Optimising CT-chest protocols and the added value of venous-phase contrast timing; Observational case-control.

Venous Chest CT

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Data availability statement

The data that supports the findings of this study are available from the corresponding author, Michael Croft, upon reasonable request.

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None to disclose.

Ethics approval statement

This study has been approved by the institution's human research ethics committee (Bellberry HREC). Protocol ID 2020-05-426.

Patient Consent statement

Waiver of consent obtained from ethics board. Patient data sufficiently anonymized.

Abstract

Introduction:

To optimize CT chest protocol by comparing venous contrast timing with arterial timing for contrast opacification in vessels, qualitative image quality and radiologists' satisfaction and diagnostic confidence in assessing for potential nodal, pleural and pulmonary disease in general oncology outpatients.

Method:

Matched case control study performed following CT protocol update. 92 patients with a range of primary malignancies with 2 CT chests in a 2-year period; one with an arterial phase protocol, and the second in the 60 second venous phase, were included. Contrast attenuation in aorta, pulmonary artery and liver were measured. Subjective measurements assessed perivenous artefact, confidence in nodal pleural and pulmonary assessment and presence of pulmonary emboli. Statistical analysis was performed using paired and unpaired t-tests.

Results:

Venous-phase CT demonstrated more consistent enhancement of the vessels, with higher attenuation of the nodes, pulmonary and pleural lesions. There was a significant reduction in perivenous beam hardening artefact on venous-phase CT ($p<0.001$). Diagnostic confidence was significantly higher for nodal assessment and pleural abnormality visibility ($p<0.001$) and pleural assessment ($p <0.05$). There was no significant difference in pulmonary mass visibility. There was adequate enhancement to diagnose significant pulmonary emboli (PE) with 4 incidental PEs detected on the venous phase, extending to segmental vessels.

Conclusion:

Venous-phase CT chest performs better than arterial-phase on all fronts, without compromising assessment of incidental pulmonary emboli. When intravenous contrast is indicated in a routine chest CT (excluding a CT-angiogram), the default timing should be a venous or 60s phase.

Keywords

Chest, Contrast media, CT protocol, Oncology, Pleura

Introduction

Computed tomography (CT) of the chest is the workhorse of diagnostic imaging in evaluation of various thoracic conditions, such as evaluation and staging of lung cancers(1). The clinical question and patient factors usually dictate if iodinated intravenous contrast is indicated or not(2), with a relative paucity of literature available in relation to the specific CT scanning protocol(1, 3-5). For the rest of the manuscript, this study focuses on routine contrast-enhanced CT and does not include pulmonary angiogram or aortic angiogram. CT-chest has been shown to not be accurate for nodal assessment (55% sensitive and 81% specific for disease) (3, 6, 7) or pleural disease(8, 9) and this may be in part, due to scanning specifications.

Recent literature has suggested that the use of venous phase imaging can aid in improved nodal, pleural and parenchymal assessment(1). The improvement in the visualization of lymph nodes is due to a reduction in beam hardening artifacts from contrast in the superior vena cava and brachiocephalic vein(4). In the venous phase, the mediastinal vessels have more homogenous enhancement and hence, do not obscure the borders of lymph nodes, making them easier to measure. The internal enhancement patterns of the nodes can also be better characterized(1, 2, 6, 7).

Venous phase timing, or delay of 55-90s after contrast injection, can improve visualization of the pleura and pleural based lesions due to greater contrast distribution into the extravascular, interstitial spaces (1, 4, 7, 10). This can aid in distinguishing enhancing pleural nodules from effusion, which often occur concurrently. This contrast timing is in line with recommendations by the British Thoracic Society (BTS) of 60s delay for the assessment of mesothelioma(11).

For the above reason, this venous-timing can also improve delineation of lung lesions from surrounding tissue, such as collapsed lung or pleura(4).

