Scientific Research Publishing

Open Journal of Medical Imaging, 2021, 11, 48-57
https://www.scirp.org/journal/ojmi
ISSN Online: 2164-2796
ISSN Print: 2164-2788

Strategies to Improve CT Dose Optimization for Hybrid PET/CT Imaging

Abdel-Baset Bani Yaseen[1], Yasmin Md Radzi[2], Hussain M. Almohiy[3], Akshay Kohli[4], Mohammad Rawashdeh[1]

[1]Faculty of Applied Medical Sciences, Jordan University of Science and Technology, Irbid, Jordan
[2]School of Physics, Universiti Sains Malaysia, Penang, Malaysia
[3]Department of Radiological Sciences, College of Applied Medical Sciences, King Khalid University, Abha, Saudi Arabia
[4]Department of Radiology, John Hunter Hospital, New Lambton Heights, Australia
Email: ambanyyasin170@ams.just.edu.jo

How to cite this paper: Yaseen, A.-B.B., Radzi, Y.Md., Almohiy, H.M., Kohli, A. and Rawashdeh, M. (2021) Strategies to Improve CT Dose Optimization for Hybrid PET/CT Imaging. *Open Journal of Medical Imaging*, **11**, 48-57.
https://doi.org/10.4236/ojmi.2021.112005

Received: March 27, 2021
Accepted: May 24, 2021
Published: May 27, 2021

Abstract

Background: To evaluate whether current dose reduction strategies for the CT component of hybrid Positron Emission Tomography—Computed Tomography (PET/CT) systems could reduce patient dose with maintaining adequate image quality for PET/CT studies. Materials and Methods: Literature survey was initially based on the selection of keywords and years of publication to identify potentially relevant articles, then the further search was conducted on the authors and references from these articles. The abstract of each article was first appraised to decide whether the content was relevant to this research question. The articles were classified into five groups: studies on dosimetry, studies on radiation-induced diseases, studies on dose reduction methods for CT-based attenuation correction (CTAC), studies on dose reduction methods for CT localization, and studies on reducing the need for a full-dose diagnostic CT in PET/CT imaging. 58 peer-reviewed articles were selected and appraised and 29 articles were used to compose this literature review. Results: The published nuclear medicine and medical physics literature were reviewed. CT dose contributed 47% - 81% of the total effective dose of a standard PET/CT study and was associated with radiation-induced diseases. The dose reduction techniques were extracted and divided into three categories: reducing the CT dose for attenuation correction (AC) and localization, selectively localizing CT use, and reducing the need for a full-dose diagnostic CT. Conclusion: Three strategies have been demonstrated, with high potential for reducing patient dose while maintaining an adequate CT image quality, used for CTCA localization and diagnosis, respectively.

Keywords

CT Scan, Radiation Dose, Hybrid Imaging, PET Systems, CTAC

1. Introduction

Over the past 30 years, PET imaging has improved from a research tool to a strong imaging tool. The continues development of hardware, software, imaging techniques and radiopharmaceuticals, lead to expanded the PET role in many areas, including, but not limited to cardiology, neurology, endocrinology, image-guided therapy planning, biopsy, delineation of pathologic volume, treatment management and pharmacology research [1] [2].

PET provides functional information according to the bio-distribution of an administered radiopharmaceutical. However, precise localization of functional information with anatomical reference is the challenging because of the relatively low spatial resolution. The theoretical spatial resolution of FDG^{18}PET imaging is approximately 1 mm, but the spatial resolution of clinical PET imaging is between 3.3 and 7 mm [3]. The anatomical landmarks that are demonstrated on CT or magnetic resonance image (MRI) images are often blurry or absent on PET images. In addition to that, the uptake of PET radiopharmaceuticals may be non-specific [3].

The first hybrid PET/CT system for clinical usage was made commercially available in 2001 [4]. Nowadays, as the significant advantage of hybrid PET/CT compared with stand-alone PET has grown, the major manufacturers do not produce stand-alone PET anymore [3] [5] [6] [7].

