge or larger catheters are generally used in order to support the flow rates. If a

patient has small or fragile veins then a smaller gauge catheter can be utilized. Similarly, if the antecubital vein is not accessible a more peripheral (i.e. hand or foot) venipuncture site can be cannulated. If a smaller angiocatheter or peripheral vein is necessary then the flow rate and CT protocol must be adjusted accordingly

The patient is instructed to notify the technologist if they experience discomfort at the injection site since this may indicate local subcutaneous extravasation. The reported incidence of intravenous contrast material extravasation related to power injected CT contrast material has ranged from 0.1% to 0.4% (36) Higher flow rates lead to a higher incidence of extravasation, which is experienced as pain, fullness or burning at the injection site

Due to the hyperosmolality of the solution extravasated iodinated contrast material are toxic to the skin and result in an acute inflammatory reaction which peaks at 24-48 hours following injection (37). Studies have shown that low osmolar contrast material is less toxic to the subcutaneous tissues than high osmolar contrast agents (38). Although this is usually a benign event other than patient discomfort, significant complications have been reported including ulceration and tissue necrosis. In the case of a significant response, sequelea can include fibrosis, muscle atrophy and compartment syndrome. The extent of injury to the tissue is related to the dose of contrast agent which has extravasated and therefore patient communication concerning discomfort is essential (39).

Venous air embolism is not unusual following the injection of contrast material and small punctuate pockets of air can be seen in the intrathoraic veins, main pulmonary arteries or right

ventricle and less frequently in the intracranial venous system (40,41). This is usually silent and of no clinical importance however if a large volume of air is inadvertently injected then clinically significant venous air embolism can lead to complications including dyspnea, chest pain, pulmonary edema, hypotension, tachycardia, and stroke. Therefore, limiting the amount of air within the power injector and ensuring appropriate positioning of the bolus during injection is important (42).

1.5.4 *The Timing of Contrast material Injection*

With decreased scan times and more rapid coverage of the thorax in spiral CT there is a corresponding decrease in the time required for vascular enhancement. With this comes the ability to utilize less volume and concentration of intravenous contrast. Thus, the volume of intravenous contrast material needed to enhance thoracic vasculature can be significantly reduced. Costello and colleagues demonstrated that with a spiral CT scanner enhancement with 60 mL of 60% iodinated contrast material provides superior vascular contrast enhancement to that of conventional CT imaging with 120 mL of 60% iodinated contrast (26). Because scanning time is shorter with spiral CT, a consistently high degree of vascular enhancement is possible at the peak of the bolus delivery. The ability to utilize less contrast provides cost savings to the radiology department in addition to benefiting the patient. By timing the spiral CT scan appropriately the images can be obtained with peak contrast enhancement or during a particular phase of enhancement. For example, the timing for a CT pulmonary angiogram ensures optimal enhancement of the pulmonary arteries to assess for thromboembolus.

At our institution a routine thoracic CT protocol utilized 100cc of contrast material injected at a

rate of 2.5 cc/sec with a 25 second delay between injection and acquisition of the helical image. A CT pulmonary angiogram was performed with 150cc of contrast material injected at a rate of 3.5cc/sec. with a 17 second delay between injection of contrast and the helical acquisition.

1.5.5 *Adverse Effects of Contrast material*

The adverse side effects of contrast material are relatively infrequent. A non-life threatening, moderate reaction requiring some treatment occurs in 1-2% of patients receiving ionic high-osmolar contrast material and in 0.2 to0.4% of patients receiving non-ionic high-osmolar contrast material. Severe, life-threatening reactions can be expected in about 0.2% of patients after injection of ionic high-osmolar and 0.04% after non-ionic low-osmolar contrast material (43). It is therefore essential for the radiologist and support staff to have intimate knowledge of the risk of reaction, methods to prevent reactions, the possible manifestations and their treatment (44,45). Virtually all life threatening reactions occur immediately or within the first 20 minutes after contrast injection. The frequency and severity of contrast reactions can be affected by the dose, route and rate of delivery.

Reactions to contrast material can be divided into:

1. Anaphylactic (idiosyncratic)
2. Nonanaphylactic
    a. Chemo toxic
    b. Vasovagal
    c. Idiopathic
3. Combination (1 and 2)

Anaphylactoid reactions mimic allergic reactions and shock (44). There is no uniform explanation for these reactions however the process likely involves many factors and bodily systems. The combined effect may lead to vasodilation of the dermis, mucosa, or peripheral blood vessels or bronchospasm (43). The likelihood of a reaction is increased if the patient has a history of asthma, allergies to food or drugs or previous contrast reaction. In these patients either a CT using low osmolality non-ionic contrast material or doing a CT scan without contrast is recommended. There is no evidence that allergy to shellfish or seafood increases the risk and an anphylactoid type reaction to contrast. (45).

Premedication with corticosteroid and antihistamine has been shown in clinical trials to decrease the frequency of anaphylactoid contrast reactions (46,47). However, no pretreatment regime can completely eliminate reactions. In addition, non-ionic low-osmolar contrast material should be utilized in at risk patients (48). The ACR has established guidelines concerning patient selection and premedication for patients who are at increased of reaction to intravenous contrast injection (35).

Chemo toxic side effects include neurotoxicity, cardiac depression, arrhythmia, electrocardiogram changes and renal tubular or vascular injury. Nonionic contrast material is associated with fewer chemotoxic side effects and some effects are agent specific (49). Most side effects are mild. Serious cardiovascular and pulmonary side effects such as significant hypotension, tachycardia and shock are rare and are idiosyncratic in occurrence. No definitive

risk factors have been described in the literature. The etiology of chemotoxic effects is complex, however the pathophysiology of some reactions such as hypotension, tachycardia, arrhythmias, and pulseless electrical activity have been established (50)

Contrast material results in increased vagal tone on the heart and blood vessels which can result in bradycardia and hypotension and a vasovagal reaction. The emotional mind set of the patient plays a large role in their response to the contrast and in some cases a vagal reaction may be related to the venapuncture or claustrophobia. A vasovagal reaction can range from light-headedness to cardiopulmonary arrest if untreated. As in any reaction to contrast material prompt attention is necessary.

Reactions to intravenous contrast for which no chemotoxic or vasovagal explanation can be found are by definition idiopathic. That is, no underlying cause for the reaction can be defined.

Combined anaphylactoid and non-anaphylactoid reactions can occur simultaneously. This can be a complicated presentation and knowledge of the patient's medical history is essential for treatment of a reaction since pre-existing conditions such as pulmonary edema and cardiac disease can effect the manifestation of reactions. Of particular importance is the patient's medication history since cardiac medication, specifically beta- blockers can inhibit a patients tachycardic response during an anaphylactic reaction. This may lead to the inappropriate diagnosis of a vasovagal reaction.

1.5.6 *Contrast-Induced Nephrotoxicity*

The use of contrast material in diagnostic and interventional procedures has been increasing as innovation and technology advance and contrast material induced nephropathy has become a major concern for radiologists and cardiologists. The importance of this topic is evident by the numerous reviews in the radiology (51,52), cardiology (53), nephrology (54,55), intensive care (56,57) literature addressing the risk factors, diagnosis, treatment and prevention of contrast material nephropathy.

The incidence of contrast material induced nephropathy has been steadily increasing. In 1977, 5% of hospital- acquired acute renal failure was attributed to intravenous contrast material and in 1987 the incidence had increased to 32% (58, 59). In 2002 Nash et al reported that toxicity induced by contrast material had become the third leading cause of hospital acquired acute renal failure (60) The exact incidence is difficult to determine due to variable contrast agents, dose, definitions of renal failure/insufficiency, populations and methods of measurement in the literature. There is no standard definition and the literature varies in the criteria for contrast material induced nephropathy. In general, it is an acute decrease in renal function after the intravenous administration of contrast material. It is has been defined both in terms of percent increase from baseline creatinine (25 percent or more) (61) and an absolute elevation (44 umol/litre) (62) from baseline after exposure to contrast material. In addition, the time frame for these changes varies ranging from 24 or 120 hours after administration of contrast material (61, 62, 63, 64, and 65). Creatinine levels typically peak 3-5 days after administration and depending on the definition the incidence of contrast material induced nephropathy may be underestimated.

Contrast material induced nephropathy can be associated with clinically important adverse short and long term outcomes. Complete recovery of renal function typically occurs in five to ten days however there may be some degree of residual renal impairment in up to 30% of patients affected by contrast material nephropathy (66). Dialysis is rarely required and other comorbid illness certainly contribute to the outcome (67,68). Levy, Viscoli and Horwitz reported a mortality rate of 34% in patients who developed contrast material-associated renal failure compared to a 7% mortality rate in APACHE-II (a severity of disease classification system which uses a point score based upon initial values of 12 physiological measurements, age and previous health status) matched controls without renal failure. They concluded that renal failure appears to increase the risk of developing severe non-renal complications that lead to death (69)

The etiology of contrast material induced nephropathy is not well understood. There has been extensive in vivo- and ex-vivo research in animals however no optimal model has been identified (70, 71, and 72). In addition, the relative rarity of contrast material induced nephropathy in humans makes the pathogenesis difficult to study. In patients with no risk factors for contrast material induced nephropathy or preexisting renal disease the incidence of nephropathy following the administration of radiocontrast material is negligible and is reported to be approximately 8% (67). There are two predominant theories which are not mutually exclusive. One theory is that the contrast agent causes acute renal vasoconstriction which causes or exacerbates renal ischemia particularly in the outer medulla which is susceptible to reductions in blood flow. The mechanism is unknown but is likely multifactoral related to the osmotic load, and intra- renal alterations in endothelin, prostaglandins, nitric oxide, and adenosine (54, 73).

Another possibility is that direct renal tubular epithelial cell toxicity, in association with the generation of oxygen free radicals contributes to the occurrence of contrast material nephrotoxicity (70, 74). It is likely that the two theories work in concert, however there is no single unifying hypothesis that has gained wide spread support.

Specific risk factors have been identified which are associated with an increase risk of acute renal function following the administration of intravenous contrast material. The understanding of these factors and their strength of association with contrast material induced nephropathy has been well elucidated. Underlying impairment in renal function has been recognized as a major risk factor with increasing levels of renal dysfunction associated with higher risk of contrast induced nephropathy (74, 75). Diabetes mellitus is a second important risk factor. Although much of the increased risk is related to renal disease, diabetes mellitus in the absence of nephropathy, especially in insulin dependent diabetics is associated with increased risk of contrast related nephropathy (67,75, 76,77) Patients with intravascular volume depletion are also at increased susceptibility to renal injury following intravenous administration as well as patient with advanced heart failure. Patients with nephrosis and cirrhosis are also at risk. In these conditions decreased effective circulating volume and reduced renal perfusion potentiate renal vasoconstriction following the administration of contrast material (55,76). A history of congestive heart failure also inflates the risk in patients with diabetes mellitus and renal insufficiency. Other predictors of contrast material nephropathy include the presence of myeloma, hypertension, age greater than 70, acute myocardial infarction within 24 hours of administration of contrast, hemodynamic instability and receipt of intravascular contrast within previous 7 days The concurrent use of nephrotoxic agents such as ACE inhibitors and

nonsteroidal anti-inflammatory have also been implicated (55,56,57).

Risk factors not related to the patient include the osmolality and content of the contrast medium and volume of contrast medium utilized (78, 79, and 80). Low osmotic contrast material are generally less nephrotoxic than high osmotic contrast material in patients with pre-existent renal insufficiency, however there is no difference in their efficacy in patients with normal renal function (68,75,81). The largest randomized controlled trial to date comparing ionized "high" osmolar agents and nonionic "low osmolar agents evaluated 1196 patients undergoing coronary angiography. This study demonstrated a reduction in incidence of contrast material induced nephrotoxicity with the use of iohexol, a low osmolar nonionic contrast agent in patients with preexistent renal insufficiency, with or without diabetes (67). A meta-analysis by Barrett and Carlisle included the results of this study made similar conclusions (81). Iodixanol is the first of the new multimeric iso-osmolar contrast agents. In low risk populations is does not provide additional protection against contrast induced nephropathy (79, 80). Iodixanol was associated with a statistically significant lower incidence of contrast induced renal insufficiency compared with Iohexol in a recent randomized trial of 129 diabetic patients with chronic renal insufficiency undergoing coronary angiography(82).

The best treatment of contrast material induced nephrotoxicity is prevention. It is important to identify patients at risk and when possible an unenhanced CT scan or alternative diagnostic procedure such as a MRI or ultrasound should be performed, particularly in patients with renal insufficiency. If contrast is necessary a nonionic contrast agent should be utilized with as low a dose as possible (78). Standard saline hydration has decreased the incidence and severity of

contrast material nephropathy. Hydration reduces the degree of vasoconstriction and increases urine output. Although there is no trial which has compared hydration to placebo it is universally recommended based on the available literature (83, 84, and 85). No pharmacological agent has yet been shown to be as beneficial. (84, 85). One proposed intervention includes the prophylactic administration of N-acetylcysteine in patients with renal impairment. N-acetylcysteine has antioxidant and vasodilatory effects and has been used in high risk patients to prevent renal toxicity however its benefit is controversial (86, 87, 88, 89, 90, 91). Tepel et al studied 83 patients with chronic renal insufficiency and randomly assigned them to placebo or N-acetylcysteine. They reported significantly less contrast material induced nephropathy with N acetylcysteine and concluded that the prophylactic administration of N acetlycysteine is an effective method of preventing contrast material induced nephropathy in patients with chronic renal insufficiency (87). Other studies however have been contradictory. In general, there is significant heterogeneity among studies which have looked at N –acetylcysteine and although recent meta analysis suggest some benefit the results should be interpreted with caution (88,89,90,91). More data is needed before N acetyocysteine can be recommended in patients at risk for the prevention of contrast-induced media nephropathy. Mannitol and Furosemide have been investigated and have not shown any advantage over saline for preventing contrast induced renal dysfunction. Mannitol may in fact be harmful. Patients with renal chronic renal failure treated with saline and mannitol have been shown to have a higher incidence of contrast induced nephropathy than those treated with saline alone (85). Various vasodilators, theophylline and aminophylline have also been investigated however to date no prophylactic agent has been identified which can consistently and significantly reduce the incidence of renal insufficiency following contrast administration in patients at risk (53, 55, 57, 83).

Various algorithms and recommendation have been published concerning the use of intravenous contrast in patients at risk for reduced renal function (35, 56, and 83). It is the responsibility of both the requesting clinician and the radiologist to be judicious when assessing a patient for a radiographic or diagnostic procedure requiring contrast material. This is particularly important in patients with preexisting renal impairment. The risks and benefits of an enhanced scan must be considered and if contrast material is deemed necessary for diagnosis or treatment then appropriate preliminary measures must be implemented to decrease the risk along with appropriate follow up measurement of renal function. Each patient must be assessed on an individual basis and a non contrast study performed if diagnostically adequate

1.6 Artifacts and Pitfalls in Spiral CT

1.6.1 *Partial Volume Averaging*

When a CT is performed the Radiologist determines the section of thickness required for a diagnostic scan taking into account the clinical presentation and diagnostic purpose of the scan. In 1 mm thick axial images for example, there is very little variation in the type of tissue included in an axial section. However, in 10 mm thick axial images a larger volume of tissue is imaged per axial cut and there is variation in the origin of the tissue within a voxel. A voxel is defined as the volume obtained from the product of pixel size and image section thickness (25). The CT number of the pixel (picture element comprising the smallest component of the digital image) is determined by the x-ray attenuation that occurs in the corresponding voxel (25). If tissues with different attenuation properties occupy the same voxel, for example blood vessels

and lung, the CT number represents the sum of different attenuation values. This is known as partial volume averaging (25). Partial volume averaging is particularly troublesome in scans that are oblique or parallel in relation to tissue boundaries. Examples include the diaphragm, the apices of the lungs and upper and lower poles of the kidneys. In the evaluation of smaller structures such as small vessels, the adrenals and bronchi partial volume averaging is also an issue. If detailed structural analysis is required for diagnosis then thin collimation is preferable. Therefore, the influence of partial volume averaging depends on the size of the structure relative to the section width and the position of the structure in relation to the scan plane (92). Structures that are oriented along the z-axis or approximately parallel to the scan plane are far more subject to partial volume averaging than structures perpendicular to the scan plane. Partial volume averaging can reduce the contrast of small pulmonary or hepatic lesions which can result in lesions being missed by the interpreting radiologist (93). In addition scans that cut through a portion of an adjacent structure can simulate lesions (94). For this reason interpretation of a single axial image in isolation is unfavorable and review of multiple slices often clarifies the finding. For example, on a single axial image the lowest part of the caudate lobe of the liver may be mistaken for a lymph node at the porta hepatis. In addition, if a tumor is detected ill defined margins due to volume averaging with adjacent structures may result in a spurious diagnosis of infiltration (95).

1.6.2 *Beam Hardening Artifact*

The photons (bundle of electromagnetic radiation that can behave like a particle and has an energy proportional to frequency) emitted from the x-ray tube of a CT scanner represent a spectrum of high and low energies (25). As the thickness of the scanned object or patient

increases, the low energy spectrum photons are absorbed more than the higher energy photons. This phenomenon is called beam hardening (25). Absorption is reduced at higher energies and increased beamed hardening artifact causes a decline in the CT numbers. The technical solution to this problem is to estimate the thickness of the object based on the x-ray absorption and mathematically correct for beam hardening based on the estimated thickness (96). One important assumption in this computer correction is that the entire object is composed of just one substance, usually water. If the local composition of the object differs markedly from that of water, such as bone, metal or concentrated contrast medium, then beam hardening artifact will continue to occur.

