Supporting Information

1. Settings for radiomic feature calculation

1.1. Settings used for Gray Level Co-Occurrence Matrix (GLCM) features:

The matrix was acquired at 16 quantized gray levels through using an 8-connected neighborhood in 2D with the corresponding direction vectors at distance 1 of: (1, 0, 0), (1, 1, 0), (0, 1, 0) and (−1, 1, 0).

2. Calculation of the Metric of Reproducibility: Overall Concordance Correlation Coefficient

The Concordance Correlation Coefficient (CCC) between values of a radiomic feature (Y) of n samples at two different CT image conditions ((Y_{i1}, Y_{i2}) , $i = 1, 2, \ldots, n$) with means of $\mu_1 = E[Y_1]$, $\mu_2 = E[Y_2]$ and variances of $\sigma_1{}^2, \sigma_2{}^2$ and correlation coefficient of ρ is:

$$\rho_c = 1 - \frac{E[(Y_1 - Y_2)^2]}{\sigma_1^2 + \sigma_2^2 + (\mu_1 - \mu_2)^2}$$

or,

$$\rho_c = CCC = \frac{2\rho\sigma_1\sigma_2}{\sigma_1{}^2 + \sigma_2{}^2 + (\mu_1 - \mu_2)^2}$$

Hence CCC is the agreement of feature (Y) within a pair of CT image conditions. The Overall Concordance Correlation Coefficient (OCCC) of a radiomic feature (Y) of n samples across M different CT image conditions ($Y_1, Y_2, \ldots, Y_M$) is the weighted average of all pairwise CCCs where higher weights are given to the pairs of conditions whose feature values have higher variances and larger mean differences:

$$OCCC = \frac{\sum_{x=1}^{M-1}\sum_{y=x+1}^{M}\xi_{xy}\rho_{xy}\chi_{xy}}{\sum_{x=1}^{M-1}\sum_{k=x+1}^{M}\xi_{xy}}$$

Where $\xi_{xy} = \sigma_x{}^2 + \sigma_y{}^2 + (\mu_x - \mu_y)^2$ and $\chi_{xy} = \frac{2\sigma_x\sigma_y}{\sigma_x{}^2 + \sigma_y{}^2 + (\mu_x - \mu_y)^2}$.

Hence agreement (OCCC) of a radiomic feature against variation of dose (across M=4 levels) in a subset (e.g. at fixed kernel $k_1$and slice thickness st_2) is:

$$OCCC_{d.k_1\_st_2} = \frac{\sum_{x=1}^{3}\sum_{y=x+1}^{4}\xi_{xy}\rho_{xy}\chi_{xy}}{\sum_{x=1}^{M-1}\sum_{k=x+1}^{M}\xi_{xy}}$$

Agreement (OCCC) of a radiomic feature against variation of kernel (across M=3 levels) in a subset (e.g. at fixed dose $d_{100}$and slice thickness $st_{0.6}$) is:

$$OCCC_{k.d_{100}\_st_{0.6}} = \frac{\sum_{x=1}^{2}\sum_{y=x+1}^{3}\xi_{xy}\rho_{xy}\chi_{xy}}{\sum_{x=1}^{M-1}\sum_{k=x+1}^{M}\xi_{xy}}$$

Agreement (OCCC) of a radiomic feature against variation of slice thickness (across M=3 levels) in a subset (e.g. at fixed dose $d_{50}$and kernel k_2) is:

$$OCCC_{st.d_{50}\_k_2} = \frac{\sum_{x=1}^{2}\sum_{y=x+1}^{3}\xi_{xy}\rho_{xy}\chi_{xy}}{\sum_{x=1}^{M-1}\sum_{k=x+1}^{M}\xi_{xy}}$$

