Radiation Exposure to Patient and Radiologist During Transcatheter Arterial Embolization Therapy for Hepatocellular Carcinoma: Multicenter Study in Japan

T. Ishiguchi1, H. Nakamura2, M. Okazaki3, S. Sawada4, Y. Takayasu5, S. Hashimoto6, S. Hayashi7, S. Furui8, S. Koyama9, and H. Maekoshi9

1Nagoya University School of Medicine, Showa-ku, Nagoya, 466-8550, Japan
2Osaka University Faculty of Medicine, Suita, Japan
3Fukuoka University School of Medicine, Fukuoka, Japan
4Kansai Medical University, Moriguchi, Japan
5Hyogo College of Medicine, Nishinomiya, Japan
6Keio University School of Medicine, Tokyo, Japan
7Interventional Radiologist, Fukui, Japan
8Teikyo University School of Medicine, Tokyo, Japan
9Nagoya University School of Health Science

INTRODUCTION

Hepatocellular carcinoma (HCC) is a primary liver cancer commonly seen in Asian countries. HCC is usually associated with chronic hepatitis or cirrhosis due to Hepatitis B or C virus infection. In Japan, more than 30,000 people die of HCC a year, which consists the fourth leading cause of death by malignant neoplasm (1). Methods of treatment of HCC include transcatheter arterial embolization (TAE), surgical resection, percutaneous ethanol injection, systemic chemotherapy, and microwave coagulation. Among these, TAE is now most commonly performed in 40 to 60% of the patients with HCC (2). Current standard technique of TAE is consisted of superselective catheterization using a microcatheter to the hepatic arterial branch(es) supplying the tumor, infusion of oily contrast material (Lipiodol) mixed with anticancer drug(s), and injection of gelatin sponge particles to occlude the arterial blood flow to the tumor (3,4). TAE is performed under image guidance by X-ray fluoroscopy and digital subtraction angiography (DSA), and a patient with HCC may commonly have repeated TAEs during life due to regrowth of the primary tumor or appearance of new intrahepatic lesions. Therefore, precise evaluation of the radiation dose to the patient and the physician during TAE procedure is essential. To date, however, there have been only limited reports regarding to radiation exposure during TAE with considerable variability in the technique and the radiological equipments (5,6). Present multicenter study was carried out to evaluate radiation exposure to patients and interventional radiologists during TAE for HCC with the currently standard technique.

MATERIALS AND METHODS

Patients and Embolization Techniques

This study was conducted from September 1998 to March 1999 including 40 patients undergoing TAE for HCC at eight institutions (5 each consecutive patients from Nagoya University School of Medicine, Osaka University Faculty of Medicine, Fukuoka University School of Medicine, Kansai Medical University, Hyogo College of Medicine, Keio University School of Medicine, Fukui Medical School and Teikyo University School of Medicine). The mean age of the 30 men and 10 women was 65 years (range; 51-80 years), and the mean height and weight were 160.6 cm (range; 143-180 cm) and 57.7 kg (range; 37-74 kg), respectively. HCCs were located in the right lobe of the liver in 21 patients, the left lobe in 8, the right and the left lobe in 9, and the right and the caudate lobe in 2 patients. Fourteen patients had a solitary tumor and 26 patients had multiple tumors. The mean diameter of the tumors was 3.1 cm (range; 1-8 cm). Digital angiography systems from General Electric (Milwaukee, USA), Siemens (Erlangen, Germany), Toshiba (Tokyo, Japan), GE-Yokogawa (Tokyo, Japan), Philips (Best, Netherlands) and Hitachi (Tokyo, Japan) were used for diagnostic angiography and TAE. The equipments had been used since installation for 1-9 years (mean; 2.5 years). Supplementary X-ray filters (0.5 to 3-mm Al or 0.2-mm Cu) were equipped in 5 systems. The standard technique of the TAE procedure was as follows, although some details were modified by each radiologist when necessary. After the baseline images of the superior mesenteric arteriography and the celiac arteriography were obtained, a guiding catheter was placed at the common hepatic artery or the proper hepatic artery, and then a microcatheter was advanced distally to the tumor’s feeding artery. The oily contrast material (Lipiodol Ultra-Fluid, Guerbet, France) mixed with anticancer drug(s) (Epirubicin, Adriamycin, Mitomycin C or Neocarcinostatin) was injected through the microcatheter. Finally, gelatin-sponge particles (Gelfoam, Pharmacia & Upjohn, Peapack, USA) were injected until the arterial flow to the tumor was terminated. Computed tomography (CT) combined with the angiography
system (GE-Yokogawa, Tokyo, Japan) was used in two of the eight institutions (Hyogo and Keio). CT images of the liver were obtained during arterial portography or hepatic arteriography to evaluate tumor vascularity, and/or during TAE procedure to confirm distribution of Lipiodol.