Beam hardening artifact is predictable on a CT scan. If both arms are left by the patient's side and in the scanning field horizontal streak artifacts will appear between the bony structures due to increased x-ray absorption and beam hardening. For this reason both arms should be placed above the patient's head. Similarly beam hardening artifact can be seen between the shoulders. Generally the denser the skeletal structures the more pronounced the artifact. Metallic objects cause significant beam hardening and can almost completely absorb the x-ray photons which results in a hyper-dense metallic implant with hyper-dense streak artifacts adjacent to it. Beam hardening artifact caused by bilateral total hip replacement can make evaluation of the pelvis quite difficult. This artifact does not generally occur with small objects such as staples due to partial volume averaging. For this reason CT is not generally useful for evaluating metallic objects.

Contrast filled structures such as vessels or the urinary bladder typically cause areas of very low attenuation to appear between the contrast filled structure and the adjacent tissue (97). If there is a particularly high concentration of contrast medium within a vessel there are often adjacent hyper dense streak artifacts. Optimal initiation of the CT scan in relation to the time of contrast injection is important to allow equilibrium of contrast with blood within the vessels. Barium within the gastrointestinal tract also results in very intense focal streak artifact. For this reason a CT examination of the abdomen should be postponed if the patient recently received barium for a diagnostic procedure and the presence of barium within the GI tract should be assessed on a preliminary scanogram.

1.6.3 *Motion Artifact*

Motion in the scanned section during one rotation of the x-ray tube will result in inconsistent projection of data because of different configurations of the scanned object in the various axial sections (97). Therefore varying degrees of motion artifact will appear throughout the reconstructed images especially in the region of the moving structures. Motion artifact occurs in predictable locations. Pulsation of the heart (98) and aorta (99,100) can cause double or multiple contours to appear on vessel and organ boundaries. When this effect occurs in the ascending aorta it can simulate an intimal flap or dissection (99). Similarly pulsations of the heart can cause streak artifacts in adjacent organs and can simulate dissection in the descending aorta (101). Vascular pulsations lead to displacement of vessels and the appearance of double contours or serration of the vessel walls. Pulmonary vascular pulsations or transmitted lung pulsation commonly occur posterior to the heart in the left lower lobe resulting in distortion.

This can mimic focal emphysema when hypodense areas appear nearby. EKG gating can to some degree suppress pulsation effects in the aorta and pulmonary vessels (98). Technological advancement with faster scanners has lead to a significant decrease in pulsation effects with newer generation CT scanners.

Insufficient breath holding can cause double contours to appear along organ boundaries which move with respiration (99). This can obscure pathology and rarely can be mistaken for true pathology. Double contours within the lung caused by rapid respiration can mimic bronchiectasis or pleural disease (102). This is particularly prominent in patients who can not hold their breath for an entire scan and take a sudden deep inspiration or start breathing towards the end of a lung CT scan. In addition, the upper border of sub diaphragmatic structures such as the upper pole of the kidneys can be distorted by respiratory motion (103).

With spiral CT scanning acceptable results can be achieved if the patient performs shallow respiration (103). Multiplanar reformations however are highly sensitive to patient motion and even small respiratory movements can cause serration of surface contours (104). Patient instruction is therefore critical in any CT scan performed in which the patient is expected to hold their breath.

1.7 Radiation Dose in CT Scanning

1.7.1 *Quantification of Radiation Dose*

Since its inception in 1973, the use of CT as a diagnostic tool has expanded rapidly. The

introduction of helical CT and more recently, multi-detector row CT has greatly increased the clinical indications. According to surveys conducted at United States medical facilities, the annual number of CT examinations performed has increased from approximately 3.6 million in 1980, to 13.3 million in 1990 and to 33 million in 1998 (105,106). Studies in the United Kingdom have shown an approximately two fold increase in the number of CT examinations performed between the late 1980's and the late 1990's (107). CT accounts for the largest proportion of the collective dose of x-rays owing to diagnostic procedures (108,109). The level of radiation dose especially in the pediatric population is of concern to radiologists, medical physicists (25), government regulators (107), and the media (110).

The quantification of ionizing radiation is a complex one (see Table 2)(25). The simplest parameter, radiation exposure is determined by measuring ionization in air caused by the x-ray beam. The measurement unit is coulombs per kilogram (c/kg). From this value one can calculate skin entrance dose, which can be relevant for certain deterministic radiation effects such as skin erythema, cataract induction and hair loss (111). The deterministic effects of radiation exposure result from cell death and occur at very high dose levels (doses greater than 0.5Grays). These effects occur in each individual who receives a sufficient dose and there is a threshold below which effects are insignificant (25).

Table 2: Methods of Quantifying Ionizing Radiation

Method	Conventional Units	International System Of Units (SI)
Radiation exposure	Roentgens (R)	coulombs per Kilogram
Absorbed Dose	rads (rad)	grays (Gy)
Equivalent dose	rems	sieverts (Sv)
Effective dose	effective dose equivalent (Sv)	sievert (Sv)

Absorbed dose is determined by measuring the energy per unit mass within an object. The measurement unit is the gray (Gy) (25). Unlike radiation exposure, the gray is dependent on the composition of the object or subject exposed to the radiation beam. However, this does not take into account the differing sensitivity of organs to radiation (112). Equivalent dose is a modification of absorbed dose which incorporates weighting factors to account for the different biological effects of various radiation sources. For x-rays, the radiation weighting factor is one and the equivalent dose has the same numerical value as the absorbed dose. (113)

The most useful and practical measurement is effective dose which estimates the whole body dose that would be required to produce the same stochastic risk as the partial- body dose that was actually delivered in a localized radiological procedure. Stochastic effects of radiation occur at lower doses (doses less than 0.5 Gy) and the severity of radiation induced damage is independent of the radiation dose (25). The radiation dose only increases the probability of the stochastic effect occurring. The existence of a threshold dose for stochastic effects is unknown and controversial. The effective dose allows us to compare radiation exposure from different

sources, such as natural background radiation. The measurement unit is the sievert (Sv) and it is calculated by summing the absorbed doses to individual organs weighted for their radiation sensitivity (114). The effective dose for chest CT can be calculated by using dose distributions for specific CT scanner geometry and beam quality (114,115). The effective dose has an inverse correlation with increasing patient weight. The values of effective dose from a chest CT scan for a 10 and 70 kg patient are 9.6 and 5.4 mSv, respectively (116)

Once the effective dose has been determined the risk estimates for stochastic effects can be produced using radiation exposure data from Japanese atomic bomb survivors. Although the stochastic effects of radiation are to some degree dependent on race and age at exposure a conservative risk estimate is 50 additional fatal cancers induced per million people of the general population exposed to 1 mSv of medical radiation (113).

1.7.2 *CT Radiation Exposure*

It is not feasible to calculate the exact effective dose for each patient examination since we cannot actually measure the absorbed dose inside a patient. However, it is possible to make a good estimate of the effective dose. Certainly, it would be useful to estimate the effective dose prior to a CT exam. To address this issue, CT scanners have incorporated data derived from measurements made in head and body phantoms (117). This is displayed as the CT dose index (CTDI) and dose length product (DLP). (See Figure 2) The CT scanner software can then be used to calculate an effective dose in a reference subject (117). CTDI takes into account the imperfect collimation of the x-ray beam and radiation scatter from adjacent scanned sections. Measurements of dose are made in the center of the phantom and close to the periphery. Due to

beam attenuation, the dose inside the phantom changes with depth and therefore a weighted CTDI is calculated. The DLP depends on the weighted DI, the pitch and the length of the CT scan. By utilizing manufacturer generated tables loaded onto the scanner software the exact DLP for a study can be calculated (117). The conversion coefficients from DLP to effective dose have been generated for different anatomic regions and radiation risk for a patient can be determined. (See Table 3) (116).

Figure 2: Algorithm for the estimation of radiation exposure from a CT scan

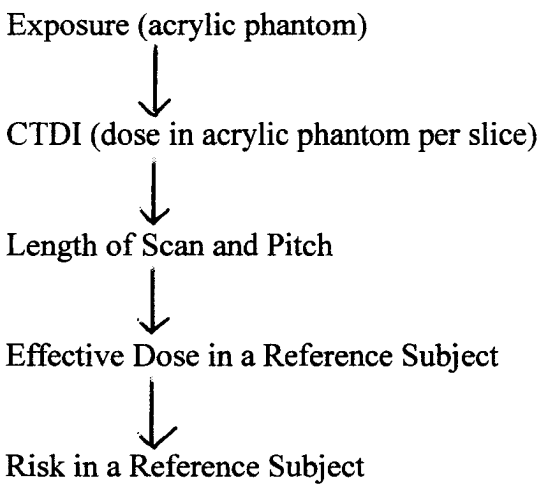


Table 3: Proposed reference dose values for routine CT examination on the basis of absorbed air

Examination	Reference Dose Value	
	CTDI w (mGy)	DLP mGyxcm)
Routine head	60	1050
Face and sinuses	35	360
Vertebral trauma	70	460
Routine chest	30	650
High resolution lung	35	280
Routine abdomen	35	780
Routine pelvis	35	570
Bony pelvis	25	520

CTDIw= weighted CT

The relative high radiation dose from CT scanning results from two properties of the technology. First, unlike analogue film radiography, the digital technology of CT enables the independent manipulation of image acquisition and display. Therefore, when the radiation dose is increased in CT the image quality improves due to decreased noise (118). Whereas, with film based imaging, increasing the radiation dose leads to over exposure and darkening of the film. Secondly, CT technology maps the entire gray scale into a preselected CT numbers scale or Hounsfield units. There is an inherent tendency to increase radiation exposure to overcome image degradation due to quantum noise and the effects of increasing radiation dose is not readily evident as with film screen technology (118). Studies assessing the subjective evaluation

of chest CT scans have demonstrated that radiologists consistently give higher image-quality scores to images obtained with a higher radiation dose (119,120).

1.7.3 *CT Scanner Radiation Efficiency*

CT scanner radiation efficiency is to some degree related to the technology of an individual manufacturer and machine. (See Table 4) (121). The shielding ability of the collimator between the patient and the detector, imperfect collimation of the x-ray beam, and movement of the true x-ray focal spot (the area of the anode within the x ray tube from which the x ray beam is produced) all contribute to wasted or non diagnostic radiation dose (25). The radiation dose is therefore increased to overcome scatter and imperfect collimation. The result of all these effects is the geometric efficiency of the CT scanner.

Table 4: Published values of CTDI from manufacturers

		Head CTDI	
Manufacturer	Model	mrad	mGy
Elscint (Rockleigh, NJ)	Twin	3200	32
GE Medical Systems (Milwaukee, Wis)	Hi Speed Advantage	4000	40
Philips Medical Systems North America (Shelton, Conn.)	Tomoscan SR	5300	53
Picker International (Cleveland, Ohio)	PQ 2000 Mark II	4200	42
Siemens Medical Systems (Iselin, NJ)	Somatom Plus 4	7300	73
Toshiba America Medical Systems (Turtin, Calif.)	Xpress SX	6600	66

Scatter radiation results from the interaction of the primary beam with the body of the patient (122). Scatter radiation exits the body in all directions and if detected it decreases contrast and generates artifacts. The extensive collimation of CT compared to plain chest radiography means 90% of detected x-rays are primary image photons compared to 50-90% with plain chest radiography. (122)

The patient dose in CT is affected by the number and spacing of adjacent sections. In CT scanners, radiation extends beyond the slice collimators or image slice because of scatter radiation, focal spot penumbra and the core beam geometry of the x-ray beam (123). Therefore, contiguous sections generate a peak radiation dose approximately 50% more than that of a single CT axial section and there is an increase in radiation dose associated with multiple adjacent CT images(124). Also the amperage is often increased to compensate for increased noise with thinner slices which leads to increased dose (119). CT studies which overlap anatomy, helical CT scans with a pitch of less than 1 or re-imaging the same region (such as unenhanced and enhanced scans) can have 2-3 time the radiation dose of non-overlapped scans (125). The radiation dose can be decreased if there are gaps between adjacent axial sections, however this comes at the expense of anatomic detail and omission of portions of anatomy. In addition, if unenhanced CT scans are performed with a high resolution technique the radiation dose can be decreased to 10% of a spiral CT with a pitch of 1. (125)

A CT examination with a pitch greater than 1 means there are gaps between the slices. This reduces the radiation dose by averaging less exposed tissue in the gaps between the CT slices with radiated tissue. A pitch of less than 1 means there is an overlap of the scanned tissue which

increases radiation dose. Exams with a pitch greater than 1 cover larger volume in shorter times, which provides either less motion artifact or thinner slices. Scans obtained with elevated pitch have lower image quality because the section profile is broadened. However, the radiation dose delivered by the exam is less by the value of the pitch (e.g. ½ the radiation exposure with a pitch of 2) if the tube voltage and current are kept constant (125). In some cases when helical CT is used to detect pulmonary embolus, it has been shown that improved image contrast can be obtained with less radiation dose by using thinner sections at pitch values of 1.5-2. (126)

Spiral CT scanners, vary in their efficiency depending on many factors including collimation and detector capability. Ideally a detector should record all incident x-ray photons. Most current detectors are solid state and can detect up to 95% of the incident x-ray beam. High pressure xenon detectors, however only detect approximately 60 %. The overall dose efficiency of CT scanner which is the product of the geometric efficiency, the quantum detection efficiency and the conversion efficiency can vary significantly between CT scanners. (127)

Noise can also vary based on scanner technology and electronics. The sum of quantum noise and electronic noise results in differences in image quality between scanners at the same radiation dose (118). CT scanners also differ in their ability to filter the x-ray beam. Filtration eliminations low-energy photons which can be preferentially absorbed relative to high energy photons and contribute to radiation dose (120).

The chest is an elliptical object and a uniform tube current at all angles around the patient leads to increased scatter. The chest has a higher attenuation from left to right than from anterior to posterior and manufacturers have introduced programs that alter tube current. Tube current modulation increases radiation dose laterally and decreases it in the thinner anterior posterior direction. This has been shown to decrease radiation exposure with minimal effect on image quality (128,129,130).

1.7.4 *Radiation Exposure and Image Quality*

The relationship between radiation exposure and image quality has been well elucidated. Generally speaking, anytime a decrease in noise is desired, the dose used to acquire the image will increase. If the tube current and scanning times are not changed, the increase in tube voltage will increase radiation dose to the patient. It is of note that the radiation exposure delivered by a given tube voltage and current setting will vary between CT scanners of different models and manufacturers because of differences in scanner geometry (x-ray tube to patient separation) and x-ray tube filtration. (See Table 4) (121).

Studies have shown that radiographers give consistently higher image quality score to images obtained with a higher radiation dose (119). There is a consistent increase in mean image quality with higher radiation exposure; however there is no significant difference in the detection of mediastinal or lung parenchymal abnormalities from 20 to 400 mAs (m) (119). The minimum dose requirement in a CT examination is determined by the acceptable amount of image noise at the required spatial resolution. Acceptable image noise in turn depends on the necessary contrast resolution, the window width that will be used, and the attenuation characteristics of the region

being scanned and the diameter of the patient. The radiation dose and image noise can be modified by adjusting the tube current, scan time and tube voltage. The dose values within a section of anatomy are determined by factors such as voltage, current, scan time, rotation angle, filtration, collimation and section thickness and spacing (118). Certainly this is a complex multifaceted balance.

Although CT is a modality with relatively high radiation dose, it has replaced many modalities with higher radiation exposure such as pulmonary angiography (131,132). CT techniques should conform to the ALARA (As Low As Reasonably Achievable) principle. As more research and understanding of the relationship between radiation exposure, image noise and diagnostic accuracy unfolds the minimum radiation dose that can provide adequate diagnostic information for clinical questions will be developed.

2.0 Scaling Responses in the Medical Sciences

2.1 Types of Responses

Responses or variables on a questionnaire can either be categorical (race or religion) or continuous (hemoglobin and blood pressure). In categorical variables, respondents choose yes or no options and therefore, the responses consist of nominal variables. Attitudes and opinions however are usually on a continuum and a categorical response ignores the continuous nature of most decision processes. This can lead to several problems:

1. The respondents may vary on what they consider a positive response.
2. Even if respondents have similar understanding of the meaning of the responses dichotomizing the variables on a questionnaire forces the respondent to make choices which do not necessarily reflect their opinion. If the respondent can only agree or disagree then the possibility that they may have an opinion between the ranges of possible choices is disregarded. This results in a loss of information and decreased reliability and validity (133).
3. By dichotomizing a continuous variable, a measurement scale becomes less efficient and more subjects will be necessary to show a statistically significant effect or trend in responses. A measurement instrument is more likely to show an effect if there are multiple choices or response levels and the outcome is measured along a continuum (133).

There is an argument that multiple response levels may introduce noise into the data, offering more responses to the subject than is necessary. If the researcher is only interested in whether

the respondent agrees or disagrees with the statement they can always create a cut off point along the continuum after the fact to categorize the responses. This ensures that no information is lost. In most instances people are capable of making finer discriminations than simply yes or no and agreeing or disagreeing.

If responses are ordered (eg.staging of breast cancer) the variables are called ordinals. In this case there is no assumption of the equality of the interval between variables. Interval variables however, assume the responses are constant (eg. temperature). If a variable has a meaningful zero point then it is considered a ratio variable, indicating the ratio between two responses has meaning (temperature in Kelvin).

The relevance of the distinction between variables is that parametric statistics can be applied to interval and ratio variables such that the data can be described in terms of mean and standard deviation. Non-parametric statistics are utilized to analyze nominal and ordinal data variables (134).

