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Cumulative radiation exposure dose of diagnostic imaging studies in breast cancer patients

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► ***Original article***

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ABSTRACT

Background*:** Breast cancer is a common disease in radiation oncology. We evaluated the radiation dose received by breast cancer patients, an often-neglected concern. ***Materials and Methods*:** The total effective radiation dose in 101 breast cancer patients was calculated by summing the effective doses of individual diagnostic imaging tests from the first hospital visit to the initiation of radiotherapy. The effective dose from general radiography and computed tomography (CT) was estimated using tissue-weighting factors and dose-length products. The effective dose from isotopes (18F-fluorodeoxyglucose and 99m Tc-methylene diphosphonate) was estimated from the radioactivity of each isotope using dose coefficients. The patient radiation exposures were analyzed using radiologic records in the Picture Archiving and Communication System. ***Results: The median duration from initial imaging to the initiation of radiotherapy was 4.5 months (range: 0.7–13.4 months). When comparing the average effective doses associated with each diagnostic modality, CT, positron emission tomography-CT, bone scanning and radiography occupied 64%, 21%, 10% and 5% of the total effective dose, respectively. Comparison of the total effective dose according to clinical factors (age, AJCC stage, T stage, N stage, operation method, and cancer location) by multivariate analysis revealed that only T stage was significantly correlated with the total effective dose (p = 0.004). The median total effective dose was 71.5 mSv (range: 11.9–131.9 mSv). ***Conclusion:*** The radiation dose received from diagnostic testing in breast cancer patients is not negligible. We need to systematically collect and manage the doses received by patients from medical procedures.

Keywords: *Effective dose, Radiation exposure, Cumulative dose, Breast cancer.*

INTRODUCTION

The development of radiology procedures such as computed tomography (CT) and positron emission tomography-CT (PET-CT) has enabled the detailed and early diagnosis of malignancies [1]. The use of radiation for medical purposes has caused human radiation exposure to increase; in fact, medical radiation is now the largest contributor to human radiation exposure [2, 3].

In Korea, the proportion of plain radiography and CT examinations has increased from 8% (2006) to 14% (2011) and the effective radiation dose from medical procedures increased by 10% between 2007 and 2011 [2]. Since the benefits of using ionizing radiation in medicine are believed to exceed the risks of radiation exposure, the use of medical radiation is currently justified; however, there is no uniform dose threshold [4].

Cancer patients are increasingly exposed to medical radiation to provide a detailed diagnosis. In addition, as cancer patients may survive for many years after their initial treatment, more emphasis is placed on diagnosing recurrence. According to the Surveillance, Epidemiology, and End Results (SEER) database from 2007 to 2013, the 5-year survival rates of early and regional breast cancer

patients reached 98.9% and 85.2%, respectively [5]. Since breast cancer patients tend to be long-term survivors, radiation protection becomes an important factor when late complications, such as secondary cancers, occur [6, 7].

At present, the amount of radiation exposure from each medical imaging device is recorded in Korea, but the measurement and management of individual patient exposures are insufficient [8-10]. This study evaluated the effective doses that the breast cancer patients received during diagnostic imaging studies from their first hospital visit to the time of the CT simulation radiotherapy planning. We also discuss the importance of reducing medical radiation exposure.

MATERIALS AND METHODS

The 101 patients included in this study were pathologically confirmed to have breast cancer from May 2015 to June 2016 and underwent CT-mediated radiotherapy planning at Korea University Guro Hospital between January and June 2016. The selected patients had Stage IIIC or lower disease, according to the American Joint Committee on Cancer (AJCC) (7th edition) staging system [11], and patients with distant metastasis were excluded. We measured the radiation exposure that resulted from imaging studies from the patient's first hospital visit for confirmed or suspected breast cancer to the time of the CT scan performed for radiotherapy planning. The diagnostic imaging studies included chest CT, abdominal CT, chest posterior-anterior (PA) plain radiography, chest lateral plain radiography, abdominal anterior-posterior (AP) plain radiography, mammography, bone scanning, PET-CT, and fluoroscopy. All results were analyzed based on the radiologic records of the Picture Archiving and Communication System (PACS). Retaken or unrecorded images were not included.