Radiation Dose Monitoring

The radiation doses of the patients and radiologists were measured with lithium-fluoride thermoluminescent dosimeters (TLDs, Nagase Landauer, Tokyo, Japan). For TLD system calibration, experimental exposures at varying kilovolt peaks, 70, 80, 90, 100, 110 and 120 kV with the effective energy of 33.0, 34.2, 36.0, 37.8, 40.0 and 42.2 keV, respectively, were made in air with an ionization chamber dosimeter (Radocon 500 and 33-mL Chamber 550-4, Victoreen, Cleveland, Ohio) placed adjacent to TLD pellets in the center of the beam. The X-ray energy response of the dosimeter was compared and calibrated with the National Standard Free Air Ionization Chamber installed at the Electrical Laboratory Agency of Industrial Science and Technology of The Ministry of International Trade and Industry. The X-ray output (R/min) was measured and the effective dose was calculated using a conversion factor (mSv/R) at each condition (7). Readings from the TLDs and the ionization chamber were compared and used to create a calibration curve for determining the dose to the patients’ TLDs.

Three each TLD pellets were sealed in a 1-cm square package, and the total of 208 packages for 40 pairs of patient and radiologist and for measuring the background dose at eight institutions were prepared at the Laboratory of Nagase Landauer Co. and delivered by mail to the institutes. At each institute, the TLD packages were stored within the radiation-shielded areas adjacent to the angiographic suite. Before the start of TAE procedure, one each TLD package was positioned at the patient’s back behind the right lobe of the liver (on the mid-clavicular line and 5 cm below the right diaphragm), the patient’s lower abdomen (above the pubic symphysis), the radiologist’s forehead, and over and under the radiologist’s lead apron (Fig. 1,2), and fixed using Scotch Tape (3M, St Paul, Minn). After the TAE procedures have been completed, the TLDs were returned to the Laboratory for read out. The read-out data of the TLD pellets were corrected by the calibration factor, and the effective radiation dose at each position was defined.

In addition, the skin doses of 30 patients in 6 institutions (Nagoya, Osaka, Fukuoka, Kansai, Hyogo and Keio) were measured using a zinc-cadmium sensor linked to a digital counter (Skin Dose Monitor, SDM, McMahon Medical, San Diego, USA) placed on the back (Fig. 1). The cumulative skin dose (mGy) shown on the SDM counter and the cumulative fluoroscopic time (min) indicated by the X-ray equipment were recorded before and after every series of DSA image acquisition, so that the absorbed radiation doses by fluoroscopy and DSA were separately evaluated. A Film badge for routine personnel monitoring (Nagase Landauer) was also placed under the apron (Fig. 2).

Figure 1. Positions of the thermoluminescent dosimeters (square) and a Skin Dose Monitor sensor (circle) for patients.
RESULTS
Thermoluminescent Dosimetry
The results from the phantom studies showed that the calibration factor for the LiF-TLD system varied from 0.88 at the x-ray tube voltage of 80 kV to 1.21 at 120 kV (Fig. 3). Because the mean tube voltage used in the clinical TAE procedures was 77.8 kV for fluoroscopy and 79.5 kV for DSA, the calibration factor for the further analysis was determined as 0.9.

![Figure 2](image1.png)

**Figure 2.** Positions of the thermoluminescent dosimeters and a film badge for radiologists.

![Figure 3](image2.png)

**Figure 3.** Calibration curve of the thermoluminescent dosimeter system.
In the 40 patients, TAE was not performed in one patient after diagnostic angiography. As a result, 39 patients underwent TAE procedures by 21 interventional radiologists whose mean career was 13 years (range; 3-23 years). The radiologists put on a 0.25-mm Pb (34) or 0.35-mm Pb (5) x-ray shielding apron. TAE was performed at the hepatic segmental artery (17), right hepatic artery (10), left hepatic artery (8), inferior phrenic artery (6), right anterior branch (8), right posterior branch (5), proper hepatic artery (2) and pancreaticoduodenal artery (2). The mean number of embolized arteries in one patient was 1.4 (range; 1-3). The mean volume of injected Lipiodol was 4.3 ml (range; 1-15 ml).

The mean X-ray tube voltage was 77.8 kV (range; 70-95 kV) for fluoroscopy and 79.5 kV (range; 70-95 kV) for DSA. Fluoroscopy was obtained by a continuous exposure in 20 patients and by pulsed exposures in 19 patients. DSA was obtained by pulsed exposures in all patients. The most frequently used field size of the image intensifier ranged from 15 to 31 cm (mean; 26 cm). The mean source-to-image distance was 104 cm (range; 95-115 cm), and the mean source-to-table distance was 79.2 cm (range; 70-95 cm). The mean fluoroscopic time during the procedure was 21.3 minutes (range; 4.0-63.1 minutes). The mean number of series of DSA acquisition was 6 (range; 2-13). Contrast material for DSA was usually injected by power injectors and, in smaller arteries, 0-7 times (mean; 1.4 times) of injection was made manually. One to 5 series (mean; 3) of CT images of the liver were obtained in 8 patients during diagnostic angiography and/or during TAE.