Although hybrid PET/CT has made a considerable clinical impact, but the frequent usage will be generating growing concern about the increase of ionizing radiation that exposure patients and lead to the possibility of radiation-induced diseases [8].

1.1. Dosimetry of PET/CT

The PET effective dose is typically calculated based on the Medical Internal Radiation Dose (MIRD) schema, that developed by the MIRD Committee of the Society of Nuclear Medicine. The CT dose of PET/CT is determined by the same way as a stand-alone CT, typically characterized by dosimetry metrics such as computed tomography (CT) dose index (CTDIvol) and dose-length product (DLP) [9].

CT dose depends on many parameters such as current, voltage, gantry rotation speed, pitch, and patient characteristics. The radiation doses of 18F-FDG PET/CT scans are different between countries, clinics, equipment, protocols and patients. The overall dose of 18F-FDG PET/CT ranges from 8 mSv to 29.8 mSv. The CT component appears to account at least 54% from the total dose of a whole-body, with a maximum of 81% [8].

A retrospective study conducted by Huang *et al.* (2009) reported that an average of 18F-FDG PET effective dose was 6.2 mSv, and CT effective dose was 13 - 24.8 mSv (accounting for 54% - 81% from the total effective dose) [10].

Wu *et al.* (2004) found that an average PET effective dose was 10.7 mSv, and for CT effective dose was 19.0 mSv (accounting for 64% of the total effective

dose) [9]. A study on oncology patients conducted by Khamwan *et al.* (2010) reported an average PET dose of 4.4 mSv and a CT dose of 14.5 mSv (contributing 77% of the total effective dose) [11]. A recent study on pediatric patients by Kornerup *et al.* (2015) found that an average of CT effective dose of 35.0 mSv, accounting for 75% of the total effective dose from PET/CT scans that have high-resolution diagnostic quality [2].

1.2. Radiation-Induced Health Risk

The relationship between ionizing radiation exposure and radiation-induced disease is becoming increasingly noteworthy. The health risks of ionizing radiation exposure from medical imaging studies have become an important issue, drawing attention from both medical professionals and the public during the past 30 years [2] [12] [13].

The research conducted by Huang *et al.* (2009) is the first studied published to investigate the rate of cancer incidence induced by ionizing radiation from hybrid PET/CT imaging, though the study covered only the U.S. and Hong Kong populations [10].

The estimation of the effective dose was based on dose coefficients and tissue weighting factors recommended by ICRP publication 80 and ICRP publication 103. The average 18F-FDG PET effective dose was 6.23 mSv. The CT effective doses varied between 7.22 mSv and 27.3 mSv [12] [13] [14].

The sum of the effective doses from PET and CT ranged from 13.45 mSv to 32.18 mSv. As a result, the CT effective dose accounted for 54% - 81% of the total effective dose. The lifetime attributable risk (LAR) of cancer was calculated by the method introduced in the BEIR VII report. Huang *et al.* (2009) [10] demonstrated that a person who received an effective dose of 32.18 mSv from an 18F-FDG PET/CT scan at the age of 20 was expected to have LAR of cancer of 0.514% (for the U.S. population) or 0.622% (for the Hong Kong population); LAR of cancer increases as age decreases ("Biological Effects of Ionizing Radiation (BEIR) VII report", Committee on the Biological Effects of Ionizing, 2006).

The BEIR VII report and its method of estimating LAR sparked a series of critical reviews from researchers, including Calabrese *et al.* (2014) [15], Crowley *et al.* (2014) [16], Einstein *et al.* (2007) [17] and O'Connor *et al.* (2015). They argued about the validity of the BEIR VII report and the hypothesized linear no-threshold model application. However, they all agreed that low-dose radiation exposure increases the lifetime probability of developing cancers and other radiation-induced diseases [18]. Furthermore, recent studies have demonstrated that the vulnerability to radiation increases dramatically with decreasing age (Rossi *et al.*, 2016) [17] [19].