3. Supplemental Figures

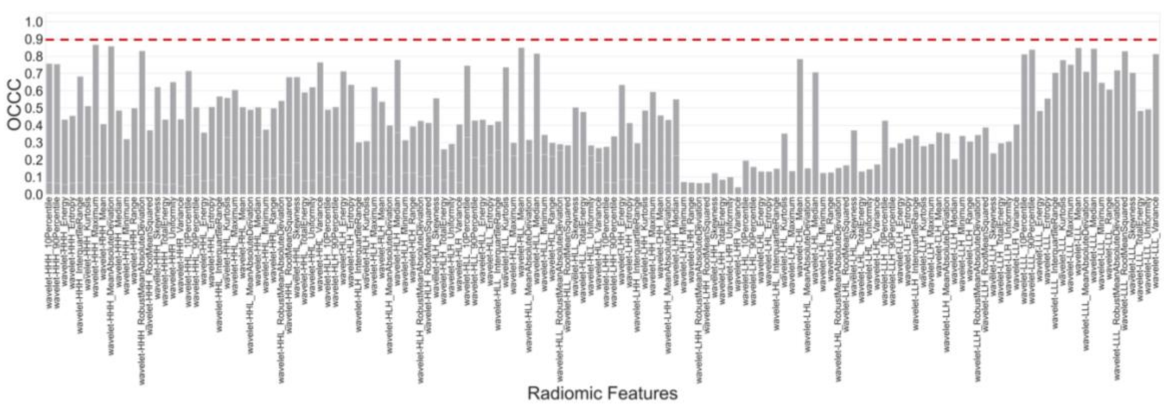


Figure S1. Inter-condition agreement of radiomic features among 36 conditions. Vertical axis shows the level of agreement (OCCC) of each feature value. The red dashed line shows the threshold of OCCC= 0.9 to indicate reproducible features

