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Lung nodules are reliably detectable on ultra-low-dose CT utilising model-based iterative reconstruction with radiation equivalent to plain radiography

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AIM: To determine if ultra-low-dose (ULD) computed tomography (CT) utilising model-based iterative reconstruction (MBIR) with radiation equivalent to plain radiography allows the detection of lung nodules.

MATERIALS AND METHODS: Ninety-nine individuals undergoing surveillance of solid pulmonary nodules undertook a low-dose (LD) and ULD CT during the same sitting. Image pairs were read blinded, in random order, and independently by two experienced thoracic radiologists. With LD-CT as the reference standard, the number, size, and location of nodules was compared, and inter-rater agreement was established.

RESULTS: There was very good inter-rater agreement with regards nodules ≥4mm for both the LD- (k=0.931) and ULD-CT (k=0.869). One hundred and ninety-nine nodules were reported on the LD-CT by both radiologists and 196 reported on the ULD-CT, with no nodules reported only on the ULD-CT. This gives a sensitivity of 98.5% and specificity of 100% for ULD-CT with MBIR. The effective dose of radiation was significantly different between the two scans ($p<0.0001$), 1.67 mSv for the LD-CT and 0.13 mSv for the ULD-CT.

CONCLUSION: ULD-CT utilising MBIR and delivering radiation equivalent to plain radiography, allows detection of lung nodules with high sensitivity. The attendant 10-fold reduction in radiation may allow for dramatic reductions in cumulative radiation exposure.

Introduction

Computed tomography (CT) has revolutionised imaging in modern medicine. Expanding indications and improvements in CT technology with subsequent higher image

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resolution has led to frequent reporting of incidental findings including indeterminate lung nodules. In contrast to recent CT screening trials for lung cancer showing mortality benefit,[1] these incidental findings are often in patients with low risk for lung cancer, and surveillance rather than invasive investigation is recommended. There are well-established protocols for surveillance of these indeterminate nodules and patients commonly require multiple CT examinations over time.[2,3] Quantifying the risk attributable to radiation from CT examinations is difficult and the magnitude and significance of this risk remains controversial[4]; however, there is an understandable concern about cumulative ionising radiation exposure, particularly in low-risk patients, and minimisation of exposure is consistently recommended.[5–7]

Low-dose (LD)-CT (∼1 mSv) utilising a technique combining filtered back projection (FBP) with statistical iterative reconstruction (SIR) has become standard of care in the surveillance of lung nodules in many institutions. Although the risk attributable to radiation from a single scan at this dose is negligible, it is likely that individuals will be exposed to medical radiation for other reasons in their lifetime. In this context, rational dose limitation is desirable, but efforts to further reduce the radiation dose have been hampered by unacceptable noise-to-signal ratio. Recent advances in computing power have allowed the introduction of an advanced model-based iterative reconstruction (MBIR) technique in CT which may address this problem.

MBIR utilises a statistical algorithm to model the system optics, production of X-rays, their attenuation within tissues, and all sources of noise, thus enabling dramatic reductions in radiation dose by reducing that noise in the reconstructed images.[4,6,8,9] CT images can thus be obtained with a radiation exposure similar to a combined posteroanterior (PA)/lateral chest X-ray (0.06–0.1 mSv). At this very low dose, MBIR images remain somewhat "noisy", but given the high contrast between air and soft tissue within the lung, MBIR CT scanning techniques may still provide adequate resolution for nodules with minimal radiation exposure.

A previous pilot study has suggested promising results for the ability of MBIR CT scanning to detect lung nodules,[10–12] but as yet, the clinical utility of this type of "ultra-low-dose" CT (ULD-CT) for the surveillance of incidental lung nodules is uncertain. This prospective study was undertaken with the aim of assessing the accuracy of ULD-CT employing MBIR and delivering a radiation dose equivalent to plain chest radiography as compared to LD-CT using SIR/FBP in detecting lung nodules.

Materials and methods

Patients

The study protocol was approved by the local Human Research Ethics Committee (ref. 13305A). Consecutive adult patients undergoing CT surveillance for indeterminate solid lung nodules were recruited from a tertiary hospital between January 2014 and February 2015. Patients unable to give consent or breath-hold, or who clinically required standard dose imaging were not recruited. Demographic information, including risk factors for lung cancer, was collected by questionnaire.