Imaging tests performed at other hospitals were excluded from the study. Tests using the ^{99m}Tc-phytate isotope were also excluded because the small amounts of isotope used made it difficult to determine individual differences between tests. Endoscopic retrograde cholangiopancreatography (ERCP), which was used in 2 patients, was also excluded because the exposure time and the amount of radiation supplied were not recorded in the PACS. Several plain radiographs that used a panorama view (1 patient, 0.01 mSv), a skull view (1 patients, 0.1 mSv for each), and a foot view (6 patients, 0.001 mSv for each), were excluded because they occurred infrequently and contributed less than 1% to the average effective doses supplied by imaging techniques.

The following imaging devices were used: Philips DigitalDiagnost (plain radiography); Philips Brilliance CT 64-Slice and GE BrightSpeed Elite 16 (CT); Selenia Dimensions (mammography); GE Dual Detector Infinia (gamma camera); Philips Gemini TF (PET-CT); and Siemens Artis Zee Biplane (fluoroscopy). The isotopes used with the nuclear medicine techniques were 9mTc-methylene diphosphonate (^{99m}Tc-MDP, bone scanning) and 18F-fluorodeoxyglucose (^{18}F-FDG, PET).

Fluoroscopy and plain radiography, including chest PA, chest lateral, abdominal AP, and mammography, were performed by the Department of Radiology using standardized methods [12]. The modality effective dose (MED) was estimated using the tissue weighting factor and the average effective dose; the radiographs were subdivided according to the Simaging type, the number of imaging procedures, and the dose received by each patient [11, 13].

CT was performed by the Departments of Radiology, Nuclear Medicine, and Radiation Oncology and also employed standardized methods (tube voltage: 120 kVp; tube current: 100–300 mA). The MED was calculated by multiplying the dose-length product (DLP) by the conversion factor (k), according to the region tested (brain: k = 0.003; abdomen to pelvic (mean): k = 0.015; chest: k = 0.014; chest to pelvic (mean): $k \times 0.0145$) [14]. For bone scanning and PET, the isotope species and the administered dose (mCi) were recorded and the average effective dose per test was used to calculate the MED [11].

Statistical analysis

The total effective dose (TED) was defined as the summation of all MEDs. Univariate analysis was performed using analysis of variance (ANOVA), and multivariate analysis was performed using linear regression. Multivariate analysis was performed for the significant factors that arose during univariate analysis. All p values < 0.05 were considered statistically significant. All statistical analyses were performed using IBM SPSS for Windows, version 20.0 (IBM Corp., Armonk, NY, USA).

Ethical approval

This study was approved by Institutional Review Board (IRB) of Korea University Medical Center Guro Hospital (IRB No.: KUGH17175-001).

RESULTS

Patient characteristics

Of the 101 patients, the median age was 52 years (range: 25–77) and the median duration between from initial imaging to CT-based radiotherapy planning was 4.5 months (range: 0.7–13.4 months). Based on the 7th AJCC staging system, 23 (22.7%), 41 (40.6%), 30 (29.7%), and 7 (6.9%) patients were stage 0, I, II, and III, respectively. Breast-conserving surgery (BCS) and modified radical mastectomy (MRM) were performed in 95.0% and 5.0% of patients, respectively. In terms of location, 45.5%, 51.5%, and 3.0% of patients had tumors in the left breast, right breast, and both breasts, respectively. The patient characteristics are described in table 1. The median TED during the study period was 71.5 mSv (range: 11.9–131.9 mSv). Comparison of the average effective doses among radiological modalities revealed that the TED was made up of diagnostic CT (35%), radiotherapy planning CT (29%), PET-CT (21%), bone scanning (10%), and plain radiography (including chest PA, chest lateral, abdominal AP, mammography, and fluoroscopy) (5%). The average values and standard deviations of the TEDs were: 23.2 mSv ± 16.1 for diagnostic CT, 19.4 mSv ± 5.8 for radiotherapy planning CT, 23.2 mSv ± 16.1 for PET-CT, 6.3 mSv ± 2.8 for bone scanning, and 3.4 mSv ± 2.7 for plain radiography (figure 1).