2.2 Visual Analogue Scales versus Likert Scales

There are many methods to quantify judgment. Direct estimates require the respondent to indicate their response by choosing a point on a line or checking a box, in this way giving a direct or exact measurement of their opinion. Two commonly used methods of health measurement are the Likert scale and the Visual Analogue Scale (VAS). A VAS provides the respondent with a 10 cm line with either end anchored with opposing statements or the minimal

and maximal extremes of the dimension being measured (see Figure 3) (134). For example, extremes of a line may be no pain versus worst possible pain. There are no specific choices indicated along the line. The respondents choose a point along the line which they feel accurately indicates their opinion or characteristic. This method has been used to assess a variety of issues such as mood (135,136,137,138), fatigue (139), respiration (140), functional capacity (141), tension (142) and in the classification of psychiatric patients (143). Visual analogue scales are often utilized to assess patient's responses before or after an intervention or treatment.

In 1952 Likert described a scale in which responses are placed and labeled along a continuum of agreeable to disagreeable. In 1957 Osgood et. al. demonstrated a differential scale in which various related topics are graded along a continuous 5 point scale with polar descriptors on either end (144,145) (see Figure 3)

Figure 3: Examples of visual analogue and Likert rating scales

a) Example of visual analogue scale and rating of pain

No pain _____ Intolerable Pain

b) Example of Likert scale and rating of pain

1	2	3	4	5
No Pain	Minimal pain	Moderate pain	Severe pain	Intolerable pain

Research has indicated that both Likert and VAS scales are reliable, valid and responsive (146,147,148,149). VAS is often used in applied research. It has been argued that VAS is relatively easier to use and understand and preferred by respondents (150,151,152,153). Some results indicate that a VAS seems to assess more closely what patients actually experience (154). Other studies however, question its user-friendliness and responsiveness in different settings (155). Studies have also shown that subjects often find VAS time consuming, cumbersome and difficult to interpret (148,156.) In addition, multiple visual measurements may be necessary to accurately and reliably assess an opinion or attribute. For example, pain is more accurately measured with multiple VAS measurements asking about the consequences of pain on activities of daily living (137). It has been suggested that a mark on the VAS has no real interpretable meaning and lay be less specific and have less precision that the Likert scale (147,148)

Whereas most studies find a significant correlation or no difference between ratings on VAS and Likert scales, some find significant differences between the two (150,156,157,158,159). Some studies suggest there is a correlation between the visual analog scale method and scales in which people are given specific intervals or choices labeled on a continuum. In addition, the VAS scale may be more sensitive to detect small differences than a Likert scale. Although these changes may be statistically significant they are not likely clinically significant changes (158).

Supporters of the Likert scale state that it is easier to use and understand both for the researcher and respondent and that coding and interpretation of the results are easier than VAS scales. It also takes less time than VAS scales (147,149,160). The wording of the descriptive categories in

Likert scales however, likely affects the responses and artificial categories may not be appropriate for a subjective questionnaire (148). There is also the issue of how many categories to provide. Too few may lead to loss of information and too many may lead to confusion.

It is clear that the opinions on VAS and Likert scales are contradictory. Therefore, it is the context and setting in which the scales are to be utilized which should determine which method is most appropriate. It is not that one scale is better than the other, but rather one may be more suitable for a particular context. In addition, there is no uniform method of comparing VAS and Likert scales and many of the studies vary in their approach to comparison. Some studies treat the VAS as interval or even ratio data (147,161) and therefore use parametric statistics. Others regard VAS as ordinal data (155,148,162) and use non-parametric statistics.

2.2.1 *Optimal Response Options on Likert Scales*

One of the main concerns when choosing the number of response options is the effect it will have on the scales reliability and ability to discriminate between the respondent's perceptions (163,164,166). Intuitively, one would think the more choices the better the reliability of the questionnaire; however this is not the case. Although there has been significant research, particularly in marketing and business, there is persistent disagreement on this issue (165,167)

The fewer the number of choices given it is possible more information will be lost in the questionnaire, particularly if the respondent is capable of more detailed discrimination. Studies have shown that reliability decreases as the number of choices decreases. In general, researchers agree that at least three choices should be given (167). From a statistical perspective there is no

maximal number of categories. In 1956, Miller et al demonstrated that the limit of short term memory is in the order of 7 chunks of information plus or minus 2 (168). Therefore, many have assumed the upper limit of choices on a questionnaire or rating scale should be set at 7. Certainly this would suggest that a VAS is subconsciously subdivided by the respondent into 7 categories or sections and therefore the theory of increased reliability and accuracy with a VAS may not exist. Many researchers assume that raters or respondents disregard the extreme choices in a rating scale and therefore the practical upper limit of choices should be set at 9 (169). This continues to be a topic of debate since some studies suggest no change in reliability over scales ranging from 5 to 100 points (166,167 and170) while others have found increased rater reliability and test reliability when utilizing two to six points (169) In a literature review, Cox concluded that there is no single number of points for a rating scale that is appropriate for all situations. In general, however, he suggested the use of five to eleven points (167). A meta-analysis of 131 studies in the marketing research literature found a positive relationship between internal reliability and the number of scale choice points (mean number of points 5). The number of choices explained five percent of the reliability variance (171).

With the varying opinions on how many choices a scale should have, it is important that the researcher take into account several key principles when designing their scale. First, what is the respondent's knowledge of the subject matter and how familiar are they with the issues being addressed. The more expertise a respondent has in the area of interest the better they may discriminate between narrower points on a scale. The respondent may prefer or provide more information with a 10 point scale as opposed to a 5 point scale. Secondly, what is the

homogeneity of the respondents. Finally, what should the anchors and labeling of the choices be? (see 2.2.3 Scale Format).

2.2.2 *Should a scale have a neutral point?*

When the respondent has an odd number of choices to choose from they have the option of neutrality or expressing no opinion on a scale from agree to disagree. They do this by choosing the neutral or central value option. Alternatively, an even number of choices forces the rater to make a positive or negative opinion as there is no neutral or middle of the road option. Therefore, the decision of even versus odd choices on a scale depends on the researchers intention and if he or she wishes to force the rater to make a decision (167).

2.2.3 *Scale Format*

Research indicates that when only the extremes of a scale are labeled the respondents tend to choose the extremes which can result in greater statistical variability. Also if only certain boxes or choices are labeled due to the prerogative of the investigator or due to lack of space then raters are more likely to choose those with labels. Reliability and validity can be significantly improved if all points on a scale are labeled with words that clarify the meaning of each point (172,173). In addition, the numbers used by researchers to label rate scale points can have unanticipated effects. Although such numbers are usually selected arbitrarily (eg. an 11 point scale labeled from 0 to 11 rather than -5 to 5) respondents sometimes presume that the numbers were selected to communicate a meaning of the scale points. Schwarz et al has shown that if the scale is numbered from -5 to 5 than 13% of the respondents used the lower half of the scale however when only positive numbers are used 34% use the lower half of the scale (176).

Therefore, the numeric values utilized can change the perception of the choices on the questionnaire (174,175). This suggests that either rating scale points should be labeled only with words or that the numbers should reinforce the meanings of the words when possible.

Although the responses on scales are often numbered, there is no guarantee the distance between the choices are equivalent. That is, the distance between strongly agree and agree is not necessarily equivalent to the distance between strongly disagree and disagree. However, statistics utilized to analyze this data make an inherent assumption of equivalence. Under most circumstances data from rating scales can be analyzed as if they are interval data without introducing bias unless the data is skewed (162).

3.0 Reliability

For a measurement method to be meaningful and useful it must be shown that is reliable (accurate and consistent and measures the same levels in stable subjects) and valid or measures what it intends to (177,178). The concept of reliability reflects the amount of error, both random and systematic, in any measurement in research. There is a certain amount of measurement error inherent in any study or calculation. For example; we all accept that there is a certain amount of error in measurements of weight and temperature. We are comfortable with the error of measurement if it is a relatively small fraction of the range of observations. For example, if we compare a 20 versus 100 point scale, a measurement error of +/- 3 is more significant on the 20 point scale. Researchers also calculate the ratio of variability between patients to the total variability. Zero indicates no reliability and one indicates no measurement error and perfect reliability. This can also be expressed more formally as variance (178).

Reliability = subject variability/subject variability plus measurement error.

Reliability is not necessarily related to agreement but can in fact be inversely related to agreement. For example, teachers have a tendency to rate their students as above average globally. Therefore if all students on an occasion are rated above average the agreement among the raters is perfect but the reliability of this descriptor by definition is 0. This is also relevant to the number of boxes or choices used in a questionnaire. As we decrease the number of choices on a rating scale the information value of any one observation is reduced and the reliability drops, although the agreement among observers will increase.

It makes no sense to speak of the error of measurement of a thermometer or the reliability of a thermometer without knowledge of the range of temperature being assessed. Small differences amongst objects of measurement are more difficult to detect than larger differences and the reliability coefficient recognizes this important characteristic (179). There are three sources of variability in any experiment: variance in the patients or subjects, variability in the observers, and random or unsystematic errors. These must be considered by any researcher when designing and interpreting the results of a study (180,181).

Reproducibility is the ability of a test to produce consistent results when completed under the same conditions and interpreted without knowing the first test results (189). Several factors can affect the reproducibility of a test including:

1. The patient and environment under which the test is repeated may not be the same.
2. The test may be affected by differences or variations in interpretation from person to person. This is known as inter-observer variability.
3. The test may be affected by variations or differences in interpretation by the same person at different times. This is known as intra-observer variability.

Whenever a judgment is made in the interpretation of a test including laboratory results, physical examination, and diagnostic imaging there is room for inter and intra variation. For example, two radiologists frequently interpret the same x-rays differently. This is known as inter observer variation. A radiology resident may interpret an x-ray differently in his or her first and fourth year of training. This is known as intra-observer variation. Certainly these variations do not

negate the usefulness of a test or its results, however all physicians must be constantly aware of the probability of variations in interpretation. It is necessary therefore to have criteria to determine how much variability can be tolerated.

Across all situations involving more than one respondent, it is important to estimate the degree of inter-observer variability, as this value has important implications for the validity of the study results. If two respondents cannot be shown to reliably rate a scale, then any subsequent analyses of the ratings will yield spurious results. Furthermore, the inter-rater reliability must be demonstrated for each new study, even if the study is using a rating scale which has been shown to have a high inter-observer variability in the past (179). Inter-observer variability is a property of the testing situation and not the rating scale itself. Intra-observer variability tests the validity of the rating scale

It is important to distinguish between reproducibility and accuracy. The accuracy of a test is its ability to produce results that are close to the true measure of the anatomical, physiological, physical or biochemical phenomena that it is meant to measure. Accuracy can be affected by both systematic error (trueness) and random error (precision) (182). Systematic error will cause the average measurement value, from multiple measurements of the same person or instrument, to be different from the true value. Precision relates to serial measurements of the same instrument or person and causes scatter in multiple measures (182). However, the average value is true. Therefore, random error affects the precision or reproducibility of a scale or system. An accurate test requires that it be reproducible and lack bias. The results must be free of systematic tendency to differ from a true value in either the positive or negative direction. A completely

accurate test is free of random outcomes as well as systematic errors or biases (182). A test may be extremely reproducible yet quite inaccurate, reproducing consistent results that are far from the true value.

There are two types of accuracies. First, there is experimental accuracy or the accuracy of a test when applied under careful controlled study conditions. Alternatively, there is clinical accuracy which is the accuracy of a test when applied under real everyday clinical conditions. Accuracy is a required property of a good test however it does not ensure validity which implies that the test is an appropriate measurement for the question being addressed. In other words accuracy does not ensure the usefulness of a test for diagnosis (180).

There are numerous statistical methods for computing inter and intra observer reliability. The simplest approach to assessing agreement would be to see how many exact agreements were observed in either repeat measurement by the same observer or between observers. However, one must take into account that there would certainly be some agreement between researchers and between interpretations by chance alone. Kappa statistic estimates the degree of consensus between two respondents after correcting the percent-agreement that could be expected by chance alone (181). Kappa can be used on nominal, ordinal and interval data (if there are few categories).

Some statistical methods are based on the assumption that it is not really necessary for two respondents to share common meaning of the rating scale, as long as each is consistent in classifying their responses according to his or her own definition of the scale. Correlation is the

method of analysis to use when studying the possible association between two continuous variables. These methods can be used on ordinal, interval and ratio data. The most popular statistical method is Pearson's correlation coefficient which is calculated when we want to measure the degree of association between two variables. An inherent assumption of Pearson's correlation coefficient is that the data underlying the rating scale are normally distributed. Therefore, if the data from the rating scale tend to be skewed toward one end of the distribution, this will attenuate the upper limit of the correlation coefficient that can be observed (182). Another measurement of association or correlation is Spearman's rank coefficient. The Spearman's rank coefficient provides an approximation of the Pearson correlation coefficient, calculated on the ranks of the observations. This statistic may be used if the data under investigation is not normally distributed It also requires that all cases be rated by both respondents (182)

4.0 Bias in Responding to Questionnaires

4.1 The Cognitive Process of Rating Scales

When a questionnaire is devised, one assumes honesty and due diligence from the respondent, however there are numerous factors that can influence a respondent's choice on a rating scale such that the results may not necessarily reflect reality. The issue of bias by raters when responding to a questionnaire has been extensively studied (183). The researcher who develops a scaled response system hopes that the respondents will inherently standardize the process by which they respond to each question. However the goal of the researcher and the respondent are not always concordant. The researcher's goal is to obtain accurate information on a questionnaire while the respondent's goal is to complete it as efficiently and quickly as possible, especially if the task ahead is time consuming. There has been significant research which provides insight into the cognitive processes by which respondents generate answers (184,185)

A great deal of cognitive work is required for a respondent to answer a question or choose a rating on a scale. First, they must interpret the question or in the current study interpret the meaning of the rating scale, then search their memory for relevant information or in the current study interpret the CT image, and then integrate this information into a single judgment, which must then translate into one of the alternatives on a rating scale (186,187).

Since a great deal of cognitive effort is required to generate an optimal answer to even a single question, the amount of effort required to complete a long series of ratings is substantial. If the

respondent is motivated and enthusiastic about the topic then they may be willing to perform the considerable cognitive tasks in a thorough and unbiased manner to complete the questionnaire. This is termed optimizing and although all researchers hope respondents will optimize throughout a questionnaire, this seems unrealistic (188).

4.2 Satisficing

If a respondent perceives that significant cognitive effort is required to fill out a questionnaire or that the reason for doing the questionnaire is trivial or unimportant they may shift their response strategy, as in filling the same box repeatedly in order to complete the task. This has been termed satisficing (183). In this situation the questionnaire has been filled out however the goal of the researcher and the respondent are at extremes and the results of the questionnaire do not accurately reflect the opinions or attributes of the person filling out the questionnaire.

The respondent may subconsciously select the first option in the list that seems reasonable and acceptable rather than carefully processing all possible alternatives. Respondents might also provide "safe" answers such as the neutral point of a rating scale if there are an odd number of choices. This can also be a source of bias since it is often perceived as easier to keep things as they are than suggest a significant change (183,185). An additional strategy is to select a response for the first question and then use the same response to all subsequent questions. This is especially a problem in Likert scales and visual analog scales where a person can simply check a box or draw on a line and go down the page indicating the same choice repeatedly. A method to counteract this respondent strategy is to vary the response order on the scale or have equal

number of questions which address the same issue (185,186). A scale for compliance with medication will have an equal number of questions where a true response and a negative response indicate compliance. Researchers can then compare responses to questions which are actually asking the same information worded in a different way within a scaling system. This however places further demands on the respondent and may lead to further satisficing. Some argue that this mental processing only plays a role when a person's knowledge of the area is limited and they are forced to choose an option however others feel it definitely exists to some degree in all respondents.

An extreme example of apathy is one in which the respondent simply flips a coin to make the choice rather than making a conscious decision. For example, if the question is a yes or no choice then the respondent may simply agree with every statement in the questionnaire. This is termed acquiescence bias. There is a tendency to give a positive response such as yes, true or often. The respondent may also choose a negative response such as no, never or rarely repeatedly throughout the questionnaire (189).

The likelihood that a respondent will satisfice when responding to a questionnaire or rating a scale may be a function of three factors (154):

1. The greater the task difficulty
2. The lower the respondent's ability
3. The lower the respondent's motivation to optimize

Ensuring that the task of completing the questionnaire is as simple as possible without compromising the validity or accuracy of the study prevents satisficing . The response should

take as little cognitive effort as possible, for example keeping the questionnaire limited to current opinions rather than having the respondent contemplate remote feelings or events. Also, questions should be kept as simple and straight forward as possible although the issue being investigated or treatment may be quite complex. If the respondents are interested in the area being investigated their diligence when rating a questionnaire is significantly greater (183). Similarly, people often loose interest as they perform a task. The shorter the questionnaire, the more likely interest does not wane. The questionnaire should be as short as possible without compromising content and reliability (183). The potential for fatigue becomes significant as the length a questionnaire increases or the questions become more difficult which can lead to further satisificing (190)

4.3 End Aversion or Central Tendency Bias

End aversion bias or central tendency bias is the reluctance of people to choose an extreme category (179). The respondent may subconsciously eliminate the extreme choices from the scale. The respondent on a 7 point scale therefore may eliminate the anchoring adjectives and effectively create a 5 point scale. This can decrease sensitivity and reliability. One way to avoid end aversion or central tendency bias is to not use extreme terms such as never and always as the end points but rather use almost never and almost always to anchor the scale. The issue with this approach is that there may in fact be some respondents who may prefer to choose the absolutes and are not given this option and certain data may be lost (179).