CT protocol and image reconstruction

Both the standard LD-CT and ULD-CT were performed at the same sitting. Each scan was performed with a single breath-hold on the CT750 HD scanner (GE Healthcare, Milwaukee, WI, USA). The following parameters were used for both the LD-CT and ULD-CT: 100 kVp (<80 kg) and 120 kVp (>80 kg), 40 mm collimation, 1.375 pitch, 0.4 second rotation speed. For the LD-CT, tube current was modulated to achieve target dose–length product (DLP) of 70 mGy.cm (<80 kg) or 105 mGy.cm (>80 kg), whereas 10 mA was used for ULD-CT. Contrast medium was administered for the LD scan if indicated clinically. For comparison to previous literature, effective radiation was calculated from total DLP using a k-factor of 0.014, in addition to the now recommended 0.021.[13] The raw data were reconstructed into three standard orthogonal planes of 5 mm thickness along with additional coronal maximum intensity projection (MIP) images. The combined FBP/Adaptive Statistical Iterative Reconstruction (ASIR, GE Healthcare) technique was used for LD-CT, whereas the MBIR technique was used for ULD-CT (VEO, GE Healthcare).

Image review

Each of LD- and ULD-CT image sets was read independently by two experienced thoracic radiologists. Although the patients were known to have nodules, the radiologists reported the scans without knowledge of previous results. The scans were read in random order, blinded to the result of the paired scan. The number, size, and location of nodules were compared. Nodules reported on the LD scan were considered true positives if reported by both radiologists in the same position with a difference in size of ≤1 mm. A consensus meeting between the two radiologists was undertaken to determine true lung nodules if there were discrepant results.

Outcome/statistical analysis

Using a power of 0.9 and a significance level of 0.05, the sample size of 100 patients was determined to detect a drop in sensitivity of 3% or more, assuming an average of two nodules per patient. A pragmatic nodule size cut-off of 4 mm was utilised for all analyses, well within the now largely proposed significant size of 6 mm.[3,14] Using the LD-CTs of chest as the reference standard, the sensitivity, specificity, positive and negative predictive value of the ULD-CT chest in detecting nodules ≥4 mm was calculated for the whole group, and then stratified for sex, body mass index (BMI), and smoking status. Interobserver agreement was assessed by comparison of the two independent radiologist assessments using the Kappa statistic (GraphPad QuickCalcs 2016; http://graphpad.com/quickcalcs/kappa2/). The effective dose of radiation was compared with a paired *t*-test (GraphPad Prism 6.07, GraphPad Software, La Jolla, CA, USA, www.graphpad.com).

Results

In total, 103 patients were recruited to the study and had both scans performed as per protocol with four subjects withdrawing consent. The demographic data of the 99 analysed subjects is in Table 1. There were approximately equal numbers of men and women, with a median age of 67 years. They were overweight on average, with 1/5 being obese. Smoking was the main risk factor and while 30% had exposure to at least one risk factor other than tobacco, the majority of these (92%) were smokers. Overall, half the cohort had any significant risk factor for thoracic malignancy, and only 15% would have been eligible for screening in the National Lung Screening Trial (NLST).

The nodules were generally well seen on both the LD and ULD scans (Fig 1). There were a total of 440 (radiologist 1) and 469 (Radiologist 2) nodules reported on the standard LD scans, with 45% and 43% of these being ≥4 mm, respectively (see Table 2). There was very good agreement between the two reporting radiologists with regards nodules ≥4 mm (kappa=0.931). This was in contrast to nodules <4 mm where the agreement was only fair between radiologists (kappa=0.277). There were 200 and 201 nodules ≥4 mm reported in 76 patients by the two radiologists on the LD scan, with 199 agreed common nodules (Table 3). The nodules had a median diameter of 5 mm (interquartile range [IQR], 4–6) with lower lobe predominance. Half of all the nodules were present in the lower lobe, 98 nodules (49%), as compared to upper lobes, 52 nodules (26%). These 199 "true-positive" nodules were then used as the reference standard against which the ULD-CT was compared.

With respect to nodules ≥4 mm, all patients with nodules identified on the LD-CT also had nodules reported at ULD-CT. Both Radiologists reported 196 of the 199 nodules on ULD-CT (Table 3), very good agreement (k=0.869), with no nodules identified on the ULD-CT that were not reported on the LD-CT. This gives a sensitivity of 98.5%, specificity of 100%, a positive predictive value of 100% and a negative predictive value of 88.4%. There was no significant drop in sensitivity when comparing the lowest to highest quartile of BMI, smoking status or sex, all maintaining a sensitivity of >95% (Table 4).