Plain radiography

The median doses and MEDs from plain radiography were 6 mSv (range: 0–19 mSv) and 0.12 mSv (range: 0–0.38 mSv) for chest PA, 5 mSv (range: 0–18 mSv) and 0.20 mSv (range: 0–0.72 mSv) for chest lateral, 2 mSv (range: 0–22 mSv) and 1.4 mSv (range: 0–15.4 mSv) for abdominal PA, and 6 mSv (range: 0–27 mSv) and 0.84 mSv (range: 0–3.78 mSv) for mammography. The median MED of fluoroscopy was 0.41 mSv (range: 0–2.58 mSv). The above data are described in table 2.

Computed tomography

In the Department of Radiology, the median number of procedures and DLP of the CT scans were 2 (range: 0–5) and 1,889.9 mGy·cm (range: 0–6,515.4 mGy·cm), respectively. For CT scans performed in the Department of Nuclear Medicine, the median number of procedures and DLP were 1 (range: 0–2) and 628.8 mGy·cm (range: 0–1,647.4 mGy·cm), respectively. The median MEDs, which were calculated from each DLP, were 27.4 mSv (range: 0–73.8 mSv) for the Department of Radiology and 9.11 mSv (range: 0 –26.0 mSv) for the Department of Nuclear Medicine. In the Department of Radiation Oncology, the median DLP of the CT scan for radiation therapy planning was 1,339 mGy·cm (range: 525.2–2224.9 mGy·cm). Based on the DLP, the median MED was 17.7 mSv (range: 7.4–32.3 mSv). The above data are described in table 3.

Radioisotope use

For PET-CT, the dose of ^{18}F-FDG administered and the median MED were 7.6 mCi (range: 0–15.3 mCi) and 5.34 mSv (range: 0–10.7 mSv), respectively. The median number of procedures was 1 (range: 0–2). The median number of bone scans performed was 2 (range: 0–2); the dose of ^{99m}Tc-MDP administered was uniformly 20 mCi and the median MED was 8.44 (range: 0–8.44).

The above data are described in table 4.

Univariate and multivariate analyses

The relationships between TED and 6 clinical factors, including age, AJCC stage, T stage, nodal status, operation method, and cancer location, were analyzed by univariate analysis. Age (p = 0.005), AJCC stage (p < 0.001), T stage (p < 0.001), and nodal status (p = 0.001) were significant factors for TED, while the operation method (BCS vs. MRM) and cancer location (left vs. right vs. both) were not. Multivariate analysis was performed using the 4 significant variables arising from univariate analysis, revealing that T stage was the only statistically significant factor related to TED (p = 0.004). These results are described in Table 1.

Table 1. Univariate and multivariate analyses relating to total effective dose.

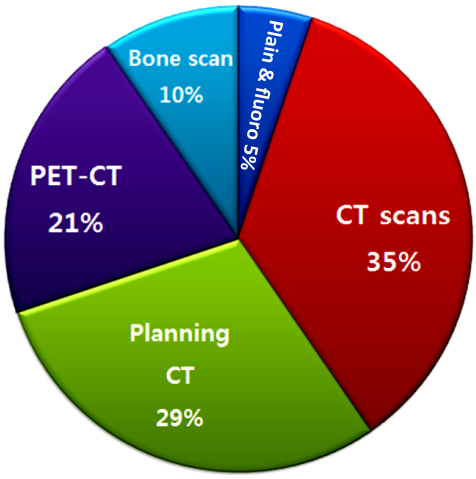
		Univariate analysis		**Multivariate analysis**	
		Total effective dose (mSv)			
	N	Mean ± SD	p value	B ± SE	p value
Age					
< 53	53	60.4 ± 29.0			
≥ 53	48	71.7 ± 24.7	**0.038**	7.93 ± 4.67	0.093
AJCC 7th stage					
0	23	42.9 ± 32.8			
I	41	65.5 ± 232.0			
II	30	79.5 ± 16.2			
III	7	83.5 ± 22.0	**< 0.001**	3.88 ± 4.63	0.403
T stage					
Tis	21	38.6 ± 30.6			
I	48	67.5 ± 22.2			
II	30	78.5 ± 15.8			
III	2	119.2 ± 18.0	**< 0.001**	14.81 ± 4.99	**0.004**
Nodal status					
LN (-)	76	60.8 ± 28.6			
LN (+)	25	80.8 ± 17.0	**< 0.001**	4.64 ± 6.48	0.476
Operation method					
BCS	96	65.9 ± 26.5			
MRM	5	63.4 ± 46.8	0.847		
Cancer location					
Left	46	65.6 ± 27.3			
Right	52	67.0 ± 27.6			
Both	3	46.8 ± 31.1	0.467		