While there is literature addressing specific indications such as lung cancer and mesothelioma, to the authors' knowledge there are no publications addressing the use of a venous chest protocol in general oncology post contrast chest imaging. Due to the evidence supporting improved outcomes with a venous chest protocol compared to an arterial phase protocol, our institution changed to a venous chest protocol for all non-angiographic post contrast CT scans performed at a general oncology outpatient centre, prior to expanding to all clinics across the network.

The aim of this study was to document the levels of diagnostic confidence in assessing mediastinal lymph nodes, pleural and pulmonary lesions on venous versus arterial phase chest CT in a general oncology outpatient clinic population. Density readings in the mediastinal vessels, lymph nodes,

pleural and pulmonary lesions and detection rates of incidental pulmonary emboli (PE) were also recorded.

Method

Ethics approval was obtained from the institution's ethics committee.

This is a retrospective, matched case-control study.

Over a 6-months period from May to October 2019, consecutive patients presenting in a single radiology outpatient oncology site for CE-CT chest were identified by searching the radiology information system (RIS) database. This followed a protocol change to use of venous phase timing in routine CE-CT chests. RIS records were accessed to determine if prior arterial CE-CT chest had been performed within our practice to be used as a control. Target sample size was determined as 100, as discussed with statistician, to achieve sufficient statistical strength.

Patient Selection: Patients with current venous phase and prior arterial phase CE-CT performed in our practice within the last 2 years (including CECT chest on its own, or if performed with other body parts such as CT-CAP). There was no minimum timeframe between the two imaging studies.

Patients were excluded if they had no prior CE-CT performed within a 2-year period, or if prior study was acquired with an angiographic protocol (Figure 1).

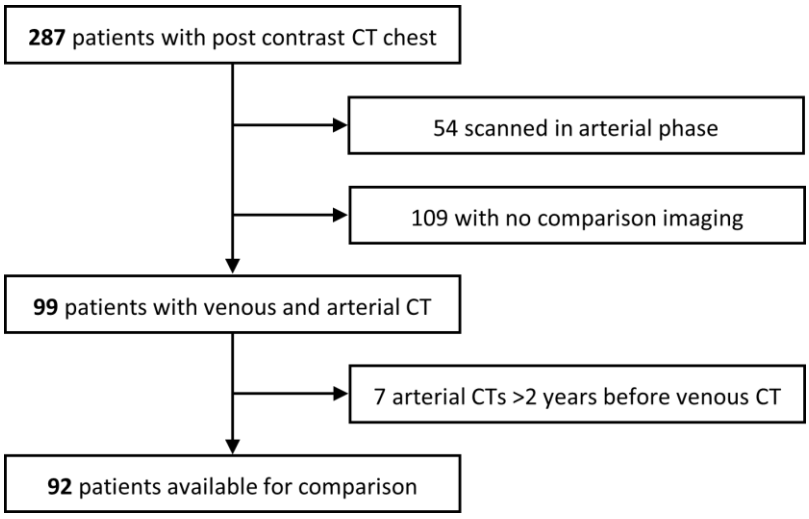

Figure 1: Study design and patient selection

Data collection: Patients were anonymized and given a numerical value. The arterial and venous studies for each patient were saved into separate folders in the picture archiving and communication system (PACS), for review later.

Scan Protocol: Arterial CE-CT chest was acquired with injection 70ml Omnipaque 350, delivered via power-injector at 4ml/s with bolus tracking in the descending aorta. Trigger of 100 Hounsfield Unit (HU) with immediate scanning from acromion to liver.

Venous CE-CT chest was acquired with injection 70ml Omnipaque 350, delivered via power-injector at 4ml/s. Bolus tracking with trigger of 100 HU in the descending aorta, with imaging performed after a 45s delay, resulting in a 60-65s post contrast scan.