In stark contrast, there was a highly significant 1-log difference between the effective dose (ED) of radiation delivered for the scans. A mean DLP of 79.33 mGy/cm equivalent to an effective dose of 1.67 mSv (SD±0.35) was delivered for the LD-CT (13), as compared to 6.23 mGy/cm, or 0.13 mSv (SD±0.04) for the ULD-CT ($p<0.0001$) when using a k-factor of 0.021 (Fig 2). Using the k-factor of 0.014 from the ICRP 60 recommendations, this equates to an effective dose of 1.11 mSv with LD-CT and 0.09 mSv with ULD-CT. When the dose was stratified for BMI, while the LD to ULD difference persisted, there was a significantly higher dose delivered in the highest quartile of BMI in the LD (1.852 versus 1.565 mSv; $p<0.0001$), but not ULD scans (0.157 versus 0.113; $p>0.05$). The radiation dose associated with the scout or "scanogram" image is not reported on this specific GE scanner and so is not factored into the effective dose reported.

Table 1
Baseline demographic information.

Scan pairs	99
Age (median [IQR])	67.4 [57.7–73.3]
Males %	51%
BMI (median [IQR])	27.3 [24.1–29.4]
BMI ≥30	21
Risk stratification	
Smoking	
Never	37 (37.4)
Ex-smoker	49 (49.5)
Smoker	13 (13.1)
Smoking intensity	
Pack years (median [IQR])	23.8 [9.7–40.5]
Years quit (median [IQR])	20 [1.5–25]
Asbestos exposure	21 (21.2)
Past extra-thoracic malignancy	20 (20.2)
Family history of lung cancer	19 (19.2)
Any risk factor[a]	50 (50.5)
30+pk years and quit <15 years	18 (18.2)
Fulfil NLST inclusion criteria	15 (15.2)

Data are *n* (%) unless otherwise indicated.
[a] Any risk factor includes ever smokers with ≥10 pack year smoking history, family history of lung cancer, past extra-thoracic cancer, or asbestos exposure.

Discussion

The discovery of indeterminate lung nodules is common at CT of the chest, coronary arteries, and abdomen. Accepted recommendations require between one and three scans for surveillance,[15] but studies have shown that concordance with surveillance guidelines is suboptimal often resulting in unnecessary scans.[16] At Monash Health, nodule incidence is similar in individuals at low and high risk for primary lung malignancy,[17] so like many others, techniques to reduce radiation exposure have been actively pursued. In the present study, ULD-CT utilising MBIR allows for the identification of nodules with high sensitivity, which is not affected by sex, BMI, or smoking status, in a cohort at varied risk for primary lung malignancy under surveillance for solid lung nodules. For these nodules (≥4 mm), there is good agreement between experienced thoracic radiologists, but this falls off sharply in nodules <4 mm. This high sensitivity is despite a more that 10-fold reduction in radiation dose to that equivalent to a PA/lateral chest X-ray, and importantly, the reduction is achievable regardless of BMI.

There is constant exposure to multiple sources of ionising radiation, both natural and man-made,[4,16] but unlike the majority of other sources, exposure to medical radiation is modifiable. CT contributes significantly to the burden of medical radiation exposure with up to 70% attributable to its use.[18] Although modelling is imperfect and highly debated, it has been estimated that a cumulative dose of <10 mSv may cause an additional cancer death in every 2500 people exposed.[19] Although this fairly modest risk is justifiable in high-risk individuals, in a younger, low-risk population, likely to have ongoing medical radiation

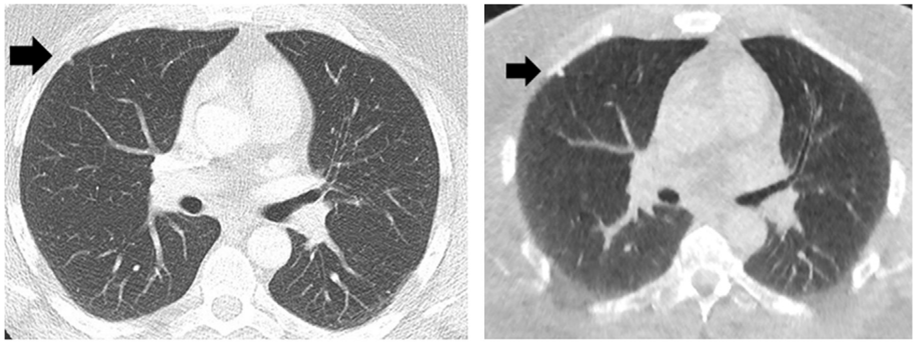

Figure 1 Nodules were clearly seen on both LD- (a) and ULD-CT (b) images.