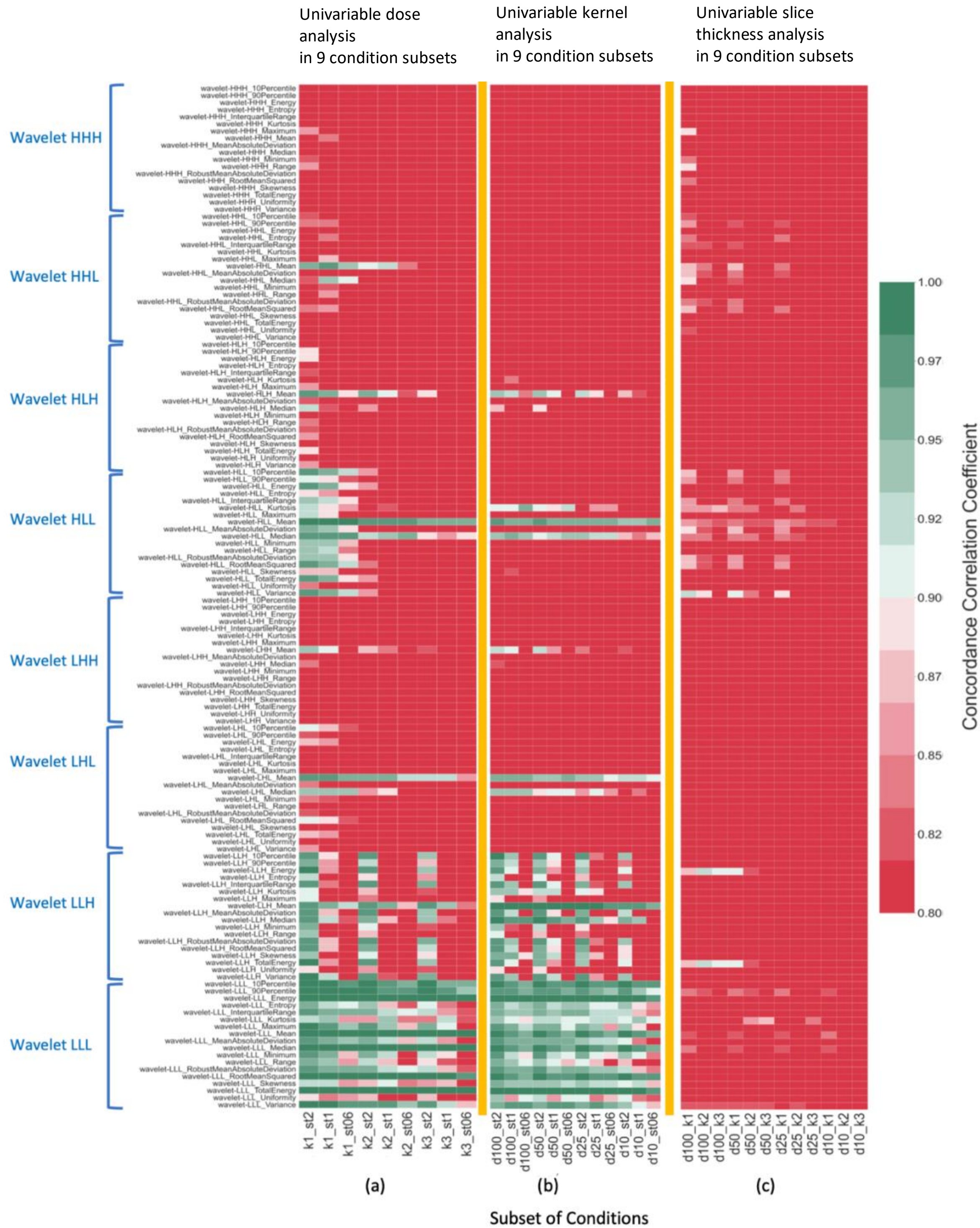
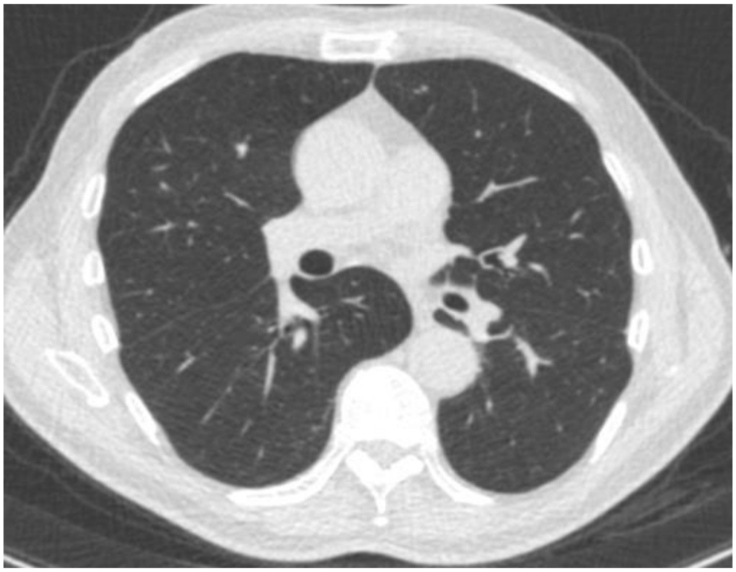
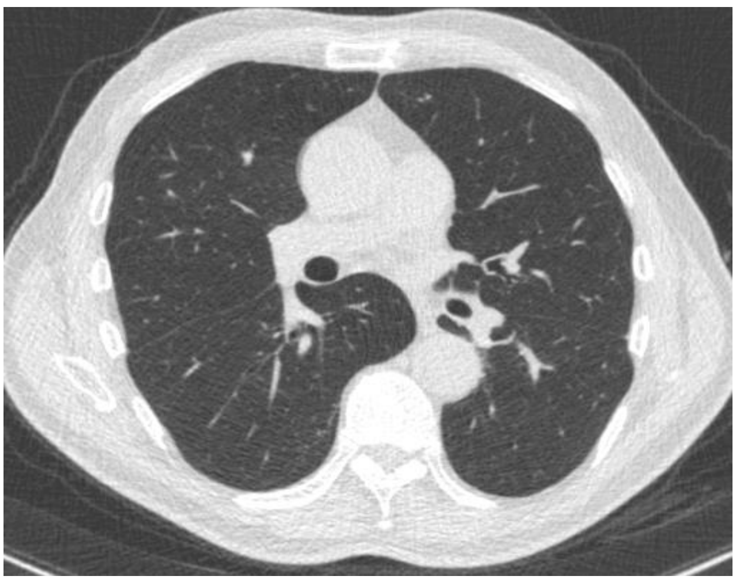