With the same radiation dose, infants were 10 times more vulnerable to ionizing radiation than adults (Goodman *et al.*, 2015) [18] [19]. The LAR of secondary cancers for a 10-year-old child was 15% per Sievert, whereas for a 40-year-old adult it was 3.8% per [12] [20]. Hence, it is essential to evaluate whether dose reduction strategies for the CT component of hybrid PET/CT sys-

tems could reduce patient dose while maintaining adequate image quality for PET/CT studies.

Was 15% per Sievert, whereas for a 40-year-old adult it was 3.8% per Sievert. Hence, it is essential to evaluate whether dose reduction strategies for the CT component of hybrid PET/CT systems could reduce patient dose while maintaining adequate image quality for PET/CT studies [21].

2. Materials and Methods

The literature survey was initially based on the selection of keywords (PET/CT; dose; reduction; CTAC and/or localization and/or diagnostic CT) and years of publication (2010-2020). Then from these results, further research was conducted on the authors and references of these articles. The abstract of each selected article was appraised to decide whether the content was relevant to this research question. Then, the selected articles were appraised and classified into six groups: studies on dosimetry; studies on radiation-induced diseases; studies on dose reduction methods for CTAC; studies on dose reduction methods for CT localization; studies on reducing the need for a full-dose diagnostic CT in PET/CT imaging; and other studies relevant to this research question.

3. Results and Discussion

3.1. Results

58 peer-reviewed articles were selected and reviewed, and 31 articles were used to compose this literature review. The published nuclear medicine and medical physics literature indicate that CT dose contributed 47% - 81% of the total effective dose of a routine PET/CT study, and was associated with radiation-induced diseases. The dose reduction techniques were extracted and grouped into three categories: reducing the CT dose for attenuation correction (AC) and localization; selectively using localization CT; and reducing the need for full-dose diagnostic CT scans. Study on automatic tube current modulation (ATCM) and reconstruction algorithms were not intentionally reviewed, as they are not dosed reduction methods specific to the CT component of PET/CT [22].

3.2. CT-Based Attenuation Correction (AC) Strategy

The CT dose for AC can be 10 - 100 times lower than that of a diagnostic CT, as the tube current of ultra-low-dose CTAC can be reduced to as low as 5 - 10 mA at reduced kVp [23] [24]. Fahey *et al.* (2007) conducted a phantom study to investigate the minimum dose required to generate an adequate CTAC map for PET imaging. Four pediatric and one medium adult-sized anthropomorphic phantoms were used for the dose measurement. The CT dose was measured at different CT tube currents (5, 10, 20, 40, 80 and 160 mA) and voltages (80, 100, 120, 140 and 160 kVp) [20].

The result showed the reduction in the current (from 80 to 10 mA) at 80 keV resulted in a 400% increase in CT noise, but only a 2% increase in the PET image

noise in all phantoms. With the pediatric phantoms, the minimum current was reduced to 5 mA at 80 kVp; with adult phantoms, the minimum current was 10 mA. An increase in CT noise did not correspond to a significant increase in PET noise; the PET images reconstructed by CTAC with different current settings (5 - 80 mA) were indistinguishable [25].

The reduction in the current (from 160 to 10 mA) and voltage (from 140 to 80 kVp) resulted in an approximately 100-fold effective dose reduction. The result of this study was consistent with the earlier study conducted by Kamel *et al.* (2002) [23], which demonstrated that the variation in tube current did not lead to a substantial difference in the quantification of 18F-FDG uptake [20] [23] [24]. Similar to Fahey *et al.* (2007) [20], two other studies conducted by Kamel (2002) [23] and Xia *et al.* (2009) [24] also focused on the reduction in CT tube current and voltage, supporting the same conclusion.

A later study conducted by Xia *et al.* (2012) [22] focused on a combination of CT modification and noise suppression methods, yielding an unbiased CTAC map at an ultra-low dose level. Xia *et al.* (2012) [24] developed further CT modifications, including tube current and voltage reduction, spectra filtration, reconstruction algorithms and post-process method. The study used a computer-assisted tomography simulator (CatSim) to simulate CT dose exposure with different parameters and imaging conditions, including tube mA and kVp, radiation dose, beam hardening, filtration, and scattering. The study simulated CT tube current at 0.5, 1, 5, 10, 20, 25, 50 and 100 mA; CT voltage at 80, 100, 120 and 160 kVp; and copper filtration at a thickness of 0, 0.25, 0.5 and 1.0 mm.