All venous phase scans were performed on a Siemens Go-Top Dual Energy CT with twin beam technology. The arterial-phase studies were predominantly acquired in the same clinic, 36 on the Go-Top and 36 on the previous Siemens Definition AS 64 Slice. 19 scans were performed at different clinics, two on 16 slice, four on 64 slice and fourteen on 128 slice scanners. All scans performed using dual energy mode were assessed on the 120kV mixed reconstructions. Image reconstructions were sent in 1mm and 3mm slices in all 3 planes, in both lung and soft tissue kernels.

Image Analysis

Imaging analysis was performed with both objective and subjective assessment:

Objective assessment was performed by a single, blinded radiologist, independent of the subjective assessment.

Measurements included: Circular region of interest (ROI) measurement on 3mm thickness reconstructions, measuring attenuation in Hounsfield units (HU) in pulmonary artery and ascending aorta at the level of the pulmonary trunk; pulmonary vein at the confluence of the pulmonary veins with the left atrium ; and mediastinal or hilar lymph nodes (Figure 2). Whenever possible, a normal node defined as non-enlarged with normal morphology including preserved fatty hilum, was used.

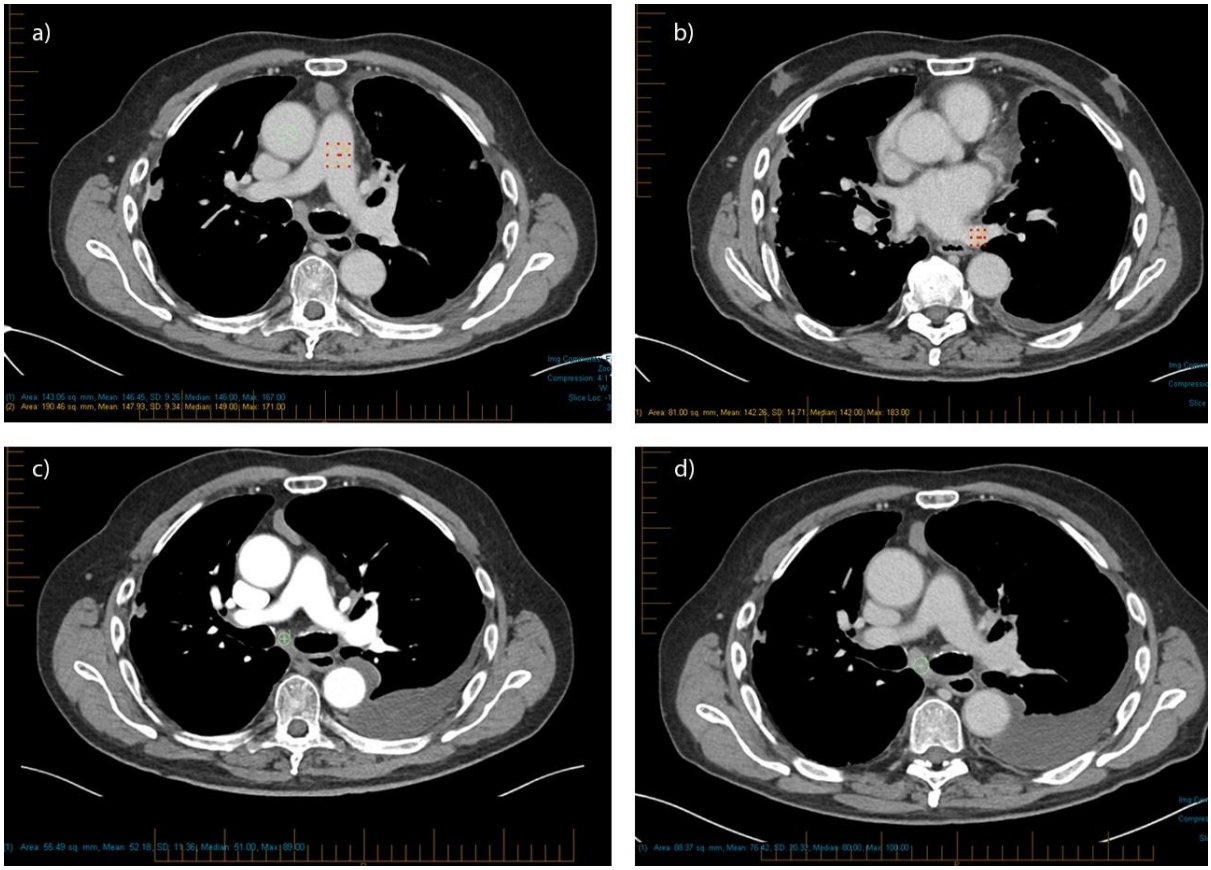

Figure 2: Measurement techniques. Axial venous-phase CT at the level of the pulmonary trunk (a) and pulmonary vein confluence (b). Region of interest (ROI) placement for pulmonary artery, ascending aorta and pulmonary vein. In a different patient, axial arterial-phase (c) and venous-phase (d) CT with ROI placed for attenuation measurement of subcarinal node. Increased attenuation of node on venous phase imaging (HU 76 versus 52). Note is made of a left-sided malignant pleural effusion from pancreatic cancer, where the pleural nodularity is better appreciated in the venous-phase (arrow).

Where present, the attenuation values were also measured in pulmonary (Figure 3 a, b) or pleural masses (Figure 3 c, d). In cases where multiple lesions were present, the largest lesion was assessed. ROI were adapted to avoid regions of necrosis, adjacent vessels, or lung. With regards to pleural mass, effort was made to not include any associated effusion.

Subjective assessment was performed by two chest radiologists with 4- and 20- years post-fellowship experience. Each assessor reviewed a different subset of 92 CT scans (46 arterial and 46 venous CTs each).

Items were scored as per the rubric in Table 1. Studies were assessed for artefact from the subclavian vein , ipsilateral to the side of contrast injection, and superior vena cava (Figure 3 e, f). Reader confidence in visualising and assessing lymph node morphology was documented.

In cases where there was pleural abnormality; tumour, effusion, scarring or atelectasis, readers assessed the ability to differentiate pleural changes from the adjacent chest wall and parenchyma, and the ability to distinguish effusion from pleural mass. The level of diagnostic confidence for this was also scored. In cases where a pulmonary nodule or mass was present, readers assessed ease and confidence of delineation of the tumour from the surrounding lung, parenchymal consolidation or collapse (Figure 3).

The presence of any incidental pulmonary emboli was recorded.