Table 2
All nodules detected by radiologist and size on low-dose computed tomography.

	Radiologist 1	Radiologist 2	Both	Agreement kappa (SE)
Total	440	469	417	0.102 (0.056) poor
≥4 mm (% all nodules)	200 (45.4)	201 (42.9)	199 (47.7)	0.931 (0.039) very good
<4 mm (% all nodules)	241 (54.6)	268 (57.1)	218 (52.3)	0.277 (0.063) fair

exposure, the benefit is less clear and minimisation of additional radiation is desirable. Until recently, the clinical utility of iterative reconstruction techniques aimed at reducing radiation exposure whilst maintaining image quality has been limited by long reconstruction times, dependent on available computing power. MBIR is the latest technique to utilise an algorithm to model the production of the X-rays, the attenuation within the tissue, and all sources of noise, thus enabling further dramatic reductions in radiation dose level.[20,21]

Naturally, much research has focused on dose reduction using MBIR in children, with comparisons to FBP, FBP/ASIR and pure ASIR, showing consistently high-quality images with superior spatial resolution and reduced noise.[22–24] Early lung work focused on image quality, noise reduction, and clarity of anatomical features, showing that MBIR was superior to FBP, ASIR, and FBP/ASIR in all cases, at very low dose.[25–27] Although not specifically looking at lung nodule detection these were noted to be seen clearly. Yamada *et al.* showed that nodule detection was significantly better when comparing ULD-CT reconstructed with MBIR to that using FBP[12,20,28,29] and showing vastly improved noise levels, with an effective dose of 0.17±0.01 mSv. Similarly, Katsura *et al.* showed that compared to a reference standard dose CT, ULD-CT with MBIR was equivalent to LD-CT with ASIR for nodule detection, with a 78% reduction in radiation dose.[10]

The present study focused on a population of both high and low risk for lung malignancy, which were under surveillance for solid, non-calcified nodules. The current standard LD-CT (reconstructed with FBP/ASIR) was used as the reference, with the aim of assessing whether ULD-CT with MBIR could be substituted into clinical practice. In contrast to previous studies, the scanning protocol for the ULD-CT resulted in radiation exposure truly comparable to a PA/lateral chest X-ray, with an average of only 0.087±0.025 mSv (±SD), or 0.13 mSv using the more contemporary k-factor. This was not significantly different when the patients were stratified for sex or BMI, and represented a 92.2% dose reduction. This magnitude of reduction is similar to previous reports,[30,31] but the actual dose received in this study was half that reported in the literature.

Importantly, of the 199 nodules of ≥4 mm reported on the LD-CT by both thoracic radiologists, 196 were identified, giving 98.5% sensitivity, comparable with previous literature, and there was no difference in sensitivity when separated on the basis of BMI, sex, or smoking status. The non-identified nodules occurred in two patients who both had at least one other nodule that was identified of equal or larger dimensions, meaning crucially neither miss would have resulted in a change in follow-up.

Limitations

Given the study cohort were those under surveillance for solid nodules, no attempt was made to assess the performance of ULD-CT with MBIR in the detection of sub-solid

Table 3
Nodules identified on scan pairs with low-dose computed tomography (CT) as the reference standard.

	Low-dose CT	Ultra-low-dose CT	
		Radiologist 1	Radiologist 2
All lobes	199	196	196
RUL	33	32	33
RML	38	37	37
RLL	45	45	44
LUL	19	19	19
Lingula	11	11	11
LLL	53	52	52

RUL, RML, and RLL: right upper, mid, and lower lobe.
LUL and LLL, left upper and lower lobe.

Table 4
Sensitivity of ultra-low-dose computed tomography (ULD-CT) stratified by body mass index (BMI), smoking status, and sex.