Abbreviations: SD, standard deviation; SE, standard error; AJCC, American Joint Committee on Cancer; LN, lymph node; BCS, breasts conserving surgery; MRM, modified radical mastectomy

Table 2. Pattern of diagnostic images.

	Number of procedures (median, range)	**Typical effective dose (mSv)**	**Modality effective dose (mSv) (median, range)**
Chest PA	6 (0 - 19)	0.02	0.12 (0 - 0.38)
Chest Lateral	5 (0 - 18)	0.04	0.20 (0 - 0.72)
Abdomen PA	2 (0 - 22)	0.7	1.40 (0 - 15.40)
Mammography	6 (0 - 27)	0.14	0.84 (0 - 3.78)
	Tissue weighting factor (chest)	**Modality effective dose (mSv) (median, range)**	
Fluoroscopy	0.12	0.41 (0 - 2.58)	

Abbreviations: PA, posterior-anterior



	plain & fluoroscopy	CT scans	Planning CT	PET-CT	Bone scan
Mean (SD)	3.4 ± 2.7	23.2 ± 16.1	19.4 ± 5.8	13.5 ± 7.9	6.3 ± 2.8

Figure 1. The contributions of each imaging modality to patient radiation exposure

Table 3. Effective dose from CT, calculated using DLP, as well as cumulative DLP.

	Number of procedures (median, range)	Average of DLP (mGy.cm)	Modality effective dose (mSv) (median, range)
CT scans	2 (0 - 5)	1889.9	27.4 (0 - 73.767)
Planning CT	1	1338.97	17.73 (7.44 - 32.26)
PET-CT (CT only)	1 (0 - 2)	628.8	9.11 (0 - 26.04)

Table 4. Radiation exposure due to isotopes at the department of nuclear medicine.

	Type of isotope	Number of procedures (median, range)	Amount of isotope administered (mCi) (median, range)	Modality effective dose (mSv) (median, range)
PET-CT (only isotope exposure)	^{18}F-FDG	1 (0 - 2)	7.6 (0 - 15.3)	5.34 (0 - 10.76)
Bone scanning	^{99m}Tc-MDP	2 (0 - 2)	20 (0 - 20)	8.44 (0 - 8.44)

DISCUSSION

According to an epidemiologic survey of atomic bomb victims by Preston *et al.* [15], the risk of solid cancer was proportional to radiation dose, even in the range of 0–150 mSv. A later study by Ozasa *et al.* [16] showed that the lowest dose range to induce a significant cancer risk was 0–200 mSv. Currently, the amount of radiation administered for medical use is generally less than 100 mSv, yet the effect of such doses on the human body has not been proven [17-19].

According to the linear no-threshold model, the probability of disability in humans increases proportionally with dose, even at low doses. Furthermore, no dose threshold exists for the prevention of cancer occurrence caused by low-dose radiation [18, 20, 21]. In the present study, the median TED during follow-up was 71.5 mSv (range: 11.9–131.9 mSv). However, this value was measured from the time of diagnosis to CT-based radiotherapy planning, which represents only a fraction of the time in which a patient can receive radiation for either diagnostic or therapeutic purposes. Considering

the no-threshold model and the common neglect of possible medical radiation hazards, it is necessary to improve the awareness of medical staff to achieve minimal patient radiation exposure.

Among the patients studied, the number of CT examinations performed varied from 0 to 5 and the mean effective dose from CT (including diagnostic and radiotherapy planning CT) comprised 64% of the total effective dose across all imaging studies. CT scans show a large variation in effective dose, depending on the target region and protocol [22, 23]. Since the mid-1990s, many studies have measured effective dose using DLP in order to establish the recommended radiation dose for administration to patients [3]. Since CT scans comprise a significant proportion of medical radiation exposure, it is necessary to create protocols and the systematic recording and management of data across all radiology departments.