Then, each combination of these three parameters was post-processed at different sinogram smoothing levels: no sinogram smoothing, 20 boxcar smoothing, and 20 3 × 3 boxcar plus adaptive trimmed mean (ATM) filtering. 1080 sets of CTAC data were simulated with different noise levels to assess PET bias. The study concluded that within: 5% of PET bias, increased filtration substantially narrowed the spectrum, resulting in increased mean energy at all kVp settings. In fact, with a tube current of 13 mA, the radiation exposure at the narrowest energy spectra of 140 kVp with 1 mm Cu filtration showed a 66% dose reduction compared to that of unfiltered 80 kVp spectra, reducing the dose from 0.42 mGy to 0.14 mGy. Also, by applying 20 3 × 3 boxcars and ATM filtering, the current could be reduced from 13 mA to less than 4 mA at 140 kVp, while the CT data still exhibited a low noise level and the PET image bias was still below 5%.

Very recently, based on the studies conducted by Fahey *et al.* (2007) [20], Brady and Shulkin (2015 [25] conducted a study on ultra-low-dose CTAC for pediatric PET/CT scans. The study evaluated an aggressive CT dose reduction method while applying 100% adaptive statistical iterative reconstruction (ASIR). They used an anthropomorphic phantom to evaluate the change in CT noise and Hounsfield units value at increasingly lower CT tube currents. The tube current modulation software controlled the tube current. For example (AutomA. and SmartmA) and gradually decreased to 10% of baseline computed tomography (CT) attenuation correction (CTAC) images was reconstructed with 100% ASIR

to reduce CT noise. Then the PET data were reconstructed using CTAC through an iterative algorithm.

The result indicated that, with A 90% reduction from the baseline CTDivol, there was no statistically significant change to the The use of standardized uptake values (SUV), background uniformity or spatial resolution of the PET images. Based on the basic phantom study, Brady and Shukl (2015) [25] implemented this 100% ASIR method in 140 accrued pediatric PET/CT scans. The current was set according to the patient's weight. There was no statistically significant difference in the noise level between the CTAC of 10 mA with 100% ASIR and the original CTAC of 80 mA. There was also no statistically significant change to the SUV in the PET images with a CTAC of 10 mA with 100% ASIR, compared with the original PET image with a CTAC of 80 mA. The estimated effective dose reduction for patients of various weights was between 62% and 86%.

As demonstrated above, Fahey *et al.* (2007) [20], Xia *et al.* (2009) [22], Alessio *et al.* (2009) [26], Xia *et al.* (2012) [24], and Brady *et al.* (2015) [25] suggested that, if diagnostic CT and detailed anatomical localization are not required, low-dose/ultra-low-dose CT is feasible for CTAC. The CTAC dose can be reduced from a range of 3.2 - 8.3 mSv to 0.9 - 3.2 mSv. This is especially beneficial for radiation-sensitive patients such as children, young adults and pregnant women [2] [27] [28] [29]. Another study conducted evaluated a new CT dose reduction method for PET/CT imaging, applying the "selective CT" technique for localization in follow-up studies of pediatric patients with Langerhans cell histiocytosis. The hypothesis was that the total dose from the combination of the low-dose CTAC and the regional localization CT was expected to be considerably lower than that of a full-range CT scan for both CTAC and localization purposes [30] [31] [32].

A group of 34 patients was imaged with the "selective CT" protocol, consisting of a low-dose CTAC scan and a regional localization CT scan. The low-dose CTAC was performed at the low-dose parameters (80 kVp; 10 mA) described by Fahey *et al.* (2007) [20], with an average effective dose of 1.65 mSv, moderately higher than that of the ultra-low dose CT protocol described by Brady *et al.* (2015) [25]. Then, a selective localization CT scan of a higher dose (100 kVp; 25 mA) was immediately repeated at the bed position of pathologic or equivocal PET findings. Another group of 17 patients was imaged using full-range CT (100 kVp; 25 mA) for both CTAC and whole-body localization.

