Whole-Body PET/CT Scanning: Estimation of Radiation Dose and Cancer Risk¹

Radiology

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**The combination of positron emission tomographic (PET) scanners
and computed tomographic (CT)
scanners, or PET/CT scanners, provides** he combination of positron emission tomographic (PET) scanners and computed tomographic (CT) coregistered images of anatomic and functional information in a single study. The technology of CT-based attenuation correction for the PET images greatly reduces scanning time compared with scanning time for conventional PET scanners, for which gamma-ray sources (such as germanium 68) have been used for attenuation correction (1), although the latter method has the advantage of increased accuracy owing to emission of the same gamma-ray energy and therefore the

Advances in Knowledge

- The effective doses from wholebody fluorine 18 fluorodeoxyglucose (FDG) PET/CT studies performed with a 64-detector CT scanner, an administered FDG activity of 370 MBq, and three diagnostic CT protocols were estimated to be 13.45, 24.79, and 31.91 mSv for female patients and 13.65, 24.80, and 32.18 mSv for male patients, respectively, with the CT component contributing between 54% and 81% of the total combined dose.
- Using tables created for estimating the lifetime attributable risk of cancer incidence according to the principles of the National Academies' Biological Effects of Ionizing Radiation VII Report, the cancer risk induced was calculated to be between 0.231% and 0.514% for 20-year-old U.S. women and between 0.163% and 0.323% for 20-year-old U.S. men; risk decreased when age at exposure increased.
- The induced cancer risks were estimated to be 5.5%–20.9% higher in the Hong Kong population than in the U.S. population for 20-year-old individuals; this is attributed to a longer life expectancy and higher baseline cancer incidence in the organs sensitive to radiation in the Hong Kong population.

same attenuation coefficient map (μ) map) as the emission scan (2).

The clinical applications of PET/CT have been expanding, mainly in oncologic diagnosis and management, as well as for other clinical indications, such as the investigation of fever of unknown origin, leading to the increasing demand for PET/CT studies and more combined PET/CT scanners being installed in hospitals and clinics worldwide (3).

However, PET/CT examinations, especially those that include diagnostic CT, result in increased patient radiation exposure compared with stand-alone CT or PET examinations, as the effective dose is a combination of the dose from PET and the dose from CT. It is well known that cancer risk is induced from radiation (4,5). Results of studies evaluating cancer risk associated with medical imaging modalities, including coronary CT angiography (6), mammography (7), and scintigraphy (8), have been reported.

To date, to our knowledge, no studies have been performed to estimate the cancer risk associated with PET/CT scanning. Therefore, we aimed to *(a)* estimate the radiation exposure of patients undergoing whole-body PET/CT examinations and *(b)* evaluate, for U.S. and Hong Kong patients, the cancer risk induced by the radiation exposure.

Materials and Methods

Whole-body PET/CT studies obtained by using a 64-detector CT system (Discovery PET/CT; GE Healthcare, Milwaukee, Wis) were evaluated. Scan coverage was from the base of the skull to the upper thighs. Direct dose measurements were performed for CT scanning, while the dose coefficients recommended by International Commission on Radiological Protection (ICRP) publication 80 (9) were

Implication for Patient Care

 \blacksquare It is suggested that risk-benefit ratios should be carefully weighed prior to every PET/CT study, especially when clinical utility is less well established or is anecdotally based and when PET/CT is used in younger patients.

applied to estimate the dose of PET scanning. Effective doses were calculated according to organ doses and weighting factors recommended in ICRP publication 103 (10). The effective dose has been used to calculate the whole-body dose arising from nonuniform dose irradiation and provides the possibility of comparing radiologic detriments from different radiation exposures. Cancer risk caused by radiation dose was estimated according to the National Academies' Biological Effects of Ionizing Radiation (BEIR) VII Report (5).