The DLP of the planning CT used in the Department of Radiation Oncology was 1,339.0 mGy·cm, which is 128% higher than the average DLP value (944.95 mGy·cm) of CT in the Department of Diagnostic Radiology. The higher radiation exposure associated with planning CT might be due to the repeated scouting for posture confirmation and the acquisition of both pre- and post-enhancement scans. Various fixation devices have been developed to stabilize the patient's posture and efforts are being made to acquire planning images through non-radiological imaging devices, such as MRI [24]. These technological advances might enable better treatment accuracy, reduce patient inconvenience, and reduce radiation exposure.

In multivariate analysis, T stage was identified as a factor that significantly affected TED. T stage is also a prognostic factor that directly affects survival and is associated with lymph node metastasis and distant metastasis; hence, patients with higher T-stage require more detailed diagnostic tests [25, 26]. According to the SEER database, the 5-year survival rate for patients with regional breast cancer was 85.2%, while the 10-year survival rate for patients with stage III cancer, which might reflect locally advanced cancers, was above 60% [5]. Long-term survival can be expected even in patients with locally advanced breast cancer; therefore, the late radiation risks should not be ignored.

Our study had several limitations. The retrospective nature meant that we could not account for imaging that occurred prior to the patient's first visit to our hospital. In addition, we did not directly measure the radiation received using a dosimeter, such as a thermoluminescence detector (TLD); instead, we estimated the effective dose based on the known dose and a reference value. However, Bor *et al.* [27] reported that the radiation dose value obtained by multiplying the DLP value by the conversion factor was similar to the radiation dose measured by TLD.

Although our study is an observational study at a single institution, considering that most tertiary centers in Korea perform similar diagnostic procedures for breast cancer patients, the results of our study can be used as the basis for future research. Further investigation is required regarding cancers with high incidence rates and possible long-term survival rates, such as gastric or colorectal cancers. Consequently, the systematic management of medical radiation exposure might be enabled, which may reduce patients' fears and decrease late radiation risks.

CONCLUSION

The breast cancer patients received a median dose of 71.5 mSv (range: 11.9–131.9) from diagnosis or suspicion of breast cancer to planning CT. The clinical factor most associated with medical radiation exposure was T stage. Future studies on radiation exposure in various cancer patients and the systematic management of medical radiation are warranted.

***Conflicts of interest*:** *Declared none.*

REFERENCES

1. Bar-Shalom R, Yefremov N, Guralnik L, et al. (2003) Clinical performance of PET/CT in evaluation of cancer: additional