With the selective CT technique, the average effective dose from low-dose CTAC settings was 1.65 mSv, whereas the average effective dose from repeated localization CT was 1.19 mSv. Therefore, the average total effective dose was 2.84 mSv. In contrast, the average effective dose from the full-range CT for both CTAC and localization was 6.3 mSv (5.2 to 7.4 mSv). As a result, a dose reduction of 54.9% from the CT component alone was achieved. Hence, Gelfand *et al.* (2015) [33] concluded that, with selective CT techniques, the effective dose from a whole-body 18F-FDG PET/CT scan can be considerably reduce.

3.3. Reduce the Need for Full-Dose Diagnostic CT

The CT component of a state-of-the-art PET/CT scanner has the same imaging capacity as a dedicated stand-alone CT scanner, offering CT images of full diagnostic quality with or without contrast enhancement. Some studies have argued that the use of contrast media in PET/CT might overestimate the standardized uptake value (SUV) due to the over-scaling of CTAC. However, recent studies by Aschoff *et al.* (2012) [34] and Muto *et al.* (2014) [31] demonstrated that the overestimation of SUV was insignificant and did not influence the diagnostic decision and patient management.

It is a standard procedure at many PET centers to perform a full-dose diagnostic CT for detecting and staging malignancies. Adding diagnostic CT to PET imaging is associated with improved diagnostic accuracy in certain scenarios [35]. An earlier study by Kuelh *et al.* (2007) [36] suggested that PET/CT imaging was recommended to be performed with full-dose contrast-enhanced CT in assessment for initial chemotherapy, radiotherapy, non-small cell lung cancer, colorectal cancer, nasopharyngeal carcinoma, gastrointestinal stromal tumors, and locally ablative therapy.

However, an additional full-dose diagnostic CT, as well as a PET/CT scan, has some considerable drawbacks, including lower patient flow, work delay and most importantly, significantly higher patient dose. The reported effective dose of a typical full-dose contrast-enhanced CT scan used in PET/CT studies may range from 11 mSv to 40 mSv [37]. Therefore, the tradeoff between image quality and patient dose should be investigated to comply with the as low as reasonably achievable (ALARA) principle as much as possible.

Another study conducted by Goodman *et al.* (2015) [18] compared the diagnostic accuracy of PET/CT imaging between low-dose CT without breath-holding (LDCD) and contrast-enhanced full-dose CT with breath-holding (CECD). The result suggested that the sensitivity and specificity were 97.1% and 95% for PET with LDCT, and 100% and 95% for PET with CECT, respectively. With similar diagnostic accuracy, low-dose unenhanced CT was associated with an average dose reduction of 4.99 mSv.

In addition, Goodman *et al.* (2015) [18] demonstrated that there was no significant difference between low-dose CT and full-dose enhanced diagnostic CT used in PET imaging for initial staging of lymphomas. As the above studies indicate, the use of additional full-dose diagnostic CT in PET studies should be carefully justified and reviewed by a nuclear medicine professional, as evidence is accumulating that the benefit of performing a full-dose diagnostic CT may not outweigh the radiation risks.

4. Conclusion

As the International Committee on Radiological Protection (ICRP, 2007) stated, firstly, a referral for a PET/CT should be justified in a patient-specific manner to avoid unnecessary exposure; secondly, the radiation exposure from a PET/CT

study should be just sufficient to generate reasonably achievable high-quality diagnostic information, while applying the As Low As Reasonably Achievable (ALARA) principle as best as possible. The three CT dose reduction strategies discussed above have a high potential for reducing patient dose while maintaining an adequate CT image quality used for CTAC, localization and diagnostic purposes, achieving better image optimization. With ongoing development in CT hardware, software and modified protocols, we can forecast a further reduction in dose from the component, and hence a further improvement in PET/CT imaging optimization.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Kapoor, V., McCook, B.M. and Torok, F.S. (2004) An Introduction to PET-CT Imaging. *RadioGraphics*, **24**, 523-543. https://doi.org/10.1148/rg.242025724