A second method of dealing with a central tendency bias is to have throw away categories at the extreme ends of a questionnaire (179). That is, if the aim is to have a 7 point scale then 9 choices are provided with the understanding that the extreme boxes will rarely be checked and primarily serve as anchors to the questionnaire. This ensures a greater likelihood that all 7 categories will be utilized and considered by the respondent. This can lead to problems with labeling. If never and always are important choices in the questionnaire then the labeling of the throw away anchor choices may be problematic.

4.4. Positive Skew

Positive skew occurs when responses are not evenly distributed but rather weighted towards the favorable end (191). This produces a ceiling effect since most of the choices are clustered at the positive extreme. It may be statistically difficult to detect differences in responses. There are two methods to counteract this phenomenon. One is to shift the average or neutral choice on a scale away from the middle. Therefore there are more options on one extreme of the scale. This allows more accurate statistical analysis and ability to detect differences. Another strategy is to offer more choices immediately above or below average in the center of the scale assuming that those choices on the extreme do not need to be as well differentiated. This type of bias is particularly evident when respondents are grading performance such as student evaluations (189,190,191).

4.5 Global Impression versus Discrimination of by Respondents

Often respondents find it difficult to evaluate a person, event or opinion over more than a few dimensions (192). That is, the respondent's global impression overshadows any specific discriminating questions addressed in the questionnaire. For example, if a radiologist is assessing the quality of a CT scan their overall impression of the CT scan may overshadow their ability to grade the more fine detail such as motion artifact or artifact related to volume averaging or contrast material. Techniques used to encourage discrimination of finer details include training the respondents, giving more options in the questionnaire and using more than one evaluator (193). Rather than simply labeling the choices on a scale, concrete examples or descriptions are given. In addition, a separate instruction sheet with details of each point on the scale may be helpful

5.0 Randomization

The reliability of the results of a study and the interpretation of the findings require the design to take several precautions to exclude and address bias. An important source of bias is the way in which subjects vary in characteristics which are not part of the design.

Clearly the best method to determine the efficacy of treatment or a diagnostic test would be to have each patient undergo both the placebo and treatment or diagnostic procedure being investigated. Each subject would become their own control, eliminating an often troublesome source of bias, that is, the way in which subjects vary in features that are not part of the design of a study. For example, a study investigating the adverse effects from an ionic and nonionic contrast material agent would have dramatically improved statistical power if every patient entered into the study had both contrast material several days apart. Many of the statistical assumptions concerning the subjects and their variability would be eliminated. The only variable would be that manipulated by the experimenters. Unfortunately, for both ethical and economical reasons in most studies the placebo and procedures or treatments can not be prescribed to every individual enrolled in the study.

The usual approach to address variation in subjects is to allocate treatments to patients at random, that is, each subject has an equal chance of being assigned to either the treatment or control group (194). Therefore, the study groups imitate the patient population under evaluation with respect to age, gender, and other unknown variables which may influence the outcome of a study (195).

All randomization methods try to eliminate allocation bias. Fixed allocations such as simple block and stratified allocation assign intervention or control to subjects with predetermined probability. The probability does not alter throughout the study. In equal allocation patients are assigned with intervention or control in a 1:1 ratio (195,196).

In 1951 Hill described a method called simple block randomization which if performed appropriately guarantees that at any point in the study there will be balance between the control and intervention groups in terms of the number and characteristics of the subjects. The number in each group will never differ more than b/2 with b equal to the size of a block (197).

Blocks of random assignment (theoretically of any size but typically 4-8 subjects) are created. Within each block an equal number of assignments are made to each of the 2 groups (treatment or control) with entirely random sequencing (182). In a block of 4 for example, 2 treatment and 2 control assignments are made. As patients are enrolled in the trial they are assigned to the next group in the sequence. This assures that the 2 groups can never be more than 2 patients out of balance. Block randomization has 3 advantages. First, it ensures that the groups are balanced in size, especially important in smaller studies. Secondly, it allows investigators to perform interim analysis of results with groups of comparable size maximizing statistical power (182).
An additional advantage of block randomization occurs if the population changes during the time frame of a study. Block randomization ensures that there are consistently comparable study groups at any point during the research (182). If for some reason there is a significant change in the population this should not have an effect on the statistical outcome of the study since the

characteristics or change would be randomly distributed between the study and placebo group.

In addition, when the means by which the patients are allocated to treatment or placebo group is established a priori, the person entering the patients into the study does not know in advance to which group a patient will be assigned. If an investigator knows the block number in a block randomization method then they can theoretically determine the allocation of the last subject entered in each block prior to the randomization of the next patient. This can create problems with the randomization process and therefore repeated blocks of two should never be utilized. This can be addressed by varying the block length in a randomized fashion (182). That is, the block length is varied using a mixture of block sizes and the blocks are randomly and blindly selected by the investigator. Large blocks are avoided since they control balance less. This would make it almost impossible to determine where a block begins and ends and difficult to predict patient allocation into the study.

The measurement of variability used in simple statistical analysis is not exactly correct if block randomization is used. Because block randomization ensures balance between groups it does improve the power of a study. If analysis assumes simple randomization then the study will have less power than it could have if an appropriate analysis for block randomization was utilized. Therefore, this analysis would tend to be conservative and is viewed by most statisticians to be acceptable (198). There are also statistical methods which incorporate the blocking used in randomization (199).

A component of any clinical trial is to avoid bias in the comparison of the study and treatment

groups and bias while the study is being run. In medical studies, the patient and the physician can be affected in the way they respond or interpret results based on their knowledge of the treatment given or allocation of the patient to a placebo group. Blinding occurs when individuals are assigned to a study group and a control group without the investigator or the subjects being aware of the group to which they are assigned (180). A study is deemed double blind when neither the patient nor the physician evaluating the patient or the diagnostic test knows which treatment was given. Whereas, if only the patient is unaware of what treatment or diagnostic procedure they have received, this is known as a single blind study.

In many areas of medicine, particularly surgery and diagnostic imaging, it is often impossible for a study to be double blind however clinical trials should use every means possible to ensure the maximum degree of blindness. In diagnostic imaging the investigation to which the patient has been assigned is often discernable to the patient, particularly if the study is comparing two different radiographic procedures (eg. ultrasound versus CT scanning for evaluation of the gallbladder). Similarly, it is evident to the radiologist what imaging modality was utilized.

II. MATERIALS AND METHODS

1. Study Approval and Consent

Prior to the initiation of this study ethics approval was granted through The Human Investigation Committee (See Appendix A). A consent form was established which outlined the purpose of the study, described a CT scan, the randomization process, and the risks related to contrast material and radiation exposure (see Appendix B).

2. Development of a rating scale

No previous study had addressed the optimal direction for CT scanning of the thorax and no standardized rating scales exist in diagnostic imaging. Following review of the literature, as discussed in the introduction, a 5 point Likert scale was developed. An odd number of choices enabled the Radiologists grading the CT scans to indicate the scan was "average" or neutral. It was felt, based on available literature, that 5 points would allow adequate discrimination between the quality of the CT images. The scale ranged from 1, indicating significant artifact, to 5, indicating no artifact.

The Likert scale was developed to assess artifact and its impact on the quality of the CT scans. We were interested in artifact secondary to motion at the lung bases and beam hardening from the superior vena cava and subclavian vein ipsilateral to the side of the contrast material injection.

The extent to which beam hardening artifact obscured adjacent structures was also assessed by evaluating the clarity of relevant vessels (hilar vessels, great vessels, and aorta) and clarity of relevant nodal stations (2R, 2L 4R 5,6,hilar lymph nodes) (see Figure 4). Clarity was graded with 1 indicating poor visualization and 5 indicating excellent visualization. The overall subjective impression of the CT scans was also graded from 1 (poor) to 5 (excellent).

Grading of motion artifact at the lung bases was based on the delineation and clarity of the pulmonary parenchyma and vessels. Grade 5 indicated excellent definition while grade 1 indicated significant blurring due to respiratory motion. Artifact from the superior vena cava and subclavian vein ipsilateral to the site of the injection was graded based on the degree of beam hardening artifact. Grade 5 indicated no artifact and grade 1 indicated severe artifact making interpretation of the adjacent structures including the lymph nodes impossible. Clarity of the hilar vessels, great vessels and aorta was based on the density and homogeneity of the vascular enhancement and clarity of vessel margins. A grade of 5 indicated excellent enhancement, well defined and clearly seen. A grade of 1 indicated no enhancement or extreme enhancement such that the vessels were obscured. Grade 5 for a nodal station indicated that a node was clearly delineated. Grade 1 indicated significant artifact from adjacent structures obscuring visualization.

Nodal stations 2R, 2L, 4R, 5, 6, and hilar nodes were assessed since these are in close proximity to vessels and are often obscured by artifact from adjacent vessels. The nodal system was anatomically divided based on the American Thoracic Society map of pulmonary mediastinal

Figure 4: Likert grading system for CHES study

CHES Study

Patient # _____ Radiologist #_____

Circle the appropriate number for each section:

ARTEFACT	Significant		Average		No Artifact
Motion	1	2	3	4	5
(at the lung bases)					
SVC	1	2	3	4	5
Subclavian vein	1	2	3	4	5
(Ipsilateral to the injection)					

CLARITY OF VASCULAR STRUCTURES

	Poor		**Average**		**Excellent**
Hilar Vessels	1	2	3	4	5
Great Vessels	1	2	3	4	5
Aorta	1	2	3	4	5

NODAL SYSTEM CLARITY

	Poor		**Average**		**Excellent**
2R	1	2	3	4	5
2L	1	2	3	4	5
4R	1	2	3	4	5
5	1	2	3	4	5
6	1	2	3	4	5
Hilar	1	2	3	4	5

OVERALL IMPRESSION

Poor		**Average**		**Excellent**
1	2	3	4	5

lymph nodes (reference 200,201,202). The radiologists were given a diagram and written definition of each nodal station (See Figure 5 and Table 5).

Figure 5: Regional lymph node stations (used with permission) (203).

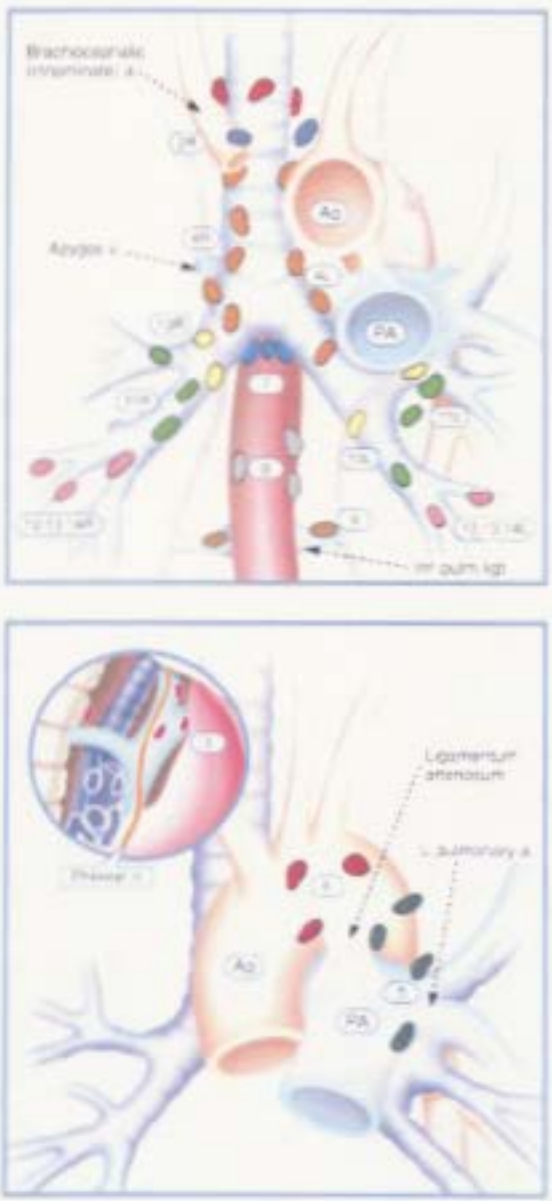


Table 5. Modified American Thoracic Society classification of regional nodal stations (201)

Nodal Station	Definition
2R	Right upper paratracheal nodes. Nodes to the right of the midline of the trachea, between the intersection of the caudal margin of the bracheocephalic artery with the trachea and the apex of the lung or above the level of the aortic arch
2L	Left upper paratracheal nodes. Nodes to the left of the midline of the trachea between the top of the aortic arch and the apex of the lung
4R	Right lower paratracheal nodes. Nodes to the right of the midline of the trachea, between the cephalic border of the azygous vein and the intersection of the caudal margin of the bracheocephalic artery with the right side of the trachea or the top of the aortic arch
5	Aortopulmonary nodes. Subaortic and Para aortic nodes, lateral to the ligamentum arteriosum or the aorta or the left pulmonary artery, proximal to the first branch of the left pulmonary artery.
6	Anterior mediastinal nodes. Nodes anterior to the ascending aorta or the innominate artery
(10R and L)	Hilar nodes. The proximal lobar nodes, distal to the mediastinal pleural reflection and the nodes adjacent to the bronchus intermeidius on the right, radiographically, the hilar shadow may be created by enlargement of both hilar and interlobar nodes

3. Inclusion and Exclusion Criteria

Between July 1998 and April 1999, 100 consecutive consenting adults, ranging in age from 21 years to 64 years (mean age 57 years) referred for clinically indicated CT scans of the chest were asked to participate in this study. The sample size was one of convenience. Exclusion criteria included:

1. There was a contra indication to receiving contrast including a documented allergy to IV contrast material or renal insufficiency. Patients were assessed by the physician obtaining consent and those felt to have little or no risk of an adverse event related to contrast material were asked to participate in the study.

2. Inability to obtain intravenous access with an 18 gauge antecubital intravenous catheter. This may be related to small or anomalous veins or previous intervention such as multiple previous intravenous access or fragile veins secondary to chemotherapy or age. Although every effort was made to cannulate the antecubital vein, in some patient's attempts were futile and unsuccessful. In this case an unenhanced CT scan was performed and if this was non-diagnostic a repeat CT scan was arranged following insertion of a central line or ultrasound guided insertion of peripheral intravenous access.

Every reasonable effort was made to obtain IV access and in many cases this required utilization of a smaller 18 gauge catheter. Many patients present to our department with intravenous access established whether peripherally or centrally. Peripheral lines although often antecubital can be

within the hand, wrist or feet. Central access may be via a femoral vein, subclavian vein or jugular vein. Inclusion into the current study required antecubital venous access with a 20 gauge catheter so that the rate at which contrast was delivered to the central vasculature and pulmonary arteries and veins was standardized. The size of the intravenous catheter and use of a jugular vein, subclavian vein, or hand or foot vein requires a change in CT protocol to compensate and ensure adequate enhancement. If the gauge of the intravenous utilized, site of venous access, contrast volume, rate and timing of the injection and the initiation of the scan along with the site of the injection are standardized then this controls for many factors which could affect the concentration of contrast and enhancement of the vasculature.

3. Intravenous contrast was not indicated for the CT scan. In many clinical settings contrast is not necessary for a diagnostic CT scan. In the absence of ancillary findings such as multiple nodules greater than 5 mm or lymphadenopathy to suggest malignancy follow up CT scans of the chest are often performed without IV contrast. Less than 1 cm pulmonary nodules are followed for 2 years without IV contrast. If stability is demonstrated over a 2 year period then they are considered benign (199). The size of a nodule and history of malignancy are also important in determining if IV contrast is necessary. In addition, in patients with a clinical history of lymphoma contrast is often used for the initial diagnostic scan but subsequent scans are generally performed without IV contrast.

4. Medically unstable, ICU or CCU patients were excluded. These patients often have medical conditions resulting in shortness of breath and many scans in these patients are performed

without a breath hold. The study protocol involved standardized instructions for a breath hold and these patients would not be capable of following the instructions.

5. The patient required a specialized protocol. CT scan protocols are prescribed based on the clinical question put forward by the attending physician. If there are concerns regarding a vascular abnormality such as dissection, a history of trauma or possible pulmonary embolus specific contrast volumes, rates of injection and delay times between the injection of contrast material and scan initiation are utilized.

4. Randomization Procedure

Once patients were recruited into the study and provided written consent (see appendix B) they were randomly allocated to either cranial to caudad or caudad to cranial CT scanning using a double blind block randomization technique (see introduction). Even numbered random blocks ranging in size from 4 to 12 CT scans, with equal number of cranial to caudad and caudad to cranial scans were computer generated. The blocks were then randomly selected and a list of 100 CT scans in either A (cranial to caudad) or B (caudad to cranial) direction created. Therefore, there were 50 CT scans performed in both directions.

5. CT Technique

CT scans were performed with a standard technique. The CT scans were performed with a single breath hold and patients were prepared for the breath hold through coached performance of a deep inspiration and expiration prior to scanning. 100 cc of ionic contrast (MD 60,

Mallinckrodt, Point Claire, PQ) or non ionic contrast (ISOVUE 300, Brachodiagnostic Canada, Mississauga, Ontario) was administered through a 20 gauge needle in either the left or right antecubital vein using a power injector with a rate of 2.5 cc per second. Patients were given MD 60 unless there was a significant risk of reaction to ionic contrast. There was a 25 second delay between injection of contrast and initiation of the scan to ensure adequate enhancement of the mediastinal vasculature (24). There is no known difference between contrast agents and the degree of vascular enhancement.

Helical CT scanning was performed with a pitch of 1.4, table movement of 10 mm per second with 7 mm axial reconstruction (Toshiba Xpress/HS1, Japan) (24). The field of view was adjusted to include the entire thorax. If images of the abdomen or pelvis were required the CT scan of the thorax was completed first as per the randomly assigned study protocol. The duration from the initiation of the scan to the final processing and printing of images was also recorded.