The results of radiation dose measurement with the TLDs during 39 TAE procedures are summarized in Table 1. The mean effective skin dose at the patient’s back behind the liver was 973 ± 681 (SD) mSv. The individual dose widely distributed, which generally increased as procedures became more complex with increasing fluoroscopic time and number of DSA acquisition (Figure 4). The maximum skin dose of 3543.2 mSv was recorded in a patient with a small solitary lesion (diameter; 1.5 cm) in the left lateral segment of the liver. TAE was performed with a microcatheter advanced to the second segmental artery. The total fluoroscopic time was 53.4 minutes and 9 series of DSA was obtained in this particular patient. No patient reported skin injury including this highest dose recipient during follow-up for 12 to 18 months. The radiation dose at the radiologist’s head was 0.04 ± 0.04 mSv (mean ± SD), and was undetectable (equal to background, calculated as 0) in 13 procedures. The dose at the radiologist’s abdomen over the x-ray shielding apron was 0.15 ± 0.19 mSv and was undetectable in 7 procedures. The dose at the radiologist’s abdomen under the apron was further smaller (0.005 ± 0.010 mSv) and was undetectable in 28 procedures (72%), which was calculated to be 3.3% of the dose in front of the apron.

Table 1. Results of thermoluminescent dosimetry.

<table>
<thead>
<tr>
<th>Position</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Mean</th>
<th>SD*</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient (n=39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Back behind liver</td>
<td>185.1</td>
<td>3543.2</td>
<td>973.0</td>
<td>681.0</td>
<td>831.8</td>
</tr>
<tr>
<td>Lower abdomen</td>
<td>0.20</td>
<td>2.91</td>
<td>0.98</td>
<td>0.69</td>
<td>0.77</td>
</tr>
<tr>
<td>Radiologist (n=39)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>0**</td>
<td>0.15</td>
<td>0.04</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>Abdomen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Over the Apron</td>
<td>0**</td>
<td>0.89</td>
<td>0.15</td>
<td>0.19</td>
<td>0.06</td>
</tr>
<tr>
<td>Under the Apron</td>
<td>0**</td>
<td>0.05</td>
<td>0.005</td>
<td>0.01</td>
<td>0**</td>
</tr>
</tbody>
</table>

* standard deviation
** equal to background
Figure 4. Distribution of effective skin dose at the patient’s back behind the liver measured by thermoluminescent dosimeters.

Real-time Skin Dose Monitoring

The results of real-time skin dose monitoring in 30 patients showed that the mean dose at the patient’s back behind the liver was 948.4 ± 485.9 mGy (range; 239.8 to 2759.4 mGy, median; 794.8 mGy). These data showed good correlation with TLD dosimetry (R² = 0.87, p<.0001). In 25 patients who did not have CT imaging during the procedures, 56% of the total skin dose was exposed by DSA and the remaining 44% was by fluoroscopy. In five patient who had CT during the procedures, the percentages for the doses by DSA, fluoroscopy and CT was 54%, 35% and 11%, respectively. The mean skin dose by one series of DSA acquisition was 90.3 mGy (range; 10.4 to 165.9 mGy), and the dose by one minute’s fluoroscopy was 16.5 mGy (range; 2.7 to 64.5 mGy). Among the six institutions, the mean dose in each institution for one series of DSA ranged from 51.1 to 122.6 mGy, and the mean dose for one minute’s fluoroscopy ranged from 6.9 to 37.4 mGy (Figure 5).

Figure 5. The mean skin dose for one minute’s fluoroscopy and one series of DSA in 6 institutions.

DISCUSSION

In recent years, various interventional radiological procedures including arterial embolization, percutaneous drainage, angioplasty and stent placement have been developed and used for treating cardiovascular diseases, malignant neoplasms and other disorders. These procedures guided by x-ray
fluoroscopy, angiography or radiography may be associated with high radiation doses that are potentially harmful to the patient and the physician (8,9). The radiation doses are assessed by means of TLD, calculation from phantom studies, dose-area product shown by the device in the x-ray equipment, or real-time dosimetry (5,6,10-16). In the present study, we used LiF-TLDs in combination with the real-time dosimeter. The TLD pellets are small, radiolucent and suitable for evaluation at the multiple sites for patient and personnel. The energy-to-sensitivity characteristics of the TLD system was evaluated