value for diagnostic imaging and patient management. *J Nuc Med*, **44(8):** 1200-1209.
2. Do KH and Jung SE (2016) Current status of medical radiation exposure in Korea - recent efforts to develop a radiation exposure control system focused on justification and optimization. *Ann ICRP*, ***45(1 Suppl):*** *113-121*.
3. Lee SY, Lim HS, Han MS (2011) The evaluation of patients' radiation dose during TACE of interventional radiology. *J Radio Sci Technol*, ***34:*** *209-214*.
4. ICRP. 1990 (1991) Recommendations of the International Commission on Radiological Protection. ICRP publication 60. Stockholm, Sweden: ICRP.
5. Howlader N, Noone AM, Krapcho M, *et al*. (eds). SEER Cancer Statistics Review. 1975-2010. National Cancer Institute. Bethesda, M.D. http://seer.cancer.gov/csr/1975_2010/, based on November 2012 SEER data submission, posted to the SEER web site, April 2013
6. Llovet JM and Bruix J (2003) Systematic review of randomized trials for unresectable hepatocellular carcinoma: chemoembolization improves survival. *Hepatology*, ***37(2):*** *429 -442*.
7. Brambilla M, De Mauri A, Lizio D, *et al*. (2014) Estimated radiation risk of cancer from medical imaging in haemodialysis patients. *Nephro. Dial Transplant*, ***29(9):*** *1680-1686*.
8. Miller DL, Kwon D, Bonavia GH (2009) Reference levels for patient radiation doses in interventional radiology: proposed initial values for U.S. practice. *Radiology*, ***253(3):*** *753-764*.
9. Chung JW (2007) Korea Food & Drug Administration. Evaluation of patient dose in interventional radiology. Seoul: Korea Food & Drug Administration.
10. Park C, Song JH, Kim YT, Yim NY, Kim JK, Kim JH, *et al.* (2013) Cumulative radiation exposures during diagnosis and treatments with diagnostic radiology tools: in patients with hepatocellular carcinoma. *J Korean Soc Radiol,* ***69(3):*** *243-250*.
11. Edge SB, Byrd DR, Carducci MA, *et al*, eds. (2009) American Joint Committee on Cancer (AJCC) Cancer Staging Manual. 7th ed. New York: Springer.
12. Sandström S, Ostensen H, Pettersson H (2003) The WHO manual of diagnostic imaging: radiographic technique and projections. Vol. 2. World Health Organization.
13. Dance DR, Skinner CL, Young KC *et al.* (2000) Additional factors for the estimation of mean glandular breast dose using the UK mammography dosimetry protocol. *Phys Med Biol*, ***45(11):*** *3225-3240*.
14. Huda W, Ogden KM, Khorasani MR (2008) Converting dose -length product to effective dose at CT. *Radiology*, ***248(3):*** *995-1003*.
15. Preston DL, Shimizu Y, Pierce DA, Suyama A, Mabuchi K (2003) Studies of mortality of atomic bomb survivors. Report 13: solid cancer and noncancer disease mortality: 1950 - 1997. *Radiation Research*, ***160:*** *381-407*.
16. Ozasa K, Shimizu Y, Suyama A, Kasagi F, Soda M, Grant EJ, Sakata R, Sugiyama H, Kodama K (2012) Studies of the mortality of atomic bomb survivors, Report 14, 1950 - 2003: an overview of cancer and noncancer diseases. *Radiation Research*, ***177(3):*** *229-243*.
17. Preston DL, Ron E, Tokuoka S, Funamoto S, Nishi N, Soda M, Mabuchi K, Kodama K (2007) Solid cancer incidence in atomic bomb survivors: 1958 - 1998. *Radiation Research,* ***168(1):*** *1-64*.
18. National Research Council (2006) Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation, Health Risks from Exposure to Low Levels of Ionizing Radiation: BEIR VII Phase 2.
19. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans (2010) IARC monographs on the evaluation of carcinogenic risks to humans. Ingested nitrate and nitrite, and cyanobacterial peptide toxins. IARC Monographs on *the Evaluation of Carcinogenic Risks to Humans,* ***94****: v*.
20. United Nations Scientific Committee on the Effects of Atomic Radiation (2009) Effects of ionizing radiation: UNSCEAR 2006 Report to the General Assembly, with scientific annexes. Vol. 2. United Nations Publications.
21. Valentin J (2006) Low-dose extrapolation of radiation-related cancer risk. London: Elsevier.
22. Smith-Bindman R, Lipson J, Marcus R, Kim KP, Mahesh M, Gould R, Berrington de González A, Miglioretti DL (2009) Radiation dose associated with common computed tomography examinations and the associated lifetime attributable risk of cancer. *Arch Intern Med,* ***169(22):*** *2078-2086*.
23. Jung SE (2008) Korea Food & Drug Administration. Evaluation study of patient radiation dose in CT. Seoul: Korea Food & Drug Administration.
24. Schmidt MA and Payne GS (2015) Radiotherapy planning using MRI. *Phys Med Biol,* ***60(22):*** *R323*.
25. (a) Cianfrocca M and Goldstein LJ (2004) Prognostic and predictive factors in early-stage breast cancer. *Oncologist*, **9(6):** 606-616; (b) Carey LA, Perou CM, Livasy CA, Dressler LG, Cowan D.
26. Conway K, Karaca G, Troester MA, Tse CK, Edmiston S, Deming SL (2006) Race, breast cancer subtypes, and survival in the Carolina Breast Cancer Study. *J Am Med Assoc,* ***295(21)****: 2492-2502*.
27. Bor D, Sancak T, Olgar T, Elcim Y, Adanali A, Sanlidilek U, Akyar S (2004) Comparison of effective doses obtained from dose–area product and air kerma measurements in interventional radiology. *Br J Radio,* ***77(916):*** *315-322*.