In many cases patients are having multiple organs investigated. This is particularly true in malignancy where metastasis disease is a concern. In liver disease an unenhanced, portal venous phase and a hepatic arterial phase CT scan are often necessary for accurate diagnosis. In addition, pancreatic tumors often require more than one phase of enhancement for characterization. If the patient required a CT scan tailored to a particular organ such as the liver or pancreas then they were excluded from the current study.

6. Image Processing

The CT scans were processed by any one of five qualified CT technologists with 12 images displayed on each sheet of film. All images were displayed on film from the lung apices to the diaphragm with both mediastinal (window length 50, window width 400) and lung windows (window length -600, window width 1200) (24).

7.0 CT Scan Interpretation and Grading

The radiologists were given a written definition of each number on the scale as it related to artifact and clarity (see Table 6). A CT image for each degree of artifact was also provided as an example. The CT scans from the first 20 patients recruited for the study were reviewed with the interpreting radiologists prior to initiation of the. The images were reviewed to ensure a consensus and understanding of the Likert scale grading and validate the Likert scale.

The CT scans were organized and numbered by an investigator not involved in the interpretation of the scans. The CT scans were numbered from 1 to 100 and all identifying information removed. The Radiologists ratings for each CT scan were recorded on a sheet of paper pre-labeled with the identification number of the radiologist and the patient. The scans were interpreted independently by a Royal College of Canada certified general radiologist with nine years experience (Radiologist 1) and a Royal College of Canada fellowship trained thoracic radiologist with two years experience (Radiologist 2). Both were blind to the direction of the CT scan and the scans were presented in a random fashion. Each CT scan was interpreted twice to

assess intra-observer agreement. The CT scans were viewed at least two weeks apart by the radiologists to prevent recall bias. Radiologists were not aware of their first interpretation at the time of the second reading. Inter-observer agreement was also measured. To limit fatigue no more than 20 CT scans were read in a 24 hour period.

Table 6: Definition of each number on Likert scale for CHES study

CHES Study

Artefact	5	no artefact
	4	minimal streak artefact not obscuring visualization of the adjacent vessels
	3	moderate artefact partially obscuring adjacent structures
	2	moderate artefact causing areas of blackening with significant obscuring of adjacent structures
	1	very severe artefact making interpretation of the adjacent structures impossible
Clarity	5	well enhanced, well defined, clearly seen
	4	enhancement either too bright or not bright enough, but still well defined and clearly seen
	3	enhancement either too bright or not bright enough with margins difficult to separate from adjacent structures (ie. Adjacent lymph nodes)
	2	poor enhancement, blending into adjacent structures
	1	no enhancement

8. Statistical Analysis

After the first 20 patients were entered into the study the Likert scale was tested for its validity by measuring inter-observer correlation (Radiologist1 compared to Radiologist 2 for the first and second reading)) and intra-observer correlations (Radiologist 1 for his first and second reading, and Radiologist 2 for his first and second reading) using the Spearman Rank Correlation coefficient. The combination of correlation (Spearman Rank Correlation) and a measure of central tendency (mean rank) between raters enabled one to detect results where the measurement of agreement (Kappa) may not be significant but the results are still of interest. If there was a trend to favor one direction of scanning over the other which was consistent among raters this is certainly of interest and can be discerned from a combination of Spearman Rank Correlation and the mean rank. For this reason the Spearman Rank Correlation coefficient was utilized instead of a weighted Kappa.

An interim analysis was performed after the first two thirds of the patients were enrolled to assess whether or not the contrast utilized affected the variables measured in the Likert scale. This was done using the Wilcoxin Rank Sum test. We compared MD 60 scaled values and Isovue scaled values for directional scanning individually and versus each other.

For statistical analysis we analyzed the individual values for each category as well as the totals. Artifact total (atot) combined the scores for artifact due to respiratory motion and beam hardening from the superior vena cava and subclavian veins. Clarity total (ctot) combines scores for the hilar vessels, great vessels and aorta. Nodal station total (NStot) combined the scores for

2R, 2L, 4R, 5, 6, and hilar nodes. In addition, we calculated a sum of the scores (a tot +c tot +ns tot). The scores for overall impression (OI) were also analyzed. The data was analyzed with the Wilcoxin Rank Sum test. Spearman Rank Correlation Coefficients were calculated to assess intra observer and inter observer correlation (182).

III. RESULTS

1.0 Study population

One hundred patients were enrolled in the study and were evenly distributed between males (49 patients) and females (51 patients). The patients ranged in age from 21 to 84 with a mean age of 57. The indications for the CT scans and patient population are listed in Table 7. 69% of the patients enrolled in the study were for investigation of a new mass, abnormal nodal enlargement noted on chest x ray or known malignancy. 25% of the patients were enrolled for investigation of a primary respiratory disease.

2.0 Validation of Questionnaire

Spearman Rank Coefficients were calculated for the first 20 patients enrolled the study. Most variables demonstrated significant intra and inter correlation within the artifact and clarity of the vessels rating. All measures for intra observer correlation were significant for the artifact and clarity of the vessels (see Tables 8 and Table9). Most measures for inter observer correlation were significant for clarity and artifact; however 2 of 16 measures failed to show significant correlation (see Table 10 and Table 11). The subclavian vein artifact showed significant correlation in reading 1 (0.823,p= 0.00)but not in reading 2 (0.359,p= 0.12) Likewise, the clarity of the hilar vessels showed significant correlation in reading 1 (0.683,p=0.001) and did not have significant correlation in reading 2 (0.413,p=0.07.)

Table 7: Indications for thoracic CT scan and study population

Indication for CT Scan	Number of Patients	# of females
Pulmonary nodule or mass	13	7
Lung Carcinoma	12	4
Breast Carcinoma	11	11
Genitourinary Carcinoma	9	3
Gastrointestinal Carcinoma	9	5
Lymphoma	9	5
Shortness of Breath	6	3
Hemoptysis	5	2
Interstitial Lung Disease	4	1
Bronchiectasis	3	1
Pneumonia	3	2
Mediastinal mass	2	1
Chest Pain	2	0
Pleural effusion	2	1
Sarcoidosis	2	2
Melanoma	2	0
Asthma	1	1
Brain tumor	1	1
Eosinophilic Granuloma	1	1
Atelectasis	1	0
Thyroid cancer	1	0
Phrenic Nerve Palsy	1	0

Table 8: Intra-observer Spearman Rank Correlation Coefficients for artifact for Radiologist 1 and Radiologist 2 (n=20). The comparative is the first and second reading .

Artifact	Radiologist	Spearman Coef.	Significance
Motion	1	0.902	0.000
	2	0.450	0.047
SVC	1	0.486	0.03
	2	0.822	0.000
Subclavian vein	1	0.729	0.000
	2	0.683	0.001
Total	1	0.696	0.001
	2	0.743	0.000

Motion= artifact at the lung bases secondary to motion
SVC= artifact from beam hardening at the SVC
Subclavian vein= artifact from beam hardening at the subclavian vein ipsilateral to the injection site
Total= motion + SVC + sobclavian vein

Table 9: Intra-observer Spearman Rank Correlation Coefficients for clarity for Radiologist 1 and Radiologist 2 (n=20). The comparative is the first and second reading .

Clarity	Radiologist	Spearman Coef.	Significance
Hilar Vessels	1	0.625	0.003
	2	0.738	0.000
Great Vessels	1	0.755	0.000
	2	0.476	0.034
Aorta	1	0.599	0.005
	2	0.713	0.000
Total	1	0.652	0.002
	2	0.694	0.001

Total= hilar vessels + great vessels+ aorta

Table 10: Inter-observer Spearman Rank Correlation Coefficients for artifact for reading 1 and reading 2 (n=20). The comparative is Radiologist 1 and Radiologist 2.

Artifact	Reading	Spearman Coef.	Significance
Motion	1	0.487	0.000
	2	0.567	0.000
SVC	1	0.733	0.000
	2	0.657	0.002
SCV	1	0.823	0.000
	2	0.359	0.12
Total	1	0.690	0.001
	2	0.679	0.001

Motion= artifact at the lung bases secondary to motion
SVC= artifact from beam hardening at the SVC
Subclavian vein= artifact from beam hardening at the subclavian vein ipsilateral to the injection site
Total= motion + SVC + sobclavian vein

Table 11: Inter-observer Spearman Rank Correlation Coefficients for clarity for reading 1 and reading 2 (n=20). The comparative is Radiologist 1 and Radiologist 2.

Clarity	Reading	Spearman Coef.	Significance
Hilar Vessels	1	0.683	0.001
	2	0.413	0.070
Great Vessels	1	0.464	0.039
	2	0.588	0.006
Aorta	1	0.759	0.000
	2	0.505	0.023
Total	1	0.732	0.000
		0.510	0.022

Total = hilar vessels + great vessels + aorta

The Correlation coefficients for the clarity of the nodal system was poor for both intra-observer and inter-observer agreement (see Table 12 and Table13). Only 2 of 6 nodal systems (2R and 4R) showed significant intra observer correlation for both radiologists. There was no significant inter-observer correlation for the clarity of any subgroup of nodal systems on both reading 1 and

reading 2. In fact, only 2 of 12 variable (2R, reading 1and 4R, reading 2) showed significant correlation.

Table 12: Intra-observer Spearman Rank Correlation Coefficients for nodal stations for Radiologist 1 and Radiologist 2 (n=20). The comparative is reading 1 and reading 2.

Clarity of NS	Radiologist	Spearman Coef.	Significance
2R	1	0.484	0.031
	2	0.524	0.018
2L	1	0.346	0.135
	2	0.283	0.227
4R	1	0.510	0.022
	2	0.867	0.000
5	1	0.325	0.162
	2	0.196	0.407
6	1	0.310	0.180
	2	0.295	0.210
Hilar	1	0.204	0.388
	2	0.566	0.009
Total	1	0.074	0.757
	2	0.616	0.004

Total = 2R + 2L + 4R + 5 + 6 + hilar nodes

Table 13: Inter-observer Spearman Rank Correlation Coefficients for the nodal stations for reading 1 and reading 2 (n=20). The comparative is Radiologist 1 and Radiologist 2.

Clarity of NS	Reading	Spearman Coef	Significance
2R	1	0.43	0.059
	2	0.353	0.126
2L	1	-0.030	0.900
	2	0.484	0.031
4R	1	0.412	0.071
	2	0.533	0.016
5	1	0.112	0.638
	2	0.416	0.068
6	1	0.410	0.070
	2	0.390	0.080
Hilar	1	0.319	0.171
	2	0.182	0.442
Total	1	0.321	0.168
	2	0.459	0.042

Total = 2R + 2L + 4R + 5 + 6 + hilar nodes

3.0 Correlation coefficients for study population

Spearman Rank coefficients were measured to assess the intra-observer correlation for the 100 patients entered into the study. Both Radiologists were consistent with their ratings of the CT scans quality for artifact, clarity of the vessels and nodal system. Radiologist 2 had stronger correlations on three of the four variables but both Radiologist 1 and Radiologist 2 were statistically significant with a $p< 0.05$. This indicates strong consistency of grading for both Radiologist 1 and Radiologist 2 (see Table14, Table 15 and Table 16). The variables which make up the total for each category were sub-analyzed and all variables showed significant intra observer correlation and all p values were less than 0.001 (see Table 17).

Table 14: Intra-observer Spearman Rank Correlation Coefficients for artifact for Radiologist 1 and Radiologist 2. The comparative is reading 1 and reading 2 (n=100).

Artifact	Radiologist	Spearman Coef.	Significance
Motion	1	0.835	0.000
	2	0.854	0.000
SVC	1	0.784	0.000
	2	0.812	0.000
SCV	1	0.833	0.000
	2	0.712	0.000
Total	1	0.786	0.000
	2	0.821	0.000

Motion = artifact at the lung bases secondary to motion
SVC = artifact from beam hardening at the SVC
Subclavian vein = artifact from beam hardening at the subclavian vein ipsilateral to the injection site
Total = motion + SVC + subclavian vein

Table 15: Intra-observer Spearman Rank Correlation Coefficients for clarity of the vessels for Radiologist 1 and Radiologist 2. The comparative is reading 1 and reading 2 (n=100).

Clarity	Radiologist	Spearman Coef.	Significance
Hilar Vessels	1	0.786	0.000
	2	0.793	0.000
Great Vessels	1	0.791	0.000
	2	0.676	0.000
Aorta	1	0.826	0.000
	2	0.773	0.000
Total	1	0.847	0.000
	2	0.786	0.000

Total = hilar vessels + great vessels + aorta

Table 16: Intra-observer Spearman Rank Correlation Coefficients for the nodal stations for Radiologist 1 and Radiologist 2. The comparative is reading 1 and reading 2(n=100).

Clarity of NS	Radiologist	Spearman Coef	Significance
2R	1	0.675	0.000
	2	0.755	0.000
2L	1	0.670	0.000
	2	0.682	0.000
4R	1	0.616	0.000
	2	0.838	0.000
5	1	0.842	0.000
	2	0.537	0.000
6	1	0.904	0.000
	2	0.842	0.000
Hilar	1	0.771	0.000
	2	0.712	0.000
Total	1	0.706	0.000
	2	0.792	0.000

Total = 2R + 2L + 4R + 5 + 6 + hilar

Table 17: Intra-observer Spearman Rank Correlation Coefficients for total ratings for Radiologist 1 and Radiologist 2. The comparative is reading 1 and reading 2(n=100).

Variable	**Radiologist 1**	**Radiologist2**
Artifact	.786*	.821*
Clarity	.847*	.786*
Nodal System	.706*	.792*
Overall Impression	.644*	.826*

Artifact = Motion + Superior Vena Cava + Subclavian Vein
Clarity = Hilar Vessels + Great Vessels + Aorta
Nodal Stations = 2R + 2L + 4R + 5 + 6 + Hilar Nodes

Spearman Rank Coefficients were measured to assess the inter-observer correlation. Both Radiologists 1 and 2 demonstrated statistically significant agreement with each other in their grading of the CT scan quality in terms of artifact, clarity of the vessels and nodal system and overall impression with $p<0.05$ (see Table 18, Table 19 and Table 20) There was stronger correlation for all variables on the first reading however both the first and second readings demonstrated statistically significant agreement. The agreement was weakest for the nodal system on both the first and second reading, however there was still statistical significant correlation within the nodal system. A more detailed analysis demonstrated statistical significant correlations for all the variables which make up the totals for each category (artifact , vessel clarity and nodal system clarity) with the exception of the first reading from nodal system 6 (0.102 p=0.211) (see Table 21)

Table 18: Inter-observer Spearman Rank Correlation Coefficients for artifact for reading 1 and reading 2. The comparative is Radiologist 1 and Radiologist 2 (n=100).

Artifact	Reading	Spearman Coef.	Significance
Motion	1	0.625	0.000
	2	0.589	0.000
SVC	1	0.641	0.000
	2	0.664	0.000
SCV	1	0.625	0.000
	2	0.4610	0.000
Total	1	0.694	0.000
	2	0.622	0.000

Motion= artifact at the lung bases secondary to motion
SVC= artifact from beam hardening at the SVC
Subclavian vein= artifact from beam hardening at the subclavian vein ipsilateral to the injection site
Total= motion + SVC + sobclavian vein

Table 19: Inter-observer Spearman Rank Correlation Coefficients for clarity of the vessels for reading 1 and reading 2. The comparative is Radiologist 1 and Radiologist 2 (n=100).

Clarity	Reading	Spearman Coef.	Significance
Hilar Vessels	1	0.720	0.000
	2	0.793	0.000
Great Vessels	1	0.387	0.000
	2	0.428	0.000
Aorta	1	0.588	0.000
	2	0.492	0.000
Total	1	0.640	0.000
	2	0.574	0.000

Total = hilar vessels + great vessels + aorta

Table 20: Inter-observer Spearman Rank Correlation Coefficients correlation for nodal stations for reading 1 and reading 2. The comparative is Radiologist 1 and Radiologist 2 (n=100).

Clarity of NS	Reading	Spearman Coef	Significance
2R	1	0.517	0.000
	2	0.479	0.000
2L	1	0.213	0.033
	2	0.229	0.022
4R	1	0.578	0.000
	2	0.515	0.000
5	1	0.469	0.000
	2	0.233	0.020
6	1	0.102	0.211
	2	0.205	0.045
Hilar	1	0.500	0.000
	2	0.580	0.000
Total	1	0.395	0.000
	2	0.236	0.000

Total = 2R + 2L + 4R + 5 + 6 + hilar

Table 21: Inter observer Spearman Rank Correlation Coefficients for total ratings for reading 1 and reading 2. The comparative is Radiologist 1 and Radiologist 2 (n=100).

Variable	**Reading 1**	**Reading 2**
Artifact	.694*	.622*
Clarity	.640*	.574*
Nodal System	.395*	.236*
Overall Impression	.615*	.580*

Artifact = Motion + Superior Vena Cava + Subclavian Vein
Clarity = Hilar Vessels + Great Vessels + Aorta
Nodal Stations = 2R + 2L + 4R + 5 + 6 + Hilar Nodes

4.0 Wilcoxin Rank Sum

The Wilcoxin Rank Sum was calculated for motion artifact at the lung bases, artifact related to beam hardening in the superior vena cava and subclavian vein, clarity of the hilar and great vessels and aorta, clarity of the nodal stations and overall impression. The results are tabulated in Tables 22, Table 23 and Table 24. In addition, the total of the artifact, clarity of vessels and nodal stations along with a sum total were tabulated and statistically analyzed using Wilcoxin Rank Sum. The results are tabulated in Table 25.