	Low-dose scan	ULD scan		Sensitivity
		Radiologist 1	Radiologist 2	
BMI lowest quartile	49	47	49	98.2
BMI highest quartile	49	48	47	95.9
Smoking status (ever smoker >10pk yrs)	97	96	94	96.9
Smoking status (never smoker)	43	42	43	97.7
Sex (M)	113	112	112	99.1
Sex (F)	86	84	84	97.7

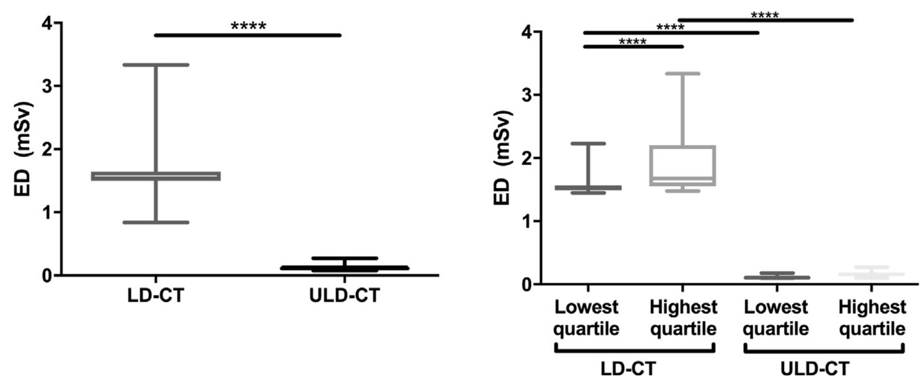

Figure 2 Effective dose of radiation delivered for ULD-CT is significantly lower than that for LD-CT regardless of BMI. ****$p<0.0001$.

nodules, although this has been evaluated previously in phantom models, with similar results to those reported here.[10,12] Although others have looked at the performance of MBIR in the context of volumetric analysis of nodules with limited success,[32] there was no attempt to investigate this in the present study as volumetric analysis is not routinely performed at Monash Health. Given the cross-sectional design of the study, the ability of ULD-CT with MBIR cannot be assessed to show change or stability of lung nodules over time.

In conclusion, ULD-CT with MBIR is able to detect solid lung nodules at a radiation dose comparable to plain chest radiography, with 98.5% sensitivity and 100% specificity. This high sensitivity is unaffected by a high BMI, sex, or position of the nodule. In addition to other measures to reduce medical radiation exposure, this MBIR technique that results in more than 10-fold reduction in radiation dose, could dramatically reduce cumulative radiation exposure. With the rapid evolution of CT technology, this MBIR or similar reconstructive technique may become standard for surveillance of solid lung nodules.

Conflict of interest

The authors declare no conflict of interest.

References

1. Holden WE, Lewinsohn DM, Osborne ML, *et al.* Use of a clinical pathway to manage unsuspected radiographic findings. *Chest J* 2004;**125**(5):1753–60.
2. Aberle DR, Adams AM, Berg CD, *et al.* Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011;**365**(5):395–409.
3. MacMahon H, Naidich DP, Goo JM, *et al.* Guidelines for management of incidental pulmonary nodules detected on CT images: from the Fleischner Society 2017. *Radiology* 2017:161659.
4. Gould MK, Donington J, Lynch WR, *et al.* Evaluation of individuals with pulmonary nodules: when is it lung cancer? Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2013;**143**(5 Suppl):e93S–120S.
5. Brenner DJ. Radiation risks potentially associated with low-dose CT screening of adult smokers for lung cancer. *Radiology* 2004;**231**(2):440–5.
6. AAPM. *AAPM position statement on radiation risks from medical imaging procedures*. College Park, MD: The American Association of Physicists in Medicine; 13 Dec 2011. Available at: http://www.aapm.org/org/policies/details.asp?id=318&type=PP2011. [Accessed 29 June 2016].
7. Smith-Bindman R, Lipson J, Marcus R, *et al.* Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med* 2009;**169**(22):2078–86.
8. ICRP. Radiological protection and safety in medicine. *Ann IRCP* 1996;**26**(2).
9. Amis Jr ES, Butler PF, Applegate KE, *et al.* American College of Radiology white paper on radiation dose in medicine. *J Am Coll Radiol* 2007;**4**(5):272–84.
10. Yamada Y, Jinzaki M, Tanami Y, *et al.* Model-based iterative reconstruction technique for ultralow-dose computed tomography of the lung: a pilot study. *Invest Radiol* 2012;**47**(8):482–9.
11. Evans K, Sych T. *White paper: new levels of CT image performance and new levels in radiation dose managment* (Intel Corporation). May 25, 2016. Published February 3, 2012. Downloaded from:, https://software.intel.com/en-us/articles/new-levels-of-ct-image-performance-and-new-levels-in-radiation-dose-management.
12. Neroladaki A, Botsikas D, Boudabbous S, *et al.* Computed tomography of the chest with model-based iterative reconstruction using a radiation exposure similar to chest X-ray examination: preliminary observations. *Eur Radiol* 2013;**23**(2):360–6.