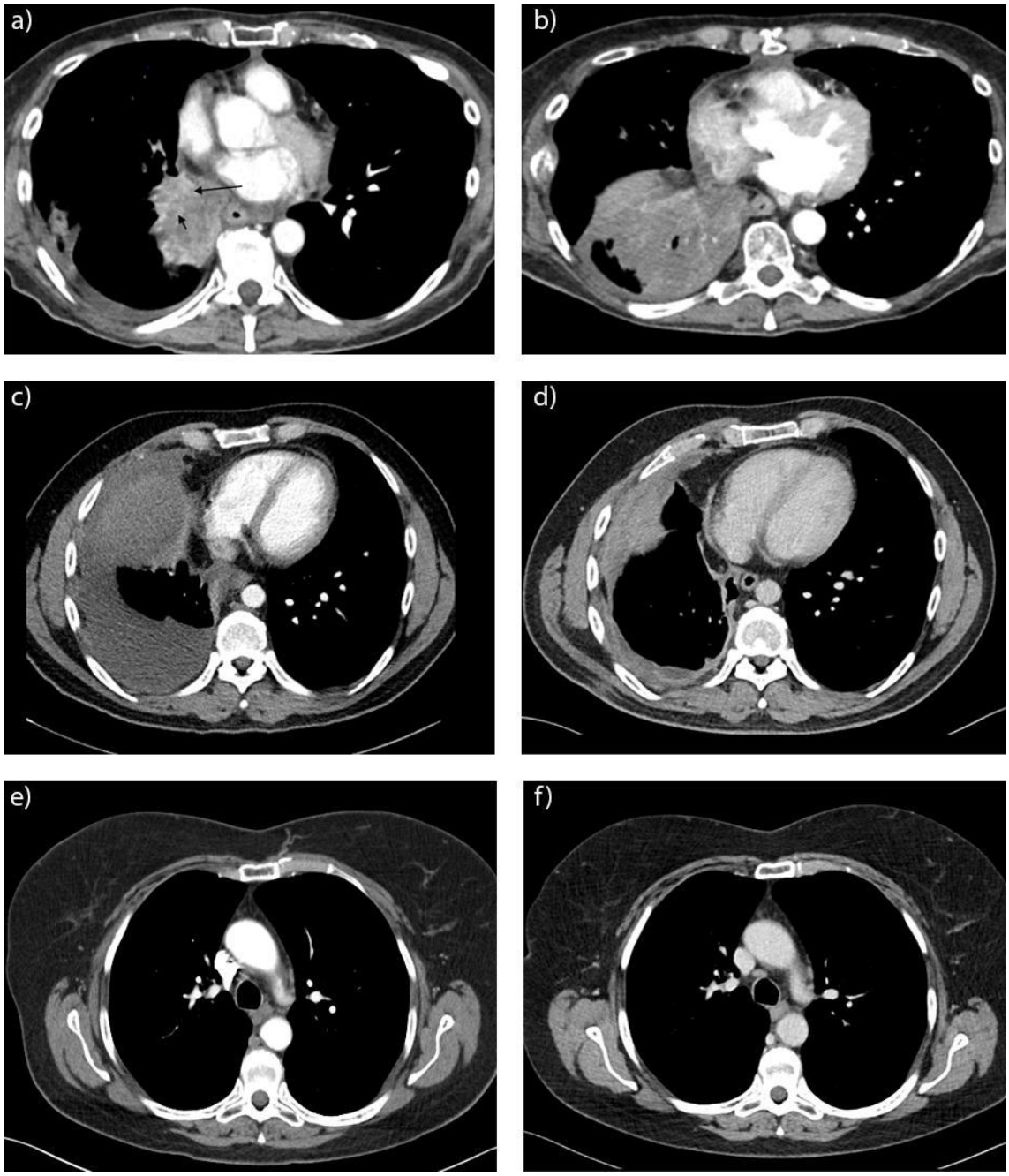

Figure 3: Contrast between arterial and venous phase CTs, with improved visualisation of parenchymal (a, b) and pleural abnormalities. Improved visualisation of nodes from reduced streak and beam artefact is also demonstrated. Venous-phase axial (a) chest CT in soft tissue window of a

69-year-old woman with primary right lower lobe lung non-small cell lung cancer, mediastinal extension and nodal involvement. The venous phase CT allows delineation of the more posterior necrotic tumour, from the more anterior, collapsed lung with normal, traversing pulmonary vessels. Level of demarcation as arrowed. This is compared with CT chest in arterial phase (b) performed a month prior, with poor delineation between tumour and collapsed lung and adjacent pleural effusion. Axial chest CT of a 42-year-old man with mesothelioma in venous (c) and arterial phase (d) performed 94 days apart. In the latter venous phase, the degree of the pleural soft-tissue rind is much better appreciated. The pleural effusion in the venous phase has reduced. With regards to the improved nodal visualisation and the reduced streak artefacts, the distal pretracheal node adjacent to the superior vena cava (SVC) in arterial study (e) was obscured by the dense contrast compared to optimised visualisation when imaging is performed in venous phase (f).

Due to obvious visual differences between arterial and venous imaging, it was not possible to blind the study protocol to the reader. In an effort to reduce recall bias, the 2 sets of studies (arterial vs venous-phase CT) were assessed more than 1 month apart.

***Statistical methods**:* Mean HU with standard deviations were obtained for the objective measurements and compared using paired t-test for nodal measures and unpaired t-test for pulmonary and pleural lesions. P-values of <0.05 were considered statistically significant.