Table 22 : Wilcoxin Rank Sum results for artifact related to motion at the lung bases, beam hardening from the superior vena cava and subclavian veins comparing directional CT scanning for cranial to caudad (down) (n=50) and caudad to cranial(up) (n=50) CT scans.

Atrifact	Direction	R1r1		R1r2		R2r1		R2r2	
		Mean	Total	Mean	Total	Mean	Total	Mean	Total
Motion	Down	46.95	2347	46.27	2313	47.84	2392	46.33	2316
	Up	54.05	2702	**54.73**	**2736**	53.16	2658	54.67	2733
	p-Value	0.116		**0.016**		0.197		0.054	
SVC	Down	42.58	2129	42.17	2108	39.64	1982	40.90	2045
	Up	**58.42**	**2921**	**58.83**	**2941**	**61.36**	**3068**	**60.10**	**3005**
	p-Value	**0.004**		**0.002**		**0.000**		**0.000**	
Subclavian vein	Down	40.87	2043	42.70	2135	36.72	1836	39.11	1955
	Up	**60.13**	**3006**	**58.30**	**2915**	**64.28**	**3214**	**61.89**	**3094**
	p-Value	**0.001**		**0.005**		**0.000**		**0.000**	
Total	Down	40.89	2044	41.84	2092	35.86	1793	37.32	1866
	Up	**60.11**	**3005**	**59.16**	**2958**	**65.14**	**3257**	**63.68**	**3184**
	p-Value	**0.001**		**0.003**		**0.000**		**0.000**	

Motion= artifact at the lung bases secondary to motion
SVC= artifact from beam hardening at the SVC
Subclavian vein= artifact from beam hardening at the subclavian vein ipsilateral to the injection site
Total= motion + SVC + sobclavian vein
R1r1 = Radiologist 1 reading 1 R1r2 = Radiologist 1 reading 2
R2r1 = Radiologist 2 reading 1 R2r2 = Radiologist 2 reading 2

Table 23: Wilcoxin Rank Sum results for clarity of the hilar vessels, great vessels, and aorta comparing directional CT scanning for cranial to caudad (down) (n=50) and caudad to cranial (up) (n=50) CT scans

Clarity	Direction	R1r1		R1r2		R2r1		R2r2	
		Mean	Total	Mean	Total	Mean	Total	Mean	Total
Hilar	Down	45.34	2267	46.39	2319	46.11	23.05	44.04	2202
	Up	55.66	2783	54.61	2730	54.89	2744	**56.96**	**2848**
	p-Value	0.064		0.1326		0.111		**0.017**	
Great Vessels	Down	47.96	2398	44.52	2226	43.65	2182	39.36	1968
	Up	53.04	2652	**56.48**	**2824**	**57.35**	**2867**	**61.64**	**3082**
	p-Value	0.359		**0.030**		**0.011**		**0.000**	
Aorta	Down	46.13	2306	45.42	2271	39.43	1971	38.97	1948
	Up	54.87	2743	55.58	2779	**62.57**	**3078**	**62.03**	**3101**
	p-Value	0.109		0.062		**0.000**		**0.000**	
Total	Down	46.03	2301	45.06	2253	39.56	1978	38.13	1906
	Up	54.97	2748	55.94	2797	**61.44**	**3072**	**62.87**	**3143**
	p-Value	0.120		0.057		**0.000**		**0.000**	

Total = hilar + great vessels + aorta

R1r1 = Radiologist 1 reading 1 R1r2 = Radiologist 1 reading 2

R2r1 = Radiologist 2 reading 1 R2r2 = Radiologist 2 reading 2

Table 24: Wilcoxin Rank Sum results for visualization of nodal stations 2R, 2L, 4R, 5,6, and hilar lymph nodes comparing directional CT scanning of cranial to caudad (down) (n=50) and caudad to cranial (up) (n=50)

Nodal Clarity	Direction	R1r1		R1r2		R2r1		R2r2	
		Mean	Total	Mean	Total	Mean	Total	Mean	Total
2R	Down	40.53	2026	43.88	2194	37.21	1860	35.75	1787
	Up	**60.47**	**3023**	**57.12**	**2856**	**63.79**	**3189**	**65.25**	**3262**
	p-Value	**0.000**		**0.015**		**0.000**		**0.000**	
2L	Down	42.41	2120	48.39	2419	41.78	2089	42.62	2131
	Up	**58.59**	**2929**	52.61	2630	**59.22**	**2961**	**58.38**	**2919**
	p-Value	**0.003**		0.424		**0.001**		**0.002**	
4R	Down	43.00	2150	41.78	2089	35.84	1792	37.70	1885
	Up	**58.00**	**2900**	**59.22**	**2961**	**65.16**	**3258**	**6303**	**1665**
	p-Value	**0.007**		**0.001**		**0.000**		**0.000**	
5	Down	49.10	2455	50.31	2515	46.91	2345	48.17	2408
	Up	51.90	2595	50.69	2534	54.09	2704	52.83	2641
	p-Value	0.586		.0940		0.091		0.195	
6	Down	49.27	2463	50.56	2528	50.00	2500	50.50	2525
	Up	51.73	2586	50.44	2522	51.00	2550	50.50	2525
	p-Value	0.626		0.981		0..317		1.0	
Hilar	Down	48.52	2426	45.10	2255	45.66	2283	44.01	2200
	Up	52.48	2624	**55.90**	**2795**	55.34	2767	56.99	2849
	p-Value	0.465		**0.039**		0.074		0.13	
Total	Down	41.04	2052	44.06	2203	36.38	1819	36.03	1801
	Up	**59.96**	**2998**	**56.94**	**2847**	**64.62**	**3231**	**64.97**	**3248**
	p-Value	**0.001**		**0.023**		**0.000**		**0.000**	

Total = 2R + 2L + 4R + 5 + 6 + hilar

R1r1 = Radiologist 1 reading 1 R1r2 = Radiologist 1 reading 2

R2r1 = Radiologist 2 reading 1 R2r2 = Radiologist 2 reading 2

Table 25: Wilcoxin Rank Sum results for total values comparing directional CT scanning for cranial to caudad (down) (n=50) and caudad to cranial (up) (n=50) CT scans

		R1r1		R1r2		R2r1		R2r2	
Parameter	Direction	Mean Rank	Sum Rank	Mean Rank	Sum Rank	Mean Rank	Sum Rank	Mean Rank	Sum Rank
Tot Artifact	Up	**60.11t**	3005	**59.16i**	2958	**65.14t**	3257	**63.68t**	3184
	Down	40.89	2044	41.84	2992	35.86	2305	37.32	1866
Tot Clarity	Up	54.97	2748	55.94	2797	**61.44t**	3072	**62.87t**	3143
	Down	46.03	2301	45.06	2253	39.56	1978	31.83	1906
Tot Nodal System	Up	**59.96t**	2998	**56.94***	2847	**64.62t**	3231	**64.97t**	3248
	Down	41.04	2052	44.06	2203	36.38	1819	36.03	1801
Overall	Up	**58.36i**	29.18	**58.16t**	2908	**64.08t**	3204	**65.98t**	3299
	Down	42.64	2132	42.84	2142	36.92	1846	35.02	1751
Sum	Up	**60.39t**	3019	**58.72i**	2936	**65.44t**	3272	**65.99t**	3299
	Down	40.61	2030	42.28	2114	35.56	1778	35.01	1750

* =p<0.05, I =p <0.011, t =p<0.001 (caudad to cranial rated significantly higher than cranial to caudad)
Tot Artifact = Motion + Superior Vena Cava + Subclavian Vein
Tot Clarity = Hilar Vessels + Great Vessels + Aorta
Tot Nodal Stations = 2R + 2L + 4R + 5 + 6 + Hilar Nodes
Sum = Atot + Ctot + NStot
R1r1 = Radiologist 1 reading 1 R1r2 = Radiologist 1 reading 2
R2r1 = Radiologist 2 reading 1 R2r2 = Radiologist 2 reading 2

Artifact was assessed by motion at the lung bases, beam hardening at the superior vena cava and subclavian vein ipsilateral to the injection of contrast material. Motion artifact, contrary to our initial hypothesis was not significantly better in scanning caudad to cranial versus cranial to caudad. In only one of four readings by the two Radiologists was there any significant difference in motion artifact. Radiologist 1 graded the artifact from motion significantly less in his second reading with p=0.016 . However, the mean rank for motion artifact tended to favor less artifact in the caudad to cranial scanning direction.

Clarity was assessed based on the enhancement and definition of hilar vessels, the great vessels and aorta. Radiologist 1 consistently rated caudad to cranial higher than cranial to caudad however this only reached statistical significance when he graded the clarity of the great vessels on his second reading with p= 0.030. Radiologist 2 consistently rated caudad to cranial better than cranial to caudad on both his first and second readings. All comparisons reached statistical significance with the exception of the clarity of the hilar vessels on his first reading (p=0.111). Radiologist 2 on both his first and second reading rated caudad to cranial scanning significantly better for total clarity. Radiologist 1 tended to rank the clarity of caudad to cranial scans better than cranial to caudad in both his first and second reading however this did not reach statistical significanc. The sum of all these variables was also significantly better for caudad to cranial scanning.

The visualization and clarity of nodal stations 2R, 2L, 4R, 5, 6 and the hilar lymph nodes was assessed. Radiologist 1 and Radiologist 2 ranked nodal stations 2R, 2L and 4R better on the caudad to cranial CT scans, with the exception of Radiologist 1 on his second reading of nodal station 2 L (p=0.424). Both radiologists could not differentiate caudad to cranial versus cranial to caudad scanning for quality of lymph node systems 5, 6 and hilar lymph nodes. However, radiologist 1 did discriminate hilar lymph nodes as being better imaged on caudad to cranial scanning in his second reading

In all mean ranks, Radiologists 2 consistently had high ratings in all comparisons compared with Radiologist 1 for caudad to cranial scans. Similarly, Radiologist 2 had consistently lower mean ratings for cranial to caudad scanning compared with Radiologist 1. There was no statistical

difference between Radiologist 1 and Radiologist 2 in their rating of CT scans in the same direction though there is certainly a trend for Radiologist 2 to score cranial to caudad higher and caudad to cranial lower than Radiologist 1. Both radiologists rated caudad to cranial scanning significantly better for total artifact, nodal system ranking and, overall impression on all readings.

5.0 Processing Time

The processing time for caudad to cranial CT scanning was longer than that for cranial to caudad. Images had to be reformatted and presented from apex to base on film to maintain the blinding effect for the radiologists. In addition, this is the standard direction of image presentation for interpretation. The average time to complete a cranial to caudad CT scan from initiation of the scan to film printing was 9 minutes compared to 11.5 minutes for caudad to cranial. The average time to complete a cranial to caudad scan of the chest followed by an abdomen was 13 minutes, compared to 15.5 minutes for a caudad to cranial CT scan of the chest followed by an abdominal CT. In order to complete an abdominal or pelvic CT scan after a caudad to cranial thoracic CT scan the patient had to be re-positioned within the gantry. When a patient was randomized to the cranial to caudad protocol the CT scan could be performed from the lung apex to the pelvis in a continuous fashion without re-positioning the patient. This accounts for the increased time it takes to complete a caudad to cranial scan followed by a CT scan of the abdomen or pelvis.

IV. DISCUSSION

The purpose of this study was to compare the quality of CT images of the chest with different scanning directions. The results clearly demonstrate that caudad to cranial CT scans are superior to cranial to caudad CT scans. Caudad to cranial CT scans have less motion at the lung bases and beam hardening artifact within the SVC and subclavian veins. They also have better clarity of the vasculature. Overall, caudad to cranial CT scans were subjectively better than cranial to caudad CT scans. In medical centers with spiral CT technology the caudad to cranial protocol would provide significantly better quality images. This in turn may improve the diagnostic utility of the images and the ability of the radiologist to interpret the CT scan and detect subtle abnormalities. In addition, better images may decrease the fatigue of the radiologists.

This is the first such study to objectively assess the impact directional scanning has on the quality of images of the thorax. As such, a 5 point Likert scale was developed, validated and then used to compare artifact and the clarity of the great vessels and nodal systems. The scores from individual comparisons were added to give a total score for each of the above.

Because no previous validated scaling system existed for grading of CT images within Diagnostic Imaging, it was essential to validate the scale used in this study. An extensive literature review (medical, psychological and business literature) comparing the types of scales, the advantage and disadvantages of each, and the optimal number of scaling points was performed (see introduction). This review suggested that our study would benefit from an odd number Likert scale. A five point Likert scale was chosen. This allowed the interpreters of the

images to suggest that a scan was average and because of their expertise in radiology, it was felt that the radiologists would not be subject to a central tendency bias. The use of our Likert scale also allowed for simplified data entry compared with VAS.

Our Likert scale was felt to be reliable based on the significant correlation found for both intra and inter-observer ratings. We analyzed the correlations with a Spearman rank coefficient and found that the three subgroups of artifact and clarity of the vessels were significantly correlated for both the first 20 patients and the final 100 patients enrolled in this study. However, we did not have consistent intra or inter-observer correlation for the clarity of subgroups of lymph nodes. Only 2 subgroups of lymph nodes showed significant intra-observer correlation while neither subgroup of lymph nodes showed significant inter-observer correlation on either the first and second readings by the study participants.

There are several possibilities why we demonstrated strong intra and inter-observer correlation for artifact and clarity of the great vessels but not for the clarity of the nodal system. Images for artifact and clarity of the great vessels were all examining significant structures in the thorax such as the pulmonary parenchyma, subclavian vein, superior vena cava and the aorta, whereas the clarity of the lymph node system was examining anatomy which is much smaller and subject to interpretation. The enhanced subclavian vein is easy to visualize but groups of lymph nodes are generally less than one cm in size unless pathologically enlarged. Therefore the radiologist needs to first find the nodal group of interest and then grade them. This can sometimes be a frustrating endeavor and although it was hoped that careful diligence is always applied in any research project, these ratings may have been tedious and fatigue may have accounted for the

lack of correlation. The correlations may have been stronger if a third party had cited the image number on the CT scan to be graded. Finally, there may not have been enough power with a sample size of only 20 to detect the agreement in the interpretation of the images.

Based on the good intra and inter-observer correlations for artifact and clarity of the great vessels, the study proceeded to enroll the targeted 100 patients. The intra and inter-observer correlations for the final 100 patients enrolled was stronger than the first 20 patients. In fact, there was only a single non-significant correlation between radiologists on the first reading of nodal station 6. This further validates our Likert scale.

The results for the statistical analysis of artifact were most interesting. It has always been assumed that beginning a CT scan at the diaphragm would provide less motion artifact than beginning at the apices. However, this analysis did not consistently show a statistical benefit for the reduction of motion artifact based on the caudad to cranial scanning direction. Only radiologist one on his second reading suggested that motion artifact was significantly reduced with this direction of scanning. All four readings favored less motion artifact with the scan beginning at the diaphragm with higher mean ranks not reaching statistical significance. This result is most likely due to the lack of power and the sample size. This study excluded sicker patients from being enrolled and because of this most patients were likely able to cooperate with the breath hold instructions. Artifact would therefore be reduced with cranial to caudad scanning. In addition, the use of a high speed spiral CT scanner in the study likely contributed to less motion artifact compared to older generation CT scanners.

Beam hardening artifact was significantly reduced with caudad to cranial scanning compared to cranial to caudad at both the subclavian vein and at the superior vena cava. The delay in the CT gantry reaching these large veins in the caudad to cranial direction allowed for more dilution and distribution of IV contrast. Unfortunately, this study did not assess whether or not the reduction in artifact allowed for better interpretation of images in the upper chest or whether the lung parenchyma or mediastinum was better visualized. However, this is the inference that would be made and the assumption that we set to prove at the onset of this study.

There was a significant improvement in clarity of all the great vessels with scanning in the caudad to cranial direction compared to cranial to caudad for Radiologist 2 but not so for Radiologist 1. Radiologist 1 tended to favor caudad to cranial scanning as all mean ranks were higher for this direction. The delay in scanning allows for venous distribution of contrast and time for a greater amount of contrast to enter the arterial circulation as well. It is difficult to be certain why Radiologist 2 clearly differentiated between caudad to cranial and cranial to caudad scanning while Radiologist 1 did not. Because of the trend to favor scanning beginning at the diaphragm, it may simply be an issue of power and 50 more patients may have been provided enough power to differentiate scanning directions. One Radiologist was a general Radiologist with 9 years in practice while the second Radiologist was fellowship trained in thoracic radiology with 2 years in practice. Radiologist 2 may have acquired certain skills in his fellowship training which made him better able to appreciate subtle differences in the CT scans resulting in better discrimination between caudad to cranial and cranial to caudad images. Radiologist 2 also tended to score at the upper and lower limits of the rating scale than did Radiologist 1. This differential rating may be due to bias, either central tendency of Radiologist

1 or Radiologist 2 trying to unblind the study by predicting direction of the scans and rating caudad to cranial higher than cranial to caudad. The differences in the mean ranks for all but 1 of 6 comparisons were quite large by radiologist 2. If Radiologist 2 were trying to favor the caudad to cranial scanning direction, one would have expected the same differentiation within the clarity of the hilar vessels which did not show a significant difference. Therefore, the more likely explanation for the difference between the interpretations of clarity of the vessels is lack of power, central tendency bias of Radiologist 1 and perhaps subtle differences in the "eye of the radiologist".

This study set out to measure the quality of CT scans through assessment of artifact (beam hardening and motion) and clarity. Beam hardening results from a high concentration of contrast material in vessels. A high concentration of contrast within a vessel also affects the visualization of the vessel wall and lumen. A vessel will bland into adjacent structures if it is not enhanced well. Alternatively, it a vessel contains a high concentration of contrast then there is significant beam hardening artifact and the lumen is obscured. Therefore, optimal contrast enhancement is important and particularity important for the assessment of lumen abnormalities such as pulmonary embolus and angiosarcomas.