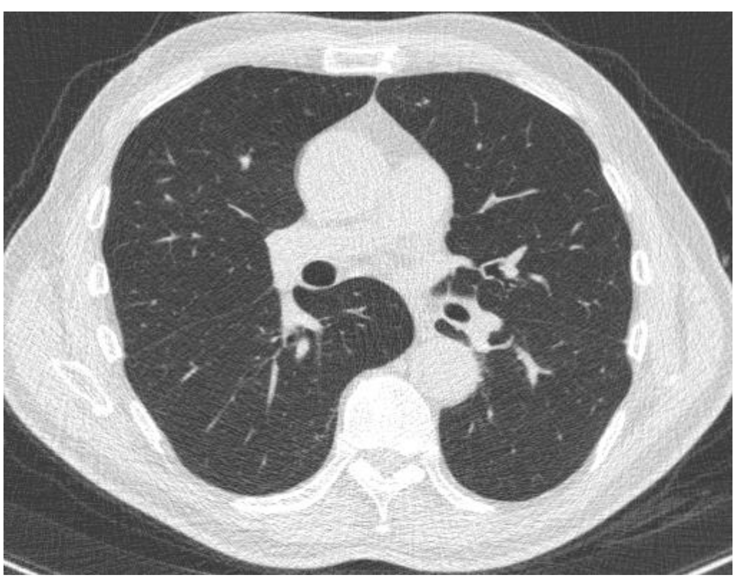
Figure S2. Agreement (OCCC) of wavelet radiomic features within condition subsets for analysis of a) impact of dose variation, b) impact of kernel variation, c) impact of slice thickness variation. Each column shows OCCC values of radiomic features within a subset that is identified on the horizontal axis. Any agreement with OCCC≤0.8 indicates extremely poor concordance and is shown in dark red.