Organ-specific CT Dose Measurement and Simulation

The dose from CT scanning was measured with an Alderson-Rando phantom (Alderson Research Laboratories, Long Island City, NY) equipped with thermoluminescent dosimeters (TLDs) (TLD-100; Harshaw, Solon, Ohio). This phantom represents a 163-cm and 54-kg female figure and was converted to a male phantom by removing the breast attachments. The variation of TLD response to uniform radiation was measured to be $\pm 5\%$. The TLDs were calibrated by using the CT scanner and an ion chamber (10X5-3CT; Radical, Monrovia, Calif). The chamber with the TLD chips attached was irradiated by the CT scanner (120 or 140 kV; 100–500 mA; pitch, 1), and linear regres-

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Abbreviations:

- $BEIR = Biological Effects of Ionizing Radiation$
- $FDG =$ fluorodeoxyglucose
- $ICRP = International Commission on Radiological$ Protection
- $LAR =$ lifetime attributable risk
- $TLD =$ thermoluminescent dosimeter

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sion analysis of the chamber and TLD chip readings was performed.

Before being inserted into the phantom, the TLDs were annealed in an oven (PTW-Freiburg, Freiburg, Germany). Twenty-four hours after irradiation by the CT scanner, the TLDs were read by a reader (model QS5500; Harshaw). The readings were then converted to exposures (in milliroentgens) by using factors acquired from the TLD calibration. Dose results were expressed in millisieverts on the basis of transfer factors from milliroentgens to millisieverts (in air, 0.0087 mSv per milliroentgen) (11).

A total of 270 TLDs were distributed in the Rando phantom, and six TLDs were used as controls (Table 1). At least two chips were used for each organ to lower the uncertainty and prevent possible damage to the TLDs. The TLD readings in specific organs were averaged to calculate the organ dose. Dose to the lens of the eye was also measured as it may be the deterministic effect in cataractogenesis.

In addition, organ doses from CT scanning were simulated by using a spreadsheet (ImPACT [12]). Scanner type and protocol parameters were entered into the spreadsheet. Because ImPACT requires input of fixed values, for protocols involving use of the AutomA technique with the GE scanner, the upper and lower limits were entered. Because ImPACT is not able to determine the tube current for each specific body region, inputting limits would provide a dose range. Effective dose was also computed in ImPACT by using the weighting factors from ICRP publication 60 (4). We then recalculated effective dose by using tissue weighting factors from ICRP publication 103 (10), which is more updated, and to maintain consistency with other effective dose calculations in our study.

Three protocols for whole-body CT scanning (A, B, and C) were studied (Table 2). Protocols A and B were identical except that tube current was set with the AutomA technique in protocol A. Protocol C had higher tube potential and tube current and also involved the AutomA technique. With the AutomA technique, tube current is adjusted according to patient anatomy to a user-selected noise level. This reduces radiation dose because the tube current is reduced for smaller anatomic regions. Protocol A is the most frequently used protocol in our unit, and protocol C is used for patients with larger body habitus. Protocol B is not used in our unit but was studied for comparison with protocols A and C, which used the AutomA technique for tube current modulation, and for comparison with published results that were obtained without the AutomA technique.

Organ-specific PET Dose Calculation

Whole-body fluorine $18 \text{ } (^{18}\text{F})$ -fluorodeoxyglucose (FDG) PET scanning with the same transverse coverage as the CT study was performed with a 2-minute 45-second acquisition per bed position, with the scanner operating in the three-dimensional mode. Normally, scans of five bed positions were obtained, and the total scanning time lasted about 20 minutes. PET doses to the lens of the eye were not calculated because there is no dose coefficient in ICRP publication 80 for the lens.

The average activity of 18F-FDG administered was assumed to be 370 MBq for adults (men and women). The organ doses can be calculated with the following equation:

 $D_{\text{T}}^{\text{PET}} = A \cdot \Gamma_{\text{T}}^{\text{FDG}}$,

where T is a specific organ or tissue, $D_{\textrm{T}}^{\textrm{PET}}$ is organ dose from the PET scan, *A* is ¹⁸F-FDG activity, and $\Gamma_{\rm T}^{\rm FDG}$ is the coefficient recommended in ICRP publication 80 (9), which is an average value for men and women.

Lifetime Attributable Risk of Cancer Incidence

The method introduced in the BEIR VII report (5) was applied to estimate the radiation-induced cancer risk in the form of lifetime attributable risk (LAR) (Appendix E1, *http://radiology.rsnajnls.org/cgi/content /full/2511081300/DC1*).

Cancer Risk Estimation for U.S. and Hong Kong Populations

To calculate the LAR for the U.S. population, the table in the BEIR VII report was updated by using the U.S. Cancer Statistics for 2001–2005 (13), the U.S.