[2] Kornerup, J.S., Brodin, P., Birk Christensen, C., Björk-Eriksson, T., Kiil-Berthelsen, A., Borgwardt, L., *et al.* (2015) Use of PET/CT Instead of CT-Only When Planning for Radiation Therapy Does Not Notably Increase Life Years Lost in Children Being Treated for Cancer. *Pediatric Radiology*, **45**, 570-581. https://doi.org/10.1007/s00247-014-3197-4

[3] Mettler Jr., F.A. and Guiberteau, M.J. (2012) Essentials of Nuclear Medicine Imaging: Expert Consult-Online and Print. Elsevier Health Sciences, Philadelphia.

[4] Beyer, T., Czernin, J. and Freudenberg, L.S. (2011) Variations in Clinical PET/CT Operations: Results of an International Survey of Active PET/CT Users. *Journal of Nuclear Medicine*, **52**, 303-310. https://doi.org/10.2967/jnumed.110.079624

[5] Blodgett, T.M., Meltzer, C.C. and Townsend, D.W. (2007) PET/CT: Form and Function. *Radiology*, **242**, 360-385. https://doi.org/10.1148/radiol.2422051113

[6] Hany, T.F., Steinert, H.C., Goerres, G.W., Buck, A. and von Schulthess, G.K. (2002) PET Diagnostic Accuracy: Improvement with In-Line PET-CT System: Initial Results. *Radiology*, **225**, 575-581. https://doi.org/10.1148/radiol.2252011568

[7] Dempsey, C. (2011) Lessons Learned from a HDR Brachytherapy Well Ionisation Chamber Calibration Error. *Australasian Physical & Engineering Sciences in Medicine*, **34**, 529-533. https://doi.org/10.1007/s13246-011-0095-z

[8] Bolch, W.E., Eckerman, K.F., Sgouros, G. and Thomas, S.R. (2009) MIRD Pamphlet No. 21: A Generalized Schema for Radiopharmaceutical Dosimetry—Standardization of Nomenclature. *Journal of Nuclear Medicine*, **50**, 477-484. https://doi.org/10.2967/jnumed.108.056036

[9] Wu, T.-H., Huang, Y.-H., Lee, J.J.S., Wang, S.-Y., Wang, S.-C., Su, C.-T., *et al.* (2004) Radiation Exposure during Transmission Measurements: Comparison between CT- and Germanium-Based Techniques with a Current PET Scanner. *European Journal of Nuclear Medicine and Molecular Imaging*, **31**, 38-43. https://doi.org/10.1007/s00259-003-1327-6

[10] Huang, B., Law, M.W.M., Mak, H.K.F., Kwok, S.P.F. and Khong, P.L. (2009) Pediatric 64-MDCT Coronary Angiography with ECG-Modulated Tube Current: Radiation Dose and Cancer Risk. *American Journal of Roentgenology*, **193**, 539-544.

https://doi.org/10.2214/AJR.08.1920

[11] Khamwan, K., Krisanachinda, A. and Pasawang, P. (2010) The Determination of Patient Dose from ^{18}F-FDG PET/CT Examination. *Radiation Protection Dosimetry*, **141**, 50-55. https://doi.org/10.1093/rpd/ncq140

[12] Valentin, J. (2007) ICRP Publication 103. *Annals of the ICRP*, **37**, 1-34.

[13] Vivekananthan, D.P., Penn, M.S., Sapp, S.K., Hsu, A. and Topol, E.J. (2003) Use of Antioxidant Vitamins for the Prevention of Cardiovascular Disease: Meta-Analysis of Randomised Trials. *Lancet*, **361**, 2017-2023. https://doi.org/10.1016/S0140-6736(03)13637-9

[14] Moussa, H.M. and Melanson, M.A. (2013) Translation of Dose Coefficients from ICRP 53 to ICRP 80. *Health Physics*, **104**, 224-226. https://doi.org/10.1097/HP.0b013e3182758035