13. ICRP. The 2007 recommendations of the international commission on radiological protection. ICRP publication 103. *ICRP* 2007;**37**(2–4):1–332.
14. Yip R, Henschke CI, Yankelevitz DF, *et al*. CT screening for lung cancer: alternative definitions of positive test result based on the national lung screening trial and international early lung cancer action program databases. *Radiology* 2014;**273**(2):591–6.
15. Wiener RS, Gould MK, Slatore CG, *et al*. Resource use and guideline concordance in evaluation of pulmonary nodules for cancer: too much and too little care. *JAMA Intern Med* 2014;**174**(6):871–80.
16. MacMahon H, Austin JH, Gamsu G, *et al*. Guidelines for management of small pulmonary nodules detected on CT scans: a statement from the Fleischner Society. *Radiology* 2005;**237**(2):395–400.
17. Robertson J, Nicholls S, Bardin P, *et al*. Incidental pulmonary nodules are common on ct coronary angiogram and have a significant cost impact. *Heart Lung Circ* 2019 Feb;**28**(2):295–301. https://doi.org/10.1016/j.hlc.2017.11.004.
18. Elgazzar AH, Kazem N. Biological effects of ionizing radiation. In: Elgazzar AH, editor. *The pathophysiological basis of nuclear medicine*. Cham, Switzerland: Springer International Publishing; 2015. p. 715–26.
19. Lee CI, Haims AH, Monico EP, *et al*. Diagnostic CT scans: assessment of patient, physician, and radiologist awareness of radiation dose and possible risks. *Radiology* 2004;**231**(2):393–8.
20. Yamada Y, Jinzaki M, Hosokawa T, *et al*. Dose reduction in chest CT: comparison of the adaptive iterative dose reduction 3D, adaptive iterative dose reduction, and filtered back projection reconstruction techniques. *Eur J Radiol* 2012;**81**(12):4185–95.
21. Beister M, Kolditz D, Kalender WA. Iterative reconstruction methods in X-ray CT. *Phys Med* 2012;**28**(2):94–108.
22. Mathieu KB, Ai H, Fox PS, *et al*. Radiation dose reduction for CT lung cancer screening using ASIR and MBIR: a phantom study. *J Appl Clin Med Phys* 2014;**15**(2):4515.
23. Fleischmann D, Boas FE. Computed tomography—old ideas and new technology. *Eur Radiol* 2011;**21**(3):510–7.
24. Hsieh J, Nett B, Yu Z, *et al*. Recent advances in CT image reconstruction. *Curr Radiol Rep* 2013;**1**(1):39–51.
25. Smith EA, Dillman JR, Goodsitt MM, *et al*. Model-based iterative reconstruction: effect on patient radiation dose and image quality in pediatric body CT. *Radiology* 2014;**270**(2):526–34.
26. Son SS, Choo KS, Jeon UB, *et al*. Image quality of CT angiography with model-based iterative reconstruction in young children with congenital heart disease: comparison with filtered back projection and adaptive statistical iterative reconstruction. *Int J Cardiovasc Imaging* 2015;**31**(Suppl. 1):31–8.
27. Ernst CW, Hulstaert TL, Belsack D, *et al*. Dedicated sub 0.1 mSv 3DCT using MBIR in children with suspected craniosynostosis: quality assessment. *Eur Radiol* 2016;**26**(3):892–9.
28. Ichikawa Y, Kitagawa K, Nagasawa N, *et al*. CT of the chest with model-based, fully iterative reconstruction: comparison with adaptive statistical iterative reconstruction. *BMC Med Imaging* 2013;**13**:27.
29. Katsura M, Matsuda I, Akahane M, *et al*. Model-based iterative reconstruction technique for radiation dose reduction in chest CT: comparison with the adaptive statistical iterative reconstruction technique. *Eur Radiol* 2012;**22**(8):1613–23.
30. Katsura M, Matsuda I, Akahane M, *et al*. Model-based iterative reconstruction technique for ultralow-dose chest CT: comparison of pulmonary nodule detectability with the adaptive statistical iterative reconstruction technique. *Invest Radiol* 2013;**48**(4):206–12.
31. Messerli M, Kluckert T, Knitel M, *et al*. Ultralow dose CT for pulmonary nodule detection with chest x-ray equivalent dose—a prospective intra-individual comparative study. *Eur Radiol* 2017;**27**(8):3290–9.
32. Chen B, Barnhart H, Richard S, *et al*. Volumetric quantification of lung nodules in CT with iterative reconstruction (ASiR and MBIR). *Med Phys* 2013;**40**(11):111902.