Life Table 2005 (14), and the principles described above. The same method was applied for calculating a LAR table for the Hong Kong population by using the Hong Kong Cancer Statistics 2005 (15) and the Hong Kong Life Table 2005 (16). The weights for the Hong Kong population were chosen to be the same as those used in the BEIR VII report, as no weights were suggested for other populations in the BEIR VII report.

According to the updated tables for U.S. and Hong Kong populations, the organ-specific LARs were calculated from organ doses by means of the linear no-threshold assumption, and these were summed to calculate the wholebody LAR. Although male breasts receive doses of radiation, the cancer risk to male breasts was not considered.

Results

Table 1

TLD Calibration

The TLD calibration result is given with the formula $E = f \cdot C$, where *E* is the

TLD Distribution

radiation exposure in air (in milliroentgens) measured in the ion chamber, *C* is the reading of the TLD chips (in nanocoulombs), and f is the calibration factor. For tube potentials of 120 and 140 kV, the calibration factors were computed to be 13.3 and 13.0 mR/nC, respectively, with an error of 1%.

Radiation Doses

The CT effective doses for protocol B calculated with ImPACT were 16.10 and

Parameters of the Three CT Protocols

* With use of AutomA.

Table 3

CT Dose for Male and Female Patients with Protocols A, B, and C

Note -- Unless otherwise specified, data are in millisieverts.

* As recommended in ICRP publication 103 (10), in which no weighting factor is defined for the lens of the eye.

[†] Sum of organ doses weighted by tissue weighting factor.

16.40 mSv for female and male patients, respectively. For protocol A with 100 and 300 mA, respectively, the effective doses to female patients were calculated to be 6.40 and 19.10 mSv, and the effective doses to male patients were calculated to be 6.60 and 19.70 mSv.

The measured organ doses and effective doses from CT scanning are summarized in Table 3. The effective doses of the three CT protocols A, B, and C, respectively, were 7.22, 18.56, and 25.68 mSv for female patients and 7.42, 18.57, and 25.95 mSv for male patients. The radiation doses to the lens of the eye from CT scanning with the three protocols A, B, and C, respectively, were measured to be 8.1, 18.4, and 27.2 mSv for female patients and 8.3, 18.6, and 27.3 mSv for male patients.

The effective dose from PET scanning was 6.23 mSv (Table 4). Doses from PET scanning to the gonads, uterus, and bladder were higher than to the other organs and were 5.0, 7.8, and 59.2 mSv, respectively. This is because of the final accumulation of 18F in the bladder. Other organ doses ranged from 2.5 to 4.8 mSv.

The total effective doses of the combined PET/CT studies, calculated by summing the effective doses of CT and PET scanning, were 13.45, 24.79, and 31.91 mSv for female patients and 13.65, 24.80, and 32.18 mSv for male patients for protocols A, B, and C, respectively. The CT component contributed 54%–81% of the total combined dose.

LAR of Cancer Incidence Estimated for U.S. and Hong Kong Populations

The LAR table of cancer incidence for the U.S. and Hong Kong populations demonstrated that excess risks for female patients were higher than those for male patients, except for the colon and bladder (Table 5). The estimated LARs of cancer incidence were particularly high in younger ages and decreased with increasing age (Figure). For example, LARs were up to 0.514% and 0.323% for 20-year-old U.S. women and men, respectively. These risks for the Hong Kong population were higher than for the U.S. population for both sexes and all ages (Figure). For example, at age 20 years, the LARs of cancer incidence in the Hong

Kong population were 5.5%–20.9% higher than those for the U.S. population, and at age 80 years, the LARs of cancer incidence were 6.5%– 47.9% higher. The difference in risks between these two populations was larger for female patients than for male patients, at older ages, and with higher-dose CT protocols. To explain the cause of the higher LAR in the Hong Kong population compared with the U.S. population, we referred to the life expectancy and cancer statistics data of the most frequent five cancers among the Hong Kong and U.S. populations (Table 6). We found the explanation to be related to the differences in life table and cancer statistics data between the two populations. First, Hong Kong residents have a longer life expectancy than Americans in which to develop cancer after radiation exposure. Second, the baseline cancer incidences of the organs more sensitive to radiation are higher in Hong Kong than in the United States. For example, the most prevalent cancer in Hong Kong is in the lung, which is given a high tissue weighting factor of 0.12 (10), while in the United States, it is in the prostate, with a tissue weighting factor of 0.013.