Subjective measurements for artefacts and reader confidence were compared with paired t-test whilst pulmonary and pleural lesions were analysed with unpaired t-test, due to the difference in size of measurable groups – in some patients, there was resolution or development of lesions in the interval between CT scans.

Subclavian and SVC Artefact	1: No artefact 2: Mild artefact not impeding diagnostic assessment 3: Severe artefact impeding assessment
Lymph node assessment	1: High confidence 2: Moderate Confidence 3: Low Confidence
Pleural abnormality visibility	0: No pleural pathology 1: Clear delineation of pleural pathology from adjacent structures 2: Partial differentiation of pleural pathology from adjacent structures 3: No differentiation of pleural pathology from adjacent structures
Pleural assessment	1: High confidence 2: Moderate confidence 3: Low Confidence
Pulmonary mass visibility	0: No pulmonary mass 1: Clear delineation from surrounding parenchymal change 2: Partial differentiation from surrounding parenchymal change 3: No differentiation from surrounding parenchymal change
Pulmonary Embolism	0: None identified 1: Present

Table 1: Scoring Rubric for subjective assessment of Chest CE-CT.

Results

Between May and November 2019, 287 consecutive patients who had non angiographic CE-CT chest were screened and 195 excluded, with 92 patients remaining for assessment (Figure 1). The majority of the 54 patients excluded due to being scanned with an arterial phase protocol, were participating in clinical trials so were not changed to the new venous chest protocol.

The patient demographics were shown in Table 2. Within the study group, there was a male to female ratio of 3:2. The mean age was 69 (age range 35-84). Average time between the two scans was 201 days, with the time difference between scans directed by the treating clinician. The majority of studies were performed for the purpose of oncology restaging, with 22% of cases having primary lung cancer and 73% non pulmonary malignancy. 7 arterial and 36 venous studies were performed in dual energy mode.

Average Age	69 (35-84)
Gender	
Male	53 (60%)
Female	39 (40%)
Average Time between scans	201 days
Type of Cancer	
Lung	20
Lower Gastrointestinal	18
Hepatobiliary	13
Prostate	11
Breast	6
Sarcoma	5
Melanoma	4
Lymphoma	4
Urinary Tract	3
Cutaneous SCC	1
Thyroid	1
Oesophageal	1
Non-malignant	
Pulmonary Nodule	4
Sarcoidosis	1

Table 2: Patient Demographics

Objective Findings:

The measured mean HU and average variation around the mean of the target structures are listed in Table 3.

The major thoracic vessels demonstrated higher attenuation values in the arterial-phase imaging, and had a greater variance in enhancement on arterial compared to venous-phase CT.

Attenuation of lymph nodes was statistically higher in the venous-phase CT, with an average difference of 23HU (p-value <0.01).

Similar observations were made in pleural and pulmonary tumours, with increased attenuation in venous-phase imaging, although pulmonary tumours did not reach a statistical significance (p-value 0.1 and 0.3 respectively) (Figure 3 a, b). This may be due to the relatively small number of cases which had measurable disease. There was a case of pericardial cyst that was mistakenly read as a node in the arterial-phase.

Mean attenuation and average variation (HU)			
	Arterial	**Venous**	***p* value**
Pulmonary Artery	294.0 (± 71.1)	160.4 (±32.3)	*<.001*
Pulmonary Vein	295.2 (±67.7)	151.4 (±26.0)	*<.001*
Aorta	299.4 (±66.6)	155.5 (±27.3)	*<.001*
Lymph nodes	65.4 (±19.9)	88.4 (±19.1)	*<.001*
Pleural Mass	48.6 (±16.3)	58.5 (±17.0)	*0.12*
Pulmonary Mass	61.1 (±26.7)	72.5 (±18.9)	*0.26*

Table 3: Objective assessment: Attenuation values of pulmonary artery, pulmonary vein, aorta, lymph nodes, pulmonary and pleural masses in arterial-phase versus venous phase contrast-enhanced CT chests.