(a) 100% dose, 1mm slice thickness, smooth kernel

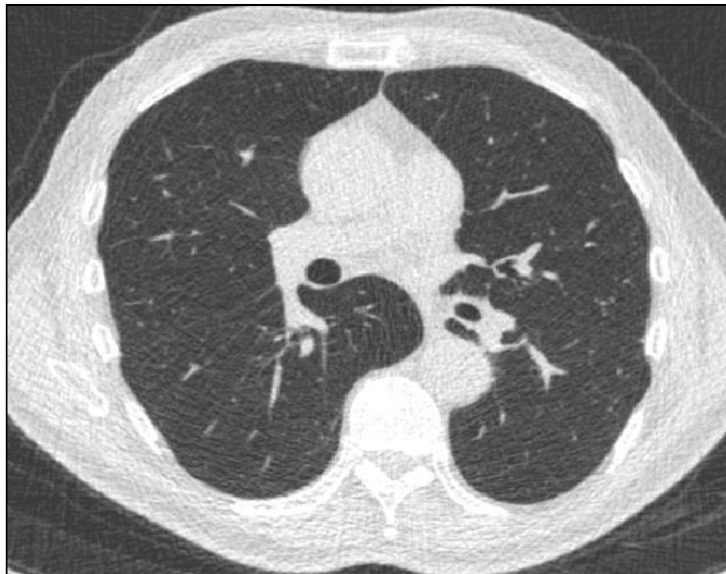


(b) 100% dose, 1mm slice thickness, medium kernel

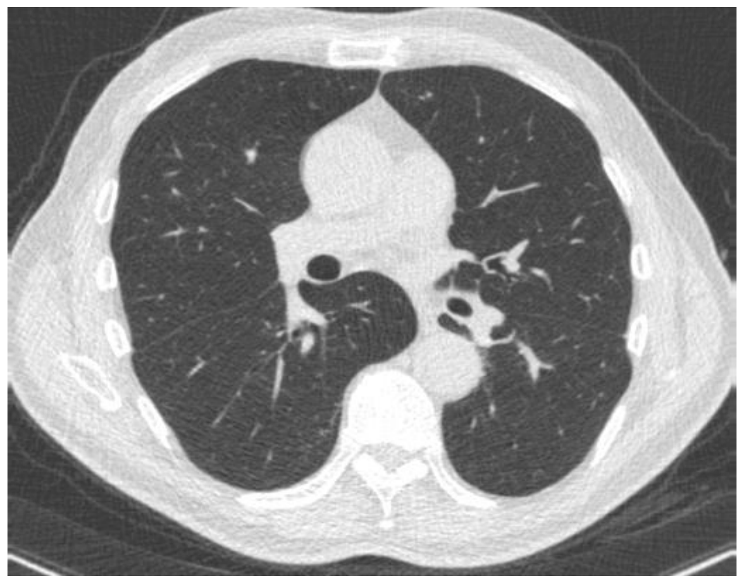


(c) 100% dose, 1mm slice thickness, sharp kernel

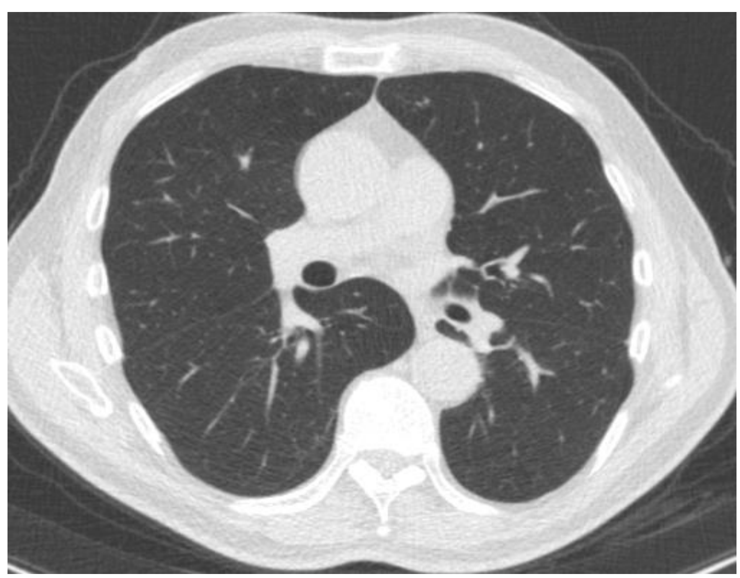
Figure S3. Lung CT images at 100% dose, 1mm slice thickness and three different kernels: a) smooth (k1), b) medium (k2), c) sharp (k3)