[15] Calabrese, E.J. and O'Connor, M.K. (2014) Estimating risk of low Radiation Doses—A Critical Review of the BEIR VII Report and Its Use of the Linear No-Threshold (LNT) Hypothesis. *Radiation Research*, **182**, 463-474. https://doi.org/10.1667/RR13829.1

[16] Crowley, S.J., Cain, S.W., Burns, A.C., Acebo, C. and Carskadon, M.A. (2015) Increased Sensitivity of the Circadian System to Light in Early/Mid-Puberty. *Journal of Clinical Endocrinology & Metabolism*, **100**, 4067-4073. https://doi.org/10.1210/jc.2015-2775

[17] Rossi, L., Zito, F., Galetta, G., Florimonte, L., Orunesu, E., Castellani, M., *et al.* (2016) 8F-FDG Whole Body PET/CT Dose Evaluation in Pediatric Patients. *Physica Medica*, **32**, 112. https://doi.org/10.1016/j.ejmp.2016.01.388

[18] Goodman, S.Z., Rosenblum, J., Tuna, I., Levsky, J.M., Ricafort, R. and Taragin, B. (2015) Is Dedicated Chest CT Needed in Addition to PET/CT for Evaluation of Pediatric Oncology Patients? *Clinical Imaging*, **39**, 794-798. https://doi.org/10.1016/j.clinimag.2015.05.005

[19] Kim, Y.Y., Shin, H.J., Kim, M.-J. and Lee, M.-J. (2016) Comparison of Effective Radiation Doses from X-Ray, CT, and PET/CT in Pediatric Patients with Neuroblastoma Using a Dose Monitoring Program. *Diagnostic and Interventional Radiology*, **22**, 390-394. https://doi.org/10.5152/dir.2015.15221

[20] Fahey, F.H., Palmer, M.R., Strauss, K.J., Zimmerman, R.E., Badawi, R.D. and Treves, S.T. (2007) Dosimetry and Adequacy of CT-Based Attenuation Correction for Pediatric PET: Phantom Study. *Radiology*, **243**, 96-104. https://doi.org/10.1148/radiol.2431060696

[21] Rodríguez-Vigil, B., Gómez-León, N., Pinilla, I., Hernández-Maraver, D., Coya, J., Martín-Curto, L., *et al.* (2006) PET/CT in Lymphoma: Prospective Study of Enhanced Full-Dose PET/CT versus Unenhanced Low-Dose PET/CT. *Journal of Nuclear Medicine*, **47**, 1643-1648.

[22] Xia, T., Alessio, A.M., De Man, B., Manjeshwar, R., Asma, E. and Kinahan, P.E. (2011) Ultra-Low Dose CT Attenuation Correction for PET/CT. *Physics in Medicine & Biology*, **57**, Article No. 309. https://doi.org/10.1088/0031-9155/57/2/309

[23] Kamel, E., Hany, T.F., Burger, C., Treyer, V., Lonn, A.H., von Schulthess, G.K. and Buck, A. (2002) CT vs ^{68}Ge Attenuation Correction in a Combined PET/CT System: Evaluation of the Effect of Lowering the CT Tube Current. *European Journal of Nuclear Medicine and Molecular Imaging*, **29**, 346-350. https://doi.org/10.1007/s00259-001-0698-9

[24] Xia, S., Zhu, Z., Hao, L., Chen, J.-G., Xiao, L., Zhang, Y., *et al.* (2009) Negative Regulation of Systemic Acquired Resistance by Replication Factor C Subunit3 in Ara-

bidopsis. *Plant Physiology*, **150**, 2009-2017. https://doi.org/10.1104/pp.109.138321

[25] Brady, S.L. and Shulkin, B.L. (2015) Ultralow Dose Computed Tomography Attenuation Correction for Pediatric PET CT Using Adaptive Statistical Iterative Reconstruction. *Medical Physics*, **42**, 558-566. https://doi.org/10.1118/1.4905045

[26] Alessio, A.M., Kinahan, P.E., Manchanda, V., Ghioni, V., Aldape, L. and Parisi, M.T. (2009) Weight-Based, Low-Dose Pediatric Whole-Body PET/CT Protocols. *Journal of Nuclear Medicine*, **50**, 1570-1578. https://doi.org/10.2967/jnumed.109.065912