Subjective Findings:

There was significant difference in the perivenous artefact reported at the subclavian vein and superior vena cava by both observers, with venous-phase having reduced beam-hardening artefact at both levels (Table 4) (Figure 3 e, f). There was a significant difference in the number of studies reported to have artefact that resulted in impedance of diagnostic assessment, with 54 arterial versus 4 venous at the subclavian vein level, and 17 arterial versus 0 venous at the SVC level.

Diagnostic confidence in assessing the supraclavicular, mediastinal, and hilar nodal stations was significantly improved with venous contrast timing.

Pleural pathology, including tumour, effusion or scarring was present in 31 arterial and 33 venous studies. There was statistically significant improvement in the reader's ability to delineate pleural lesions, as well as distinguishing effusion from pleural mass on venous CT. This included detection of nodularity or solid components within pleural effusion.

Pulmonary lesions were present in 24 arterial and 31 venous studies. There was no observed difference in reader ability to identify or delineate pulmonary tumours between the two protocols.

As each reader assessed a different subset of 46 cases, subjective analysis was assessed combined and individually for each reader. There were no significant differences in findings between reader 1 and reader 2.

As a secondary finding, pulmonary emboli were identified in 1 patient on arterial CT and 4 patients on venous CT .

Score	Arterial	Venous	*p* value
Subclavian Vein Artefact			
1	9	66	
2	29	22	
3	54	4	
Average	2.49	1.33	*<.001*
SVC Artefact			
1	21	86	
2	54	6	
3	17	0	
Average	1.96	1.07	*<.001*
Lymph Node Assessment			
1	37	80	
2	45	12	
3	10	0	
Average	1.7	1.13	*<.001*
Pleural Abnormality Visibility*			
1	13	29	
2	17	4	
3	1	0	
Average	1.52	1.18	*<.001*
Pleural Assessment*			
1	15	27	
2	14	6	
3	2	0	
Average	1.64	1.18	*.002*
Pulmonary Mass Visibility*			
1	18	26	
2	6	5	
3	0	0	
Average	1.25	1.16	*.30*

Table 4: Subjective assessment: Perivenous artefacts, lesional, nodal, pleural and vascular assessment for arterial and venous-phase CTs. Scores as per Table 1.

**only cases with visible pleural or pulmonary disease were included.*

Discussion

This study demonstrates the differences between arterial and venous-phase imaging of the chest in a general oncology population. It has shown that venous-phase imaging confers a more consistent enhancement of vessels, significant reduction in perivenous artifact and increased enhancement of nodes when compared to arterial-phase timing. This is in line with other earlier publications(4, 11). We demonstrated a statistically-significant increase in the number of nodes assessed with high confidence on the venous phase, with the majority of the arterial-phase nodes recording only a moderate-low confidence in assessment. Further benefits of improved nodal assessment include easier measurements of nodal size due to unobscured borders, as well as improved morphological assessment and visibility of the internal nodal architecture. This is considered to be of particular benefit in this patient cohort, with the ability to appreciate increased nodal enhancement and central necrosis useful in oncological assessment. As with intra-abdominal nodes, a change in morphology may be an indicator of malignancy or a response to treatment, and this information is poorly assessed on the arterial phase.

There was also a statistically-significant increase in confidence of assessment of pleural lesions. In the venous-phase study, 82% (27/33) of pleural lesions were assessed with high reader confidence, compared to only 48% (15/31) on the arterial phase. Delineation from adjacent structures was also improved with 88% (29/33) considered to have clear delineation compared to 42% on the arterial phase. This is consistent with available literature and provides the benefit of optimal pleural assessment in all oncology patients rather than just mesothelioma. Anecdotally, it has been noted since the change in CT protocol, there appears to be an increase in the number of pleural metastases being detected. While this has not been quantified, it is presumed related to improved visualisation rather than any change in prevalence of pleural disease

This study did not demonstrate a significant difference in pulmonary lesion assessment between either contrast timing. This may be due to the small sample size of the current study, as other publications have found this to be of benefit, particularly in lung cancer follow-up (11). Most of the parenchymal lesions reviewed here were pulmonary metastasis, where surrounding aerated lung confers adequate delineation from the lesion regardless of contrast protocol. There are instances where pulmonary lesions approximate atelectatic lungs, where accurate, prospective size measurement will be important, for both staging and treatment planning.