(a) 100% dose, 0.6mm slice thickness, medium kernel

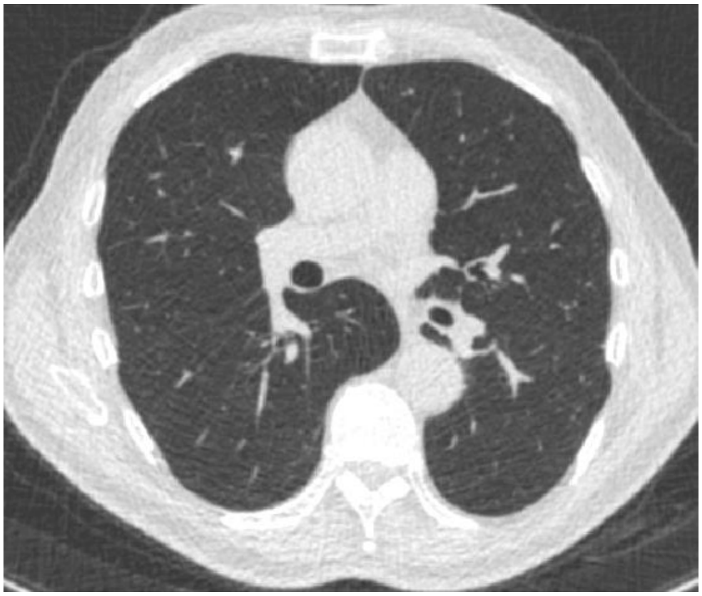


(b) 100% dose, 1mm slice thickness, medium kernel

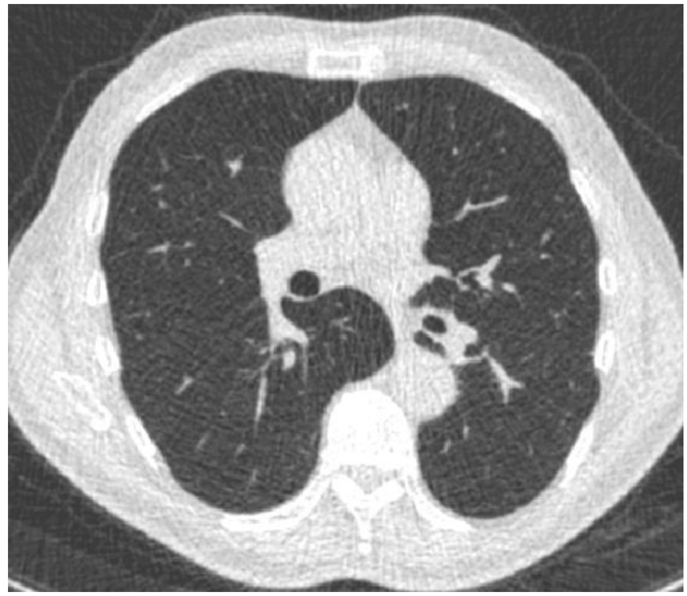


(c) 100% dose, 2mm slice thickness, medium kernel

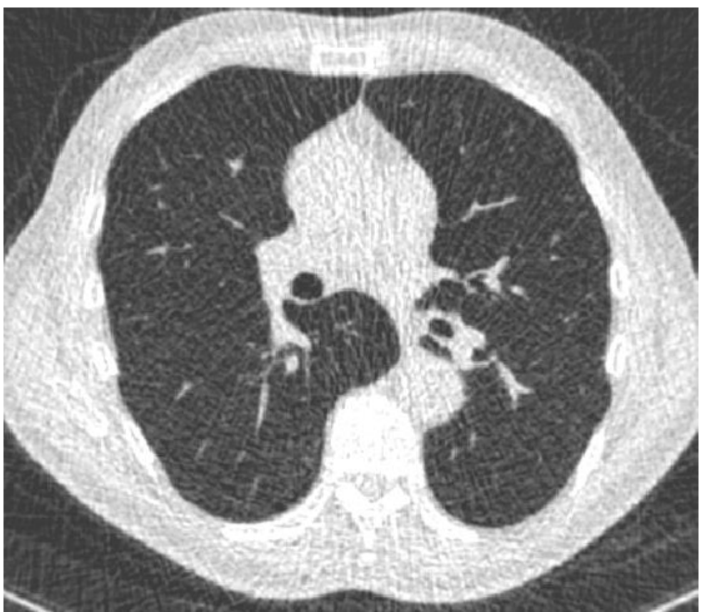
Figure S4. Lung CT images at 100% dose, medium kernel and three different slice thicknesses: a) 0.6mm, b) 1mm, c) 2mm.



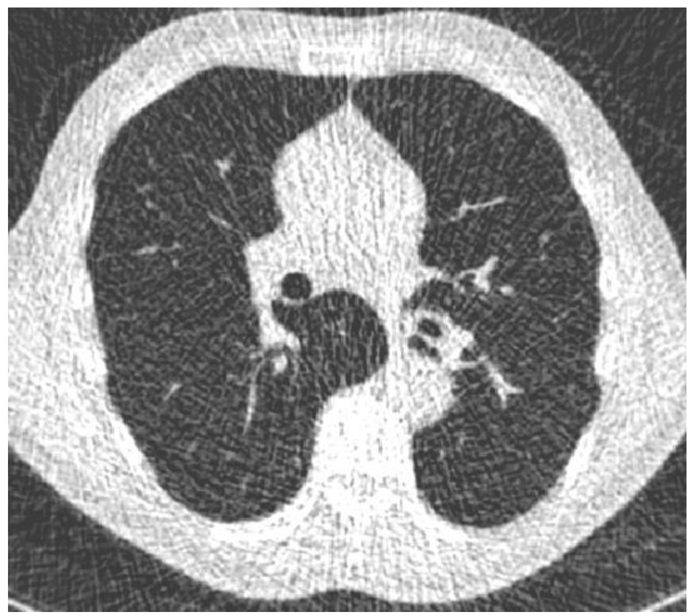
(a) 100 % dose, 0.6mm thickness, smooth kernel



(b) 50 % dose, 0.6mm thickness, smooth kernel



(c) 25 % dose, 0.6mm thickness, smooth kernel



(d) 10 % dose, 0.6mm thickness, smooth kernel

Figure S5. Lung CT images at 0.6mm slice thickness, smooth kernel and four different dose levels: a) 100%, b) 50%, c) 25%, d) 10%.