[27] Quinn, B., Dauer, Z., Pandit-Taskar, N., Schoder, H. and Dauer, L.T. (2016) Radiation Dosimetry of 18F-FDG PET/CT: Incorporating Exam-Specific Parameters in Dose Estimates. *BMC Medical Imaging*, **16**, Article No. 41. https://doi.org/10.1186/s12880-016-0143-y

[28] Brix, G., Lechel, U., Glatting, G., Ziegler, S.I., Münzing, W., Müller, S.P., *et al.* (2005) Radiation Exposure of Patients Undergoing Whole-Body Dual-Modality 18F-FDG PET/CT Examinations. *Journal of Nuclear Medicine*, **46**, 608-613.

[29] Zytoon, A.A., Mohamed, H.H., Mostafa, B.A.A.E. and Houseni, M.M. (2020) PET/CT and Contrast-Enhanced CT: Making a Difference in Assessment and Staging of Patients with Lymphoma. *Egyptian Journal of Radiology and Nuclear Medicine*, **51**, Article No. 213. https://doi.org/10.1186/s43055-020-00320-0

[30] ter Voert, E.E.G.W., van Laarhoven, H.W.M., Kok, P.J.M., Oyen, W.J.G., Visser, E.P. and de Geus-Oei, L.-F. (2014) Comparison of Liver SUV Using Unenhanced CT versus Contrast-Enhanced CT for Attenuation Correction in ^{18}F-FDG PET/CT. *Nuclear Medicine Communications*, **35**, 472-477. https://doi.org/10.1097/MNM.0000000000000086

[31] Muto, G., Yamashita, H., Takahashi, Y., Miyata, Y., Morooka, M., Minamimoto, R., *et al.* (2014) Large Vessel Vasculitis in Elderly Patients: Early Diagnosis and Steroid-Response Evaluation with FDG-PET/CT and Contrast-Enhanced CT. *Rheumatology International*, **34**, 1545-1554. https://doi.org/10.1007/s00296-014-2985-3

[32] Dougeni, E., Faulkner, K. and Panayiotakis, G. (2012) A Review of Patient Dose and Optimisation Methods in Adult and Paediatric CT Scanning. *European Journal of Radiology*, **81**, e665-e683. https://doi.org/10.1016/j.ejrad.2011.05.025

[33] Gelfand, M.J., Sharp, S.E. and Palumbo, J.S. (2015) Selective CT for PET/CT: Dose Reduction in Langerhans Cell Histiocytosis. *Pediatric Radiology*, **45**, 81-85. https://doi.org/10.1007/s00247-014-3103-0

[34] Aschoff, P., Plathow, C., Beyer, T., Lichy, M.P., Erb, G., Öksüz, M.Ö., *et al.* (2012) Multiphase Contrast-Enhanced CT with Highly Concentrated Contrast Agent Can Be Used for PET Attenuation Correction in Integrated PET/CT Imaging. *European Journal of Nuclear Medicine and Molecular Imaging*, **39**, 316-325. https://doi.org/10.1007/s00259-011-1919-5

[35] Inoue, Y., Nagahara, K., Tanaka, Y., Miyatake, H., Hata, H. and Hara, T. (2015) Methods of CT Dose Estimation in Whole-Body 18F-FDG PET/CT. *Journal of Nuclear Medicine*, **56**, 695-700. https://doi.org/10.2967/jnumed.114.153718

[36] Kuehl, H., Veit, P., Rosenbaum, S.J., Bockisch, A. and Antoch, G. (2007) Can PET/CT Replace Separate Diagnostic CT for Cancer Imaging? Optimizing CT Protocols for Imaging Cancers of the Chest and Abdomen. *Journal of Nuclear Medicine*, **48**, 45S-57S.

[37] Avramova-Cholakova, S., Ivanova, S., Petrova, E., Garcheva, M. and Vassileva, J. (2015) Patient Doses from PET-CT Procedures. *Radiation Protection Dosimetry*, **165**, 430-433. https://doi.org/10.1093/rpd/ncv128