Discussion

One important aspect in evaluating the use of PET/CT scanning in medical practice is the potential risk from radiation exposure, and this should be quantified and understood so that risk-benefit ratios can be assessed. In our study, the effective dose from 18F-FDG PET/CT scanning with a diagnostic CT protocol and an administered FDG activity of 370 MBq was calculated to be up to 32.18 mSv, and the associated lifetime cancer incidence was estimated to be up to 0.514% for the U.S. population and up to 0.622% for the Hong Kong population (for patients 20 years of age). The results are important from both an individual and a public health perspective.

The total effective dose from each PET/CT study was about five to 13 times the worldwide average effective dose from background radiation over 1 year,

Table 4

Note.—The overall effective dose (the sum of organ doses weighted by the tissue weighting factor) was 6.23 mSv. * As recommended in ICRP publication 80 (9).

† As recommended in ICRP publication 103 (10).

which is estimated to be about 2.4 mSv (17). Generally, higher tube current and potential and lower noise levels provide better-quality CT images but impart a higher radiation dose and, consequently, a higher cancer risk. This underscores the fact that a balance between image quality and radiation dose should be achieved in PET/CT scanning protocols.

Compared with the measured CT doses, the effective doses calculated by using ImPACT for protocol B were 12%–13% lower. For protocol A with the AutomA technique, the measured doses (about 7 mSv) were within the range of the doses calculated by using ImPACT but were at the low end because a high noise level of 20 was selected for the scanning. Because it has been reported that ImPACT underestimates CT radiation dose by about 18% (18), we conclude that the results from ImPACT were in good accordance with the TLD measurements. Nevertheless,

we suggest that the ImPACT software should be updated for dose calculation.

The results of our research are comparable with the PET/CT radiation doses reported in the literature (using the same FDG activity of 370 MBq). Some variability exists because of the differences in CT protocols, PET dose estimating methods, and PET/CT scanners. The total effective dose of a wholebody PET/CT study has been estimated to be between 6.34 and 9.48 mSv for the average Japanese individual (19). This lower dose was due to the use of a screening CT protocol that applied lower tube current and potential. Our results were in good accordance with those of Brix et al (20), who measured the effective doses of PET/CT examinations with four diagnostic CT protocols and found them to range from 23.7 to 26.4 mSv. Brix et al used the same CT and PET dose-estimating method we did, but their CT scanners were two-, four-, or 16-detector scanners. In another study, Wu et al (21) reported effective dose at diagnostic CT (140 kV ; 80 mA; 0.8 second; pitch, 3) to be 18.97 mSv and PET effective dose to be 10.72 mSv by using a coefficient of 2.9×10^{-2} mSv/MBq for calculating the PET effective dose.

We measured specifically the dose imparted to the lens of the eye by CT scanning, although this is not relevant to effective dose calculation because the main risk from dose to the lens is the deterministic effect of cataractogenesis rather than the stochastic effect (cancer risk) (4,10). The dose to the lens is much lower than the dose threshold (around 500 –2000 mGy) for this deterministic effect (4).

Cancer risks induced by other diagnostic imaging modalities have been reported in the literature (6,22–26). Einstein et al (6) reported that the LAR of cancer incidence associated with coronary CT angiography was 0.7% for 20 year-old women, which is the highest

cancer risk induced from the various diagnostic radiology examinations reported, and this reported risk is higher than our results.

There were inherent errors and limitations in our study. At TLD measurement, there was 5% error from the readings of the TLDs, 2% directionality error associated with the edge and surface of the TLDs (27), and an estimated 1% error in the TLD calibration procedure. Also, although we used as many TLDs as possible and averaged the TLD readings, dose uncertainty was unavoidable because radiation exposure varies with positions. Uncertainties in PET dose were produced from inherent errors of the coefficients used for PET dose estimation, which were calculated on the basis of approximation of FDG accumulated in the human body and physics simulation of 18F-FDG radioactivity transportation. There are several uncertainties in estimating LAR by using the method in the BEIR VII report, such as the excess relative dose and excess absolute dose models themselves, the dose and dose rate effectiveness factor, and the radiation-induced risk transport from the Japanese to the U.S. population. Moreover, in our study, there was additional uncertainty from the use of the same weights for the risk transport between the Japanese and Hong Kong populations, as they may differ from between the Japanese and U.S. populations. Our study was limited by the fact that the risk transport analysis, which was based on complex analyses, including comparisons of the factors that increase cancer rate and the effect of radiation on these factors in both populations, has not been studied for the Hong Kong population. Finally, we estimated the cancer risk induced from the PET dose by using the BEIR VII method based on external radiation exposure. Although there are no conclusive data to show that the risk from internal exposure would differ from that for external exposure, there is additional uncertainty (5).