A proposed drawback of venous-phase CT is potential reduction in the identification of incidental pulmonary emboli (PE). This is not an uncommon finding in this patient demographic (12, 13) and although not the primary goal when considering routine malignancy evaluation, these patients are at increased risk of thromboembolic disease and detection allows appropriate treatment (12). The venous-phase has consistently achieved acceptable pulmonary-arterial density and whilst there was only a small cohort of acute PEs; 1 in arterial-phase and 4 in venous, the cases in the venous phase were detected as far as the segmental vessels. None of these went on to have formal pulmonary angiograms prior to treatment. The ability to diagnose pulmonary emboli on delayed venous imaging of the chest has been recently reviewed by Foti et al who found that venous-phase dual-energy CT was an accurate tool in identifying emboli in oncology patients when compared to conventional CT pulmonary angiogram (13). There has also been a transition of our practice to use dual-energy CT in many oncology patients and 38 venous-phase CTs were performed as such, with low keV images reviewed routinely. This can only serve to further improve the capabilities to detect incidental pulmonary emboli, even without specific perfusion workups.

There was also initial concern about the lack of arterial phase imaging through the liver. However in most indications a venous phase is sufficient. The protocol can be adapted for hypervascular tumours requiring an arterial phase upper abdomen, by incorporating a late-arterial liver CT prior to the venous phase chest run. This means only those patients requiring arterial and venous phase liver imaging receive this protocol, resulting in dose savings. Given the observed diagnostic benefits of the venous chest in thoracic oncology, we changed our CT chest, abdomen and pelvis protocols to incorporate a single pass venous study which can also incorporate tailored use of an arterial upper abdomen prior to the venous pass in only those patients who need it, with significant dose savings (unpublished data).

The benefits of venous-phase timing also extend to include the reduction in contrast media, as the timing of the scan allows for peak enhancement with a lower volume of iodinated contrast (5).

In terms of applicability, this protocol has since been implemented for all clinical indications of non-angiographic post contrast CT chest studies at all our sites.

Limitations to the study include; this being a retrospective study with only a small number of cases with measurable pulmonary or pleural lesions. Nevertheless, this data is in line with the other published literature, in support of venous-phase timing. Due to the obvious visual differences between arterial and venous-phase imaging, it was not possible to blind the readers to the imaging protocol and this could potentially lead to reader bias. In order to reduce recall bias as the same

patient was scanned with both protocols, the cases were read separately, at least one month apart. The matched cohort negates other potential factors that may affect the appearances of the images or degree of contrast enhancement, such as patient weight and cardiac status. Finally, in terms of generalizability, we have worked out that the trigger delay for older16-slice CTs in our network needs to be 40s instead of 45s, in order to achieve equivalent venous-phase imaging.

Further studies will be required to reassess the sensitivity and specificity of nodal and pleural assessment, and to determine if change in scanning protocol and adaptation of venous-phase imaging has a positive impact in patient management.

Conclusion

In the assessment of primary and secondary lung and pleural malignancy, a 60-second venous-phase contrast enhanced chest CT results in reduced perivenous beam hardening artefact and improved tissue and lesion enhancement characteristics. This provides increased reader's diagnostic confidence, with a significant improvement in mediastinal lymph node and pleural assessment compared to conventional arterial imaging. This study confirms the viability of venous-phase imaging in routine clinical practice, with no observed detrimental trade-off. We recommend a venous phase should be used as the standard post contrast CT chest protocol.

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