The assessment of the clarity of the nodal system resulted in both radiologists interpreting images of caudad to cranial scanning statistically better than cranial to caudad for lymph nodes in the upper chest (2R, 2L and 4R). Although Radiologist 1 did not grade NS2L statistically significantly better on the second reading but not for the lower chest (5 and 6) and hilar nodes. This may be accounted for by the proximity of the lymph nodes to relevant vessels. 2R, 2L, and

4R are more superior in the mediastinum and may be more susceptible to beam hardening artifact from the adjacent subclavian vein, superior vena cava and great vessels. 5 and 6 hilar nodes are more inferior in the mediastinum and less affected by affected by beam hardening due to their location. In addition, lymph nodes more superior in the mediastinum may be more susceptible to motion with respiration. Therefore, caudad to cranial scanning may improve their delineation compared to cranial to caudad scanning. Lymph nodes 5, 6 and hilar nodes may be more anatomically stationary and therefore, not susceptible to movement from patient respiration. This study utilized a standard protocol with a pitch of 1.4, table movement of 10mm per second and 7mm axial reconstruction. Perhaps if we had utilized thinner collimation or a higher pitch the lymph nodes would have been better delineated. However, based on our study results the direction of a CT scan of the thorax has no impact on the clarity of lymph node stations 5 and 6 or hilar lymph nodes.

When the ratings are totaled for each category on the Likert scale the results indicate that scanning the thorax from caudad to cranial has less artifact related to beam hardening from the superior vena cava and subclavian veins secondary to concentrated intravenous contrast compared to cranial to caudad imaging. This is true for both radiologist 1 and Radiologist 2 on their first and second reading. For radiologist 2 on his first and second interpretation of the CT scans this reached a clinical significance of $P< 0.001$. For radiologist 1 on his second reading this reached a significance of $P<0.01$. On his first reading this reached a significance of $P<.001$. Radiologist 2 on both his first and second reading consistently rated clarity of the vascular structures including the hilar vessels, great vessels and aorta significantly better than caudad to cranial imaging ($P<0.001$). Radiologist 1 tended to rank the clarity of caudad to cranial scans

better than cranial to caudad scans in both his first and second reading however this did not reach statistical significance. Both radiologist 1 and 2 ranked caudad to cranial CT scans superior clarity of the nodal system. This reached a significance of $P<0.001$ for radiologist 1 on his first reading and $P<0.05$ on his second reading. For Radiologist 2 this reached significance of $P<0.001$ on both his first and second reading. For overall impression radiologist 2 on his first and second reading and Radiologist 1 on his second reading indicated significantly better images with caudad to cranial scanning ($P<0.001$). Radiologist 1 on his first reading was not quite as strong with $P<0.01$.

Prior to the initiation of this study both Radiologist 1 and Radiologist 2 underwent training sessions on grading the CT scans. The initial 20 patients enrolled in the study were used for this procedure. The questionnaire was reviewed for each of the 20 patients with very specific definitions given for each choice on the questionnaire. In addition, written definitions were given for each choice on the questionnaire and a diagram of the nodal systems being investigated supplied. These were readily available for reference to the radiologists during the entire length of the study. Although this does control for differences in how the radiologists interpret the questionnaire a certain amount of individual interpretation is inevitable. This may also account for radiologist 1 not reaching statistical significance in his first or second reading for total clarity. He may have misinterpreted the definition for the choices on the questionnaire. Alternatively, he may have understood the choices but chose to use his own inherent method of assessing the vascular structure.

The study is strengthened by it's randomized double block design.. The randomization list was compiled using a variable block size method. Any one of 6 radiologists or 12 residents who were available could obtain consent but they were unaware of the scanning direction until consent was obtained. Based on the number of people involved in this portion of the study it would be extremely difficult for one individual to predict the next allocation on the randomized list and subconsciously bias the patients consent.

Artifacts, whether due to motion or beam hardening from prosthesis or intravenous contrast can seriously degrade the quality of CT images, often to the point of making them diagnostically unusable. In order to optimize image quality, it is necessary to understand why and how artifacts occur and how they can be prevented. CT artifacts can include physics based artifacts, those related to the acquisition of the CT data and patient based artifacts related to movement or the presence of metallic prosthesis. There are numerous methods for decreasing or dampening artifacts. Some artifacts can be diminished by manipulation of the CT data and use of scanner software. However, in many instances appropriate preparation of the patient, patient positioning and selection of appropriate scan parameters are paramount.

Detectors can be calibrated and compensate for beam hardening effects of different parts of the patients body. However patients come in varying sizes and shapes and the phantoms can not fully mimic the human body. The avoidance of beam hardening artifact is to some degree operator dependant. The CT technologist must select the appropriate field of view, ensure the scanner uses the correct calibration and beam hardening algorithm and appropriate filters. It is important that patients are asked to remove metal objects such as jewelry prior to a scan.

Permanent items such as prosthesis and surgical clips can be avoided during the scan in some cases by using gantry angulation to exclude the metal inserts from scans of nearby anatomy. If it is impossible to avoid a metallic object then techniques such as adjusting kilo voltage or using thinner axial slices can be utilized to reduce beam hardening artifact.

Steps can be taken to prevent voluntary motion during a CT scan however involuntary motion is unavoidable. The rapid motion of the heart can lead to severe artifact on images of the heart, adjacent lung, and vascular structures. This can be dampened by combining EKG gating techniques with special methods of image reconstruction.

There are operator dependant means of avoiding voluntary motion artifact. Usually the use of positioning aids and patient comfort is sufficient to prevent voluntary movement. In some cases however such as the pediatric population or patients in severe pain sedation may be necessary to immobilize the patient. In addition using as short a scan time as possible minimizes artifact and respiratory motion.

Human variability may have played a minor role in the outcome of this study. There were five CT technologists performing the scans. The CT technologist was instructed in which direction the scan should be performed. The CT technologist would then discuss the breath hold with the patient, position the patients arms above their head, set up the intravenous contrast for injection and perform the CT scan, including establish the scan parameters. The instructions for breath hold during the CT scans were pre-recorded and automated. The study protocol was well

established with the CT technologists prior to initiation of the study. Therefore, this is unlikely a source of bias within the study.

At the time of this study our institution operated a Toshiba Xpress-HSI 1 Helical which is capable of cardiac gating however this was not utilized during the study. Every attempt was made to control for patient voluntary and involuntary motion and other artifact sources during this study, however some technologists may have been more diligent or astute than others. Although the CT technologists had similar capabilities and training certainly some may have been better at positioning the patients or instructing the patients than others. This may have lead to variability with the quality of the CT scans. If only one CT technologist performed all the scans this would control for this variable, however within our busy and productive radiology department this was not realistic.

Another source of bias and perhaps a more important one would be the radiologist interpreting the scan. Although both radiologists were blind to the direction of the scan at the time of interpretation they were aware of the purpose of this study. At the time of this study all CT scans were printed on film for interpretation. Every attempt was made to ensure the presentation of the CT scans on film, regardless of the direction of the scan, was consistent. Therefore all CT scans were printed apex to base and patient information omitted. The scans were also randomly presented to the radiologist in a controlled setting with only 20 CT scans read per sitting and no more than 20 CT scans read within a 24 hour period. Any identifying information or factors which may have indicated the direction of the scans were omitted from the film. Assessment or interpretation of CT scans however is subjective. Although a controlled setting was used,

knowing the direction of the scan may have affected ones perception of the images. If in fact radiologist 2 was better able to appreciate subtle differences in the scans and draw conclusions concerning the direction of a scan he may have subconsciously ranked caudad to cranial direction higher than cranial to caudad. As mentioned previously, if this was the case one would expect the same bias in the clarity of the hilar vessels, which did not show a significant difference. The current study used a Likert scale with 5 choices ranging from 1 indicating a poor test with significant artifact and 5 indicating no artifact and an excellent image. The use of 5 choices meant that the radiologist could choose a neutral central value indicating an average image. The range of choices on the Likert scale is sufficient since there is a significant difference between caudad to cranial and cranial to caudad scanning excluding radiologist 1 and his rating of clarity. He did, however, demonstrate a tendency to rank caudad to cranial scans better than cranial to caudad scan. If 7 choices had been provided to radiologist 1 his ability to discriminate difference in clarity between the two scans may have reached statistical significance. In addition, this may have made the remainder of the results more statistically significant.

The environment in which radiologists interpret diagnostic images is important and should optimize contrast discrimination. In ideal conditions the radiology workstation is dark with most of the extraneous light removed. A small amount of ambient light is useful and may enhance the radiologist's ability to focus without distractions. The reading room cannot be entirely dark since the radiologist may need to read requisitions or reports or view patient data. Poor room design and extraneous light may lead to ocular fatigue which in turn decreases productivity. Ideally, the reporting room should be quiet and void of extraneous noise unless the radiologist

finds background low volume white noise useful. There should be no interruptions during the interpretation of images. Unfortunately, these conditions are difficult to reproduce in everyday practice. In many group practices, radiologists have a shared reporting area with individual work-stations. In addition, phone calls, pages, and interruptions concerning patient assessment are a necessity of everyday practice.

Every effort was made to minimize fatigue and optimize the viewing conditions in this study. Our images were graded and reviewed in a private room with a multi-viewer machine, thus providing an environment conducive to focusing on the task assigned. Fatigue is an issue for radiologists who may interpret more than 100 different images in a day. In the current study the influence of fatigue and the radiologist's diligence in grading the CT scans is difficult to assess. Fatigue was controlled within the study setting in that the radiologists did not interpret more than 20 scans at one sitting and no more than 20 scans within a 24 hour period. However one can not control for fatigue related to the day to day practice of radiology and certainly on any given day radiologist 1 or Radiologist 2 may have been more astute or better able to concentrate depending on the complexity and number of images they had reviewed that day. In addition, the frequency of night call may have played a role.

Recall bias was also controlled. In order to ensure the radiologists could not recall their initial interpretation of a scan on the second reading the CT scans were randomly distributed and there was no identifying information. However patients may have unique anatomy or pathology and recall bias cannot be completely excluded. Radiologist 2 may in fact have been better able to

recall the findings on his initial interpretation and this may also account for the higher intra observer correlation when grading artifact, nodal stations and overall impression.

Artifact secondary to intravenous contrast is an issue in all enhanced CT scans regardless of the operator, the patient, or the CT machine. Numerous studies have investigated techniques to reduce perivenous artifact. Nakayama et. al found that squeezing a hand size ball during the delivery of contrast material significantly reduced perivenous artifact from the subclavian vein and improved image quality (204). Haage et. al found that injection of contrast material followed by a saline solution bolus using a double power injector when performing a thoracic helical CT scan allowed a 20% reduction of contrast material with a similar degree of enhancement. In addition, perivenous artifacts from the superior vena cava were significantly reduced (205). Studies have also shown that when the dose of intravenous contrast material is tailored to the patient's body weight better arterial and venous enhancement was obtained as compared to a fixed dose (206).

Rubin et. al investigated the effect of varying iodine concentration on material enhancement and perivenous artifact during thoracic spiral CT scanning. They concluded that reducing iodine concentration diminishes perivenous artifact and results in improved arterial enhancement during thoracic spiral CT. In this study patients received undiluted contrast medium, 1-1 normal saline dilution or 3-1 normal saline dilution. Contrast medium was injected at a flow rate determined to deliver the entire iodine dose within 40 seconds. Perivenous artifacts were statistically significantly reduced with successive of iodine dilution. Arterial enhancement was also better with diluted iodine (207). Interestingly, it was also postulated in this study that caudad to cranial

scanning would diminish perivenous artifact. They set out to investigate this hypothesis however at their institution CT scans performed in the caudad to cranial direction required images be presented on film in the same direction. These images were difficult for the radiologists to interpret and therefore this part of the study was abandoned. At our institution it was possible to program the processor to present the images on film in a cranial to caudad order irrespective of the direction in which the scan was performed

The current study utilized 100 cc of undiluted ionic or non ionic contrast administered through an antecubital vein using a power injector with a rate of 2.5 cc per second and a 25 second delay between injection of contrast and initiation of the scan. Based on previous studies if a smart preparation software program, hand exercise on the side of the injection, a saline flush, or if the dose of contrast was tailored to the patient's weight then contrast enhancement of the mediastinal vasculature may have produced less beam hardening artifact and therefore better visualization of the adjacent structures. It is unclear if combining all of these methods would in fact decrease artifact such that the direction of scanning would no longer impact the quality of the images. This study proposed that with caudad to cranial CT scanning the contrast would be less concentrated in the vessels in the superior mediastinum leading to less beam hardening artifact. Perhaps if we had a longer delay of 30 to 35 seconds in the cranial to caudad direction the results would be similar to our caudad to cranial results for vascular enhancement and beam hardening.

The current study utilized both MD60 and Isovue contrast material. At the time of this study nonionic contrast material cost approximately three times as much as ionic contrast. Therefore the cost savings was significant if MD 60 was utilized in patients with minimal risk of adverse

effects. The standard of practice at our institution involved a staff radiologist or radiology resident obtaining verbal informed consent for intravenous contrast prior to the CT scan. The risks were discussed with each patient. If the patient had no history of allergies or received ionic contrast in the past without any adverse event they were again given MD60. Patients were given Isovue if they had a history of environmental or drug allergies or a previous reaction to ionic contrast. The main disadvantage of non ionic contrast material is the higher cost and at our institution this was the driving factor behind this practice.

The effect of rapidly injected ionic or non ionic contrast material on patient motion and scan quality in spiral CT has been investigated (208). Stockberger et al attached a rod to the anterior abdomen with tape and objective measurements of motion were determined by means of computer reconstruction of the rod in 3 dimensions. The rods deviation from its estimated position in the motionless state was calculated. Subjective techniques for assessing patient motion have been shown to correlate well with more objective methods (209). The results demonstrated statistically significant increase in motion with ionic contrast versus non ionic contrast. There was less patient motion along with a better scan quality with non ionic contrast. The conclusion was that less patient motion occurred and scan quality improved with spiral CT when non ionic contrast material was utilized.

The use of both ionic and non ionic contrast material in the current study is a weakness in the design. In addition, the decreasing cost of non ionic contrast material has lead to its mainstream use at many institutions. Repeating the study with the exclusive use of non ionic contrast

material would increase the power of the results. However one could postulate that the results of this study could be applied to an institution exclusively using non ionic contrast.

Variables inherent to the patient, or institution can not be controlled for. In addition, the clinical conditions of the patient, particularly in relation to shortness of breath, and cardiac output, which can influence delivery of contrast material to the vessels, are beyond the control of the investigators. If each subject recruited into the current study had sequential CT scans in both the cranial to caudad and caudad to cranial direction several days apart the statistical power of this study would improve dramatically. Many of the statistical assumptions concerning the subjects and their variability would be eliminated. The only variable would be those being manipulated by the experimenters. There would be economical and ethical considerations with this approach particularly due to the double dose of intravenous contrast and the increased radiation exposure.

There have been great strides in technology within the last several years. CT images in the past were usually printed on film for image review. With the introduction of picture archiving and communication systems (PACS), the printing of CT images is increasingly abandoned in favor of direct viewing on CRT or flat screen monitors and storing image data in a digital archive. This has numerous benefits to a radiology department. Although the initial overhead cost for installation of a PACS system is quite significant the long term benefits include cost and space savings related to the elimination of film and the decrease in manpower needed to process, organize, manipulate, and retrieve film. In addition with a film system if a radiologist requires images of varying window widths and window lengths or 3D reconstructions these would have to be produced at the CT scanning station and then printed on film. A CT scanner has a limited

storage capacity and at a certain point images are downloaded to a disk. Therefore, manipulation of the data and production of additional images becomes more time consuming and costly. With the advent of PACS the images are immediately available to the radiologist for viewing. In addition the radiologist can manipulate the images to view varying window widths, window lengths and 3D reconstructions at the work. This saves time for both the radiologist and the CT technologist. In the current study extra time was necessary for the CT technologist to reverse caudad to cranial images for print on film in the cranial to caudad direction. This extra processing time would be eliminated with new PACS technology since CT scanners could automatically transfer images to PACS in a certain format.

Helical CT scanners from other vendors such as GE or Siemens may have varying degrees of software capabilities for reducing artifact. Each CT scanner is different in its capacity to address and minimize motion artifact and beam hardening. Although some institutions may be better at reducing artifact due to technology, more effective use of software or better operator understanding of the methods, the current technology can not completely eliminate these problems. Therefore the results of this study are applicable to all spiral CT scanners irrespective of the vendor, software, or operator.

The new detector array technology of multi slice CT offers three significant advantages including shorter acquisition times, decreased section collimation with longer scan ranges and reduction in contrast volume requirements The temporal and spatial resolution are improved and the slice thickness of reconstructed images can be manipulated retrospectively (179). Multi slice CT scanners provide a significant gain in performance. The newest CT scanners offer third

generation technology with a synchronously rotating tube and detector array as well as solid state detectors. The performance of the system is further improved by a faster rotation time. A 4 detector row scanner has approximately 8 times higher performance than a conventional single detector scanner and is at least four times faster than spiral CT. With newer 64 detector technology this can exceed 40-60 time faster (180,181). Technology initially became available in 1998 starting with a 2 detector multi slice CT scanner. Today over 200 detector CT scanners are utilized at research centers. Currently 64 detector multi slice CT scanners are available and considered leading edge for community and academic radiology departments (181). This technology is improving at an exponential rate and as multislice installation increases spiral CT scanners will be replaced.