Table 5

LARs of Cancer Incidence for U.S. and Hong Kong Populations

Note.—Data are numbers of cancer cases in the lifetimes of 100 000 persons exposed to a radiation dose of 100 mSv. LARs were calculated as described in Appendix E1 *(http://radiology .rsnajnls.org/cgi/content/full/2511081300/DC1)* and by applying the Hong Kong Cancer Statistics 2005 (15) and Hong Kong Life Table 2005 (16).

b.

(a– c) Graphs show excess cancer incidence risks estimated to be associated with radiation from a single whole-body 18F-FDG PET/CT examination at a given age. PET/CT was performed with three CT protocols (A, B, and C), as shown in (a), (b), and (c), respectively.

Although some other methods have been recommended for estimating radiation-induced cancer risks (4,5,28–31), we used the method of the BEIR VII report because it is based on review of current research. However, this method is controversial in that it may overestimate risk. To calculate LAR, this method sums the risks from the age at 5 years after exposure to the age of 100 years, which is above the average natural life span. Controversy also arises from the assumptions for risk from lowdose (or low– dose rate) radiation exposure. First, whether cancer is a risk of low-dose radiation is still unproven, as there have not been any epidemiologic studies to date to support this (23,32). However, there are direct epidemiologic data in 30 000 atom bomb survivors who were on the peripheries of Hiroshima and Nagasaki and who were exposed to the same low-dose range as CT scanning (5–100 mSv) that show a small but statistically significant increase in cancer risk (33). Second, there are no experimental data to sup-

Table 6

Top Five Cancer Sites in U.S. and Hong Kong Populations

Note.—Hong Kong data are from Hong Kong Cancer Statistics 2005 (15), and U.S. data are from the National Cancer Institute (13). As shown, the leading cancer sites in Hong Kong have higher tissue weighting factors—that is, they are more sensitive to radiation dose—than the leading cancer sites in the United States.

* Number of cases in a given site divided by number of all cancer cases.

† As recommended in ICRP publication 103.

port the linear no-threshold extrapolation for low-dose risk estimation. However, the majority of organizations have advised that the linear no-threshold assumption best fits the data $(5,28,34)$, and therefore, linear extrapolation of cancer risk from low doses should be the most appropriate method (35).

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As whole-body PET/CT scanning is accompanied by substantial radiation dose and cancer risk, risk-benefit ratios should be carefully weighed prior to every study. This is especially important when clinical utility is less well established or is based on anecdotal evidence and when PET/CT is used in younger patients. In the evaluation of patients known to have cancer, although cancer risks from radiation may be of less impact, the information is still of interest and relevant to patient education. Moreover, patients with cancer often undergo multiple PET/CT examinations for response assessment and treatment monitoring, and survival rates are markedly improved nowadays. Currently, common indications for PET/CT are for cancer staging and restaging, response assessment, and detection of unknown primary cancers. Less common indications are for fever of unknown origin and to evaluate the extent of systemic infection. Clinicians should familiarize themselves with the current literature of the recommendations on the use of FDG PET in oncology (36,37), and more work should be done to evaluate the evidence of the clinical utility of PET/CT in large-scale prospective studies. In our institution, a tertiary referral center serving the general population on Hong Kong Island, PET/CT studies for patients younger than 20 years are relatively infrequent, comprising less than 3% of the total number of studies. Seventy percent of the studies are performed in adults older than 50 years. This reflects the low incidence of cancer in the young age groups in the population. From a public viewpoint, the dose of up to 32 mSv per study adding to the background radiation is nonnegligible. Therefore, PET/CT scanning protocols should be optimized for reducing dose and its associated cancer risk.

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