Online Data Supplement

**Manuscript title:**

# Pulmonary angiopathy in severe Covid-19: surrogate physiologic, imaging and hematologic observations

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## Supplementary Methods

### *Computed Tomography (CT) & Dual-Energy CT Acquisition*

Free-breathing non-contrast-enhanced CT was acquired using 120 peak kilovoltage (kVp) tube voltage, 30-70 mAs, 0.5 s rotation time, 128 x 0.6 mm collimation, and pitch of 0.8. Images were reconstructed using a medium kernel (B40f), 1 mm slice thickness and 1 mm increment. Dual energy pulmonary angiographic images (i.e. lung and mediastinal images) and perfusion images were acquired and generated, the latter using the dual-energy post-processing software, Syngo Via Dual Energy, Siemens Healthineers. Vendor recommended kVp settings for DECT were 100 and 140Sn kVp, Scanning parameters were as follows: quality reference mAs of 89 for 100 kVp and 76 for 140Sn kVp, 64 mm × 0.6 mm collimation with z-flying focal spot, 0.285 s rotation time, and pitch of 0.55. Images were reconstructed at 2 x 1.4 mm slice thickness using a D30f kernel. Contrast volume was calculated by using a weight based algorithm ranging from 70-100 ml of Omnipaque (Iohexol, GE Healthcare, Oslo, Norway) with an injection rate of 5 mL/s through a femoral or internal jugular central venous catheter or an 18G cannula in the antecubital vein, a triphasic injection protocol delivered the first half of the contrast bolus followed by a 50:50 mixture of normal saline and contrast, followed by a 30 ml normal saline chaser to minimise streak artifact. Bolus tracking was used with a region of interest (ROI) on the main pulmonary artery.

A caudocranial scan direction was used and all patients were imaged with their arms extended cranially; three patients were imaged in the prone position to alleviate oxygen requirements. Radiation dose in terms of dose length product (DLP) was recorded and for the purposes of this study, DECT effective dose was obtained by multiplying the median DLP value by the adult chest k-factor of 0.014 mSv*mGy−1*cm−1. Patients with a body mass index over

35 and patients who could not lift their arms underwent CTPA but did not undergo DECT to mitigate artifact as a result of beam hardening.

***Quantification of Morphologic CT Abnormalities***

Morphological abnormalities were reviewed in consensus by two thoracic radiologists (AD & SRD with 14 and 24 years' experience respectively). Observers recorded the following CT features:

i) Presence/absence of pulmonary arterial filling defects indicating thromboembolic disease [E1,E2] and, if present,

ii) The 'highest' order of vessel (1, main pulmonary artery [PA]; 2, right and/or left main PAs; 3, lobar PAs; 4, segmental PAs and 5, subsegmental PAs);

iii) Presence/absence of deep venous thrombosis in lower limb or upper limb veins based, when available, on findings of compression Doppler ultrasound or CT venography;

iv) Overall extent of abnormal lung (quantified to the nearest 5% on visual inspection) and sub-quantified as the percentage of ground-glass opacification and dense parenchymal opacification (denoting consolidated and/or atelectatic lung), up to total of 100% as a component of abnormal lung;

v) Presence of dilated (branching and tortuous) vessels in the peripheral lung. Identification and evaluation of these vessels was aided by the use of images viewed on maximum intensity projection (MIP) reconstructions, as necessary; the number of segments with dilated peripheral vessels was also recorded (NB for the purposes of quantification the lungs were considered comprising 19 segments as follows: right upper lobe = 3, right middle lobe = 2, right lower lobe = 5; left upper

lobe = 3, lingula = 2 and left lower lobe = 4). Dilated peripheral vessels were recorded only in patients who had at least two lobes with assessable lung parenchyma (defined lobes with at least 50% of lobe not obscured by dense parenchymal opacification).

***Evaluation of Perfusion on Dual-Energy CT***

DECT pulmonary blood volume (PBV) images were reviewed in consensus by two thoracic radiologists (CR and SPGP; 14 and 30 years' experience respectively) independent of the review of CT abnormalities detailed above. Patients with dense parenchymal opacification (i.e. consolidated and/or atelectatic lung) in two or more lobes, and studies with severe motion and beam-hardening artefact were excluded from analysis. Perfusion images were viewed using "dense lung" color map maximum threshold of -200HU to avoid artefactual perfusion defects due to densely consolidated lung. PBV images were then rated as normal or abnormal and the proportion of involved segments and lung parenchyma was estimated using the Boyden segmental classification. Perfusion abnormalities were categorised as follows: i) wedge-shaped, ii) mottled or iii) mixed (*Figure 1 and videos 1-3*). The presence of at least one hypo-perfused bronchopulmonary segment led to the final diagnosis of a perfusion defect; this was defined as one segmental region of hypoperfusion on pulmonary blood volume (PBV) color maps with a threshold of < 20 relative HU compared to the pulmonary artery [E3]. The possibility of false positives in the setting of air trapping, consolidation, motion and streak artefact were considered by the authors [E4]. For this reason, the following measures were employed: (1) only aerated segments of lung free from dense consolidation were assessed, (2) PBV maps were reconstructed using a segmentation

threshold of -200 HU to include regions of lung with GGO, and (3) regions of artefactual perfusion or motion abnormalities were excluded from analysis.

***Thromboelastography***

Overall coagulation state was assessed using Thromboelastography (TEG 6, Haemonetics®, UK) mainly focusing the R time (time of the first measurable clot) and MA (maximal amplitude) which is the maximal clot strength as determined by platelet number and function, as well as fibrin cross-linking to form a stable clot with or without heparinase to assess the effect of heparin.

# Supplementary Video files

**Videos files 1-4:**

Morphologic patterns of DECT PBV maps with corresponding axial CT images.

***Video E1a - Wedge DECT.avi:*** PBV images demonstrate a wedge-shaped perfusion defect in the posterior and apical segments of the right upper lobe in the absence of pulmonary embolism.

***Video E1b - Wedge CT.avi*** (to be viewed alongside 1a) Axial CT images demonstrate diffuse ground glass opacity and branching nodules in the non-dependent lung in the upper lobes consistent with COVID-19 pneumonia.

***Video E2a - Mottled DECT.avi:*** PBV images demonstrate mottled perfusion defects throughout all aerated segments of the lungs in the absence of PE.

***Video E2b - Mottled CT.avi*** (to be viewed alongside 2a): Axial CT images demonstrate vascular tree in bud nodules, diffuse ground glass opacity, and mosaic attenuation consistent with COVID-19 pneumonia.

***Video E3a - Mixed DECT.avi*** PBV images demonstrate mixed (wedge shaped plus mottled) perfusion defects in a patient receiving ECMO therapy. Wedge shaped defects predominate in the aerated upper lobes while the right lower lobe have a diffusely mottled appearance.

***Video E3b - Mixed CT.avi*** (to be viewed alongside 3a): Axial CT images demonstrate demonstrate extensive ground glass opacity which correspond with the upper lobe perfusion defects, while dependent atelectasis is seen in the lower lobes, where there is a segmental pulmonary embolism, in addition mosaic attenuation and subpleural sparing is seen in all lobes, an appearance described in COVID-19 pneumonia.

***Video E4 - Normal DECT:*** Axial perfused blood volume images of the lungs in a 32-year-old female patient without Covid-19 or pulmonary embolism. Axial images demonstrate a homogenous color map consistent with normal iodine distribution.