Multi slice technology has overcome one of the most significant limitations of spiral CT, namely the inverse relation between scanning range and section collimation. The shorter scan duration reduces the risk of motion artifact. This is particularly important to trauma patients or patients who are short of breath (210). Shorter scan duration also allows for scanning of the liver and other organs at a better defined phase of contrast enhancement. The longer scan ranges are particularly important for CT angiography such that the entire abdominal aorta and the peripheral run off vessels down to the feet can be imaged. The whole aorta can be scanned along with the carotids from the aortic arch to the intra cranial circulation. In addition entire body scans involving the head, neck, chest, abdomen and pelvis are no longer time consuming and the entire body can be scanned within 10 seconds in a 64 detector multi slice CT scan (211,212,213).

The multi slice technology explosion has resulted in a significant increase in data load. A single CT scan of the chest and abdomen may produce up to and above 800 images depending on the degree of overlap. Therefore most institutions reconstruct with thicker sections and use scanning protocols which are modified versions of the standard spiral CT protocols with a somewhat thinner section collimation. However multi slice CT scanners do give radiologists and technologists an opportunity to revisit the data and manipulate images post processing to aid in diagnosis. Multi slice CT requires a similar dose as spiral CT (211,212,213).

One of the pitfalls with the current investigation was that if the patient required a CT scan of the abdomen and/or pelvis subsequent to a caudad to cranial CT scan of the additional time was required to reposition the patient in the gantry. This variable is eliminated with multi slice CT scan due to the increase software technology, ability to program protocols and the significant increase speed of the CT scanners. For this reason caudad to cranial CT scans may be more feasible with a multi slice CT scan.

The results of this study apply to spiral CT scanners. The rapid acquisition of images during a multi slice CT scan means that motion artifact whether related to voluntary movement or patient breathing is not as significant an issue. In addition, the rapid rate at which the CT scans can be performed with multi slice CT enables better manipulation of timing and rate of contrast administration. Although beam hardening artifact related to contrast concentration is still an issue, parameters such as collimation, pitch, rate and timing of injection are all factors which can be fine tuned with multi slice CT. Further studies using multi slice CT scanners would be

required to assess if caudad to cranial imaging have any advantage over cranial to caudad imaging with this new technology.

In conclusion, this study clearly demonstrates that caudad to cranial CT scans are superior to cranial to caudad scans for spiral CT. Caudad to cranial CT scans have less motion at the lung bases and beam hardening artifact within the SVC and subclavian veins. They also have better clarity of the vascular structures. Overall caudad to cranial CT scans were subjectively better than cranial to caudad scan. In centers which continue to utilize a spiral CT scanner the caudad to cranial protocol would provide significantly better quality images which may improve the diagnostic capability of the images decrease fatigue for the radiologist. There are certain pitfalls to caudad to cranial scanning including increased time required to reposition the patient within the gantry if they require additional images of the abdomen and/or pelvis, along with increased processing time for film.

The current study to some degree is limited in its application to the significant advance in technology. The increasing wide spread use of multi slice CT requires a revisit of the theory that caudad to cranial images are significant since many of the technological advances with multi slice overcome some of the limitations of spiral CT images. In addition the advent of PACS means that the pitfalls of film processing with caudad to cranial images are overcome. This would allow caudad to cranial imaging to be more easily incorporated into a standard protocol for patients requiring a CT scan of the chest.

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APPENDIX A

HUMAN INVESTIGATION COMMITTEE - APPLICATION FORM

FACULTY OF MEDICINE - MEMORIAL UNIVERSITY OF NEWFOUNDLAND
AND
HEALTH CARE CORPORATION OF ST. JOHN'S

Forward 20 copies of application and consent forms to:
Office of Research (HIC), Room 1759, Health Science Centre. (Phone 737-6974)

1. Investigators.

Principal Investigator:	If a student, indicate program and name of supervisor
Carla Pittman, MD	Diagnostic Radiology; Dr. R. Bhatia; Dr. G. Fox; Dr. P. Parfrey
Mailing Address. Telephone Number: 22 Golf Avenue 709 722-9339 St. John's, NF A1C 5C7	Co-Investigators: Dr. R. Bhatia

2. Title of study. Include protocol number, if any.

A comparison of cranial to caudad versus caudad to cranial CT scanning of the chest

3. Starting and ending dates.

Proposed start date: (at least 4 weeks from date of submission)
March 1, 1998

Anticipated completion date:
We do approximately 25 CT scans of the chest per week, assuming a 25% volunteer rate, then completion is September 1998.

4. Please fill in the appropriate information, if any. Check applicable boxes.

Hospital or Community Setting Involved	Involves		
	Patients or Residents	Records	Facilities
Health Sciences Centre	Patients		CT Scanner

5. **In the space provided**, list the main objectives of the investigation. No attachments please.

The objective of this study is to determine if caudad to cranial imaging of the chest is superior to cranial to caudad imaging for visualization of the pulmonary vasculature tree and if caudad cranial imaging has less artifact and, therefore, better visualization of mediastinal structures.

6. Introduction to study.

(a) What is the scientific background to the study?

The development of spiral CT has enabled thoracic imagers to acquire CT images of the chest in a single breath hold. However, a strategy for optimal imaging of the chest using spiral CT has not been developed. It is hypothesized that caudad-cranial direction of scanning is superior to cranial caudad for visualization of the pulmonary vascular tree, along with having less artifact. This would increase the sensitivity and specificity of CT scans of the chest and improve conformity among radiographers. To date this has not been tested.

(b) What is the rationale for the study?

i) To establish a protocol for the direction of CT scanning of the chest and, therefore, lead to conformity among chest imagers when ordering and interpreting chest CT scans.

ii) Improve visualization of the pulmonary vascular tree and mediastinal structures.

(c) Summarize any relevant human or animal studies already conducted.

As yet, there has been no published study regarding the direction of CT scanning of the chest. Rubin and colleagues (1) studied various protocols for contrast administration to optimize thoracic spiral CT. In another study Goodman et al (2) suggested it would be better to scan in the caudad cranial direction, however, no data concerning this was collected in their study.

7. Blood or other tissue sampling.

(a) List samples to be taken from participants. State type of sample, frequency and amount

No samples will be taken.

Will any samples be kept after the completion of the study? Y / N If yes, include section 9 on consent form.

8. Research interventions.

(a) List any procedures, tests or substances to be administered to participants: e.g. imaging, special diets, drugs (state dose and frequency), isotopic tracers, ECGs etc. **List only those that are not part of normal patient management.**

All patients will receive IV contrast (MD 60 or Isovue) as part of their CT scan as ordered by the referring physician.

(b) List questionnaires, interview scripts or chart audit forms to be used: Attach copies of each.

Nil

9. For studies involving patients.

(a) What treatment do ***you*** now use for patients who would meet the inclusion criteria for this study? (i.e. How would you manage these patients if they did not go into this study?) Is this considered "standard treatment"?

Currently, all patients presenting for a CT scan of the chest receive 100cc of contrast (MD60 or Isovue) at a 25 second delay with a cranial caudad scan direction (10 mm axial cuts),unless the radiologist involved orders a caudad cranial scan, which is often done at other centers.

(b) Is this an application for a clinical trial? Yes / No

If yes, what phase is this trial? I II III IV

What is the design of the trial (e.g. open, double blind, crossover etc.)?

10. **In the space provided**, give a brief description of the design of the study, including participant selection, interventions and outcome measurement. (Attach one copy of a protocol if available).

100 consecutive adult patients without contraindications to intravenous contrast referred to the Health Sciences Centre for CT scanning of the chest will be recruited into the study. Only those patients considered medically stable will be recruited. Each patient will be randomized using block randomization to be imaged in either the cranial to caudad or caudad to cranial direction. All patients will receive 100cc of IV contrast at a delay of 25 seconds. The images will be acquired from the base of the neck to the diaphragm with 7mm reconstructed images.. This will be done with a single breath hold. Images will be reviewed blindly and independently by three radiologists who will assess the quality of the images. Specifically, using a grading scale, motion artifact, vessels enhancement and beam hardening artifact will be evaluated. Statistical analysis will be performed to assess inter and intra-observer correlation. All patients will be asked for informed consent prior to being entered in the study.

11. Participants.

Number of participants at this site. 150	Will pregnant women be excluded? Y / N
Is this part of a multi-centre study? Y / N	If Yes, what is the total number of participants at all sites? _____

How will participants be recruited?

All consecutive, medically stable patients presenting to the Health Sciences Centre for CT scans of the chest will be eligible. All will be questioned concerning contraindications to contrast. Those patients eligible for contrast will receive MD 60 or Isovue.

12. What is the basis for the choice of sample size? (Consider the total number of participants for multi-centre studies).

No previous studies have been done concerning the direction of CT scanning of the chest. Therefore, a sample size of 100 patients was chosen for convenience.

13. What risks, discomforts or inconveniences are involved?

(a) risks: reaction (allergic/idiosyncratic) to ionic contrast; exposure to radiation

(b) discomforts: insertion of IV for contrast administration

(c) inconveniences: time to explain study/give informed consent/some patients will return for a second CT scan of the chest

14. Benefits.

Are there any immediate benefits arising out of the study for the participants (including controls)? Y / N Please specify.

No.

15. Confidentiality.

(a) What steps will be taken to preserve confidentiality?

The names of all patients involved in the study will remain confidential. All patients will be given a study number and this will be used when referring to the patient/CT scan. The three radiologists reading the CT scans will be blinded to the patients name/age/clinical history/direction of scan.

(b) List names of all personnel who can access information that could be linked to individual participants.

Dr. Carla Pittman (Radiology resident and principle investigator)

16. Consent process.

(a) Who will make the initial contact with the participant? CT Technologist

(b) Who will obtain the consent of the participant? Dr. Carla Pittman, Dr. R. Bhatia

(c) Explain procedure for obtaining consent.

All patients eligible for the study will be interviewed and the study explained to them. The investigators will be available to all patients who volunteer should any questions arise during or after the CT scan.

17. Vulnerable populations.

Will participants include: Minors (less than 19yrs) ? Y / N or Persons incompetent to give consent? Y* / N

If so, please justify. Outline the measures that will be used to protect their rights (attach separate sheet if required)

* Usually prohibited by Provincial legislation on Advanced Health Care Directives. (Situation as of November 1997)

18. Debriefing.

Explain the mechanism, if any, for feedback to participants.
The reports of all Ct scans will be sent to the referring patient's physician. Participation in the study will in no way delay the timely reporting of CT scans.

19. Payments.

(a) Will participants receive: reimbursement for expenses incurred? Y / N payment for participation in the study? Y / N	Please specify on separate sheet according to "Guidelines for the Remuneration of Research Subjects."* Please see Budget re reimbursement for hospital parking fee.
(b) Will there be any payment to a third party for referral of patients? Y / N	Please specify on separate sheet according to "Guidelines for Payment of Finders' Fees."*

* Available in the HIC office and on HIC web page.

20. Budget

Please enclose a copy of the budget for this study, including source of funding. Application for funding has been sent to the NYCOMED Research Fund.
Will the budget be administered through the University Finance Office? Y / N If no, where?
Will any investigator receive financial or other benefit by virtue of conducting this study? Y / N. If yes, specify.

21. Ownership of data.

Will data become the exclusive property of a pharmaceutical company or other external agency? Y / N
If yes, what is the policy of the company regarding publication of the data?

22. Reminders.

We would like to remind you that it is your responsibility to ensure that permission is obtained from clinicians, departments, institutions or communities whose patients / residents will be involved in the study.
We would also like to remind you that you must read "Guidelines on Research Involving Human Subjects" (MRC. 1987) or such guidelines as may supercede these. (available in the HIC Office and on HIC Web Page.)

Signature of principal investigator.	Signature of supervisor, in case of student application.
Date	

Adverse Reactions to Contrast Media

The minor possible adverse reactions to contrast media in descending order are:

1. hot flush, especially affecting the face, neck and external genitelia
2. pruritis, minor hives or urticaria
3. nausea, vomiting, disordered taste, sneezing
4. the general feeling of anxiety by the patient
5. coughing and dyspnea
6. pain at the injection site some time projecting proximally along the vein

The incidence of these events is 2-4%.

Intermediate Adverse Reactions

- more serious degrees of the symptoms listed above
- bronchospasm with increasing dyspnea and moderate hypertension may occur and the patient may feel apprehensive and anxious
- the incidence of these intermediate reactions is about .01 - .25%

Severe Adverse Reactions

Severe adverse reactions are usually severe manifestations of the above mentioned minor and intermediate reactions, especially dyspnea, bronchospasm, hypotension, severe apprehension, sometimes accompanied by uncontrolled restlessness, angioneurotic edema of the glottis, one or more grand mal convulsions with disturbed consciousness. Bronchospasm may become severe and the airway may be threatened by severe laryngeal and neck edema. Cardiovascular collapse may develop suddenly with pulmonary edema, severe hypotension, shock with diminished cardiac venous return, cardiac arrhythmias and possibly cardiac arrest. The incidence of these severe reactions is 0.04%.

Death

The most common causes of death are cardiorespiratory collapse, pulmonary edema, deepening coma, irretractable bronchospasm and airway obstruction. There is a mortality rate of .9/100,000.

Most serious reactions occur in the immediate post injection period. Delayed reactions have been reported but are rarely serious and almost exclusively mild in character.

REFERENCES;

1. Optimization of Thoracic Spiral CT: Effects of Iodinated Contrast Medium Concentration. Rubin GD, et al. Radiology 1996; 201: 785-791.

2. Detection of Pulmonary Embolism in Patients with Unresolved Clinical Scintigraphic Diagnosis: Helical CT Versus Angiography. Goodman LR, et al. AJR June 1995; 164: 1369-1374.

APPENDIX B

DISCIPLINE OF RADIOLOGY
FACULTY OF MEDICINE-MEMORIAL UNIVERSITY OF NEWFOUNDLAND
AND
HEALTH CARE CORPORATION OF ST. JOHN'S

Consent To Participate In Bio-medical Research

TITLE: Bottom to top CT scanning of the chest versus top to bottom CT scanning

INVESTIGATOR(S): Carla Pittman, MD
Rajdeep Bhatia, MD, FRCPC

SPONSOR: N/A

You have been asked to participate in a research study. Participation in this study is entirely voluntary. You may decide not to participate or may withdraw from the study at any time without affecting your normal treatment.

Information obtained from you or about you during this study, which could identify you, will be kept confidential by the investigator(s). The investigator will be available during the study at all time should you have any problems or questions about the study.

1. Purpose of study:

Advances in the technology of CT scans has enabled doctors to obtain a CT scan of the chest with a single breath hold by the patient. This shortens the amount of time it takes to do a CT scan. However, the best direction of scanning (ie. Head to toe or vice versa) has not been established. Many radiologists believe that scanning from the bottom of the lung to the top is better than scanning from the top of the lung to the bottom for seeing the blood vessels of the lung on the CT scan. However, this has never been proven with research, and, currently, radiologists use both methods depending on why your doctor has asked for a CT scan to be done. The purpose of the current study is to determine if one direction of scanning is better than the other.

2. Description of procedures and tests:

You will have a CT scan of the chest as requested by your doctor. You will receive dye through an intravenous. The length of the scan will be 10 minutes. You will be placed in either the bottom to top or top to bottom group. You will have a 50:50 chance of being assigned to either group.

For the purpose of this study your scan will be assigned a study number and your name removed from the films during their interpretation ands reporting by the radiologist. This ensures that the radiologist interpreting your scan does not know your identity or the direction of your CT scan.

Your participation in this study will in no way alter the timely interpretation and reporting of you CT scan. Your referring physician will receive a report indicating that you have been involved in this study and the direction of your scan. The results of this study will be made available to your referring physician upon completion of the research.

3. Duration of participant's involvement:

A CT scan (including preparation and the CT scan itself) takes approximately 10 minutes.

4. Possible risks, discomforts, or inconveniences:

The risks associated with a CT scan include:
1) Reaction to dye. The side effects from CT scan dye can range from and include flushing, itching, hives, a change in blood pressure, shortness of breath, and wheezing. These can range in severity, with mild side effects occurring 2-4% of the time and severe reactions occurring 0.04% of the time. A physician is immediately available at all times to address and treat any reaction you may have.
2) CT radiation. One CT scan of the chest results in the bone marrow exposure of approximately 500 mrem. This is approximately 100 times the dose that would be received from a normal chest x-ray. It is however, comparatively less than the dose which would be received from a barium enema study. The minimal amount of radiation dose will be used to obtain a diagnostic examination.

5. Benefits which the participant may receive:

There are no benefits to the patient.

6. Alternative procedures or treatment for those not entering the study:

If you do not enter this study you will receive a standard CT scan of the chest in the top to bottom or bottom to top direction. Both of these methods are accepted.

7. Liability statement.

You signature indicates your consent and that you have understood the information regarding the research study. In no way does this waive your legal rights nor release the investigators or involved agencies from their legal and professional responsibilities.

Patient initials_____

Bottom to top CT scanning of the chest versus top to bottom CT scanning

Investigators: Carla Pittman, MD
Rajdeep Bhatia, MD

Signature Page

Title of Project:

Name of Principal Investigator:

I, , the undersigned, agree to my participation in the research study described above.

Any questions have been answered and I understand what is involved in the study. I realize that participation is voluntary and that there is no guarantee that I will benefoit from my involvement.

I acknowledge that a copy of this form has been given to me.

(Signature of Participant) (Date)

To be signed by participant
(Signature of Witness) (Date)

To the best of my ability I have fully explained the nature of this research study. I have invited questions and provided answers. I believe that the participant fully understands the implications and voluntary nature of the study.

(Signature of Investigator) (Date)

Phone Number

To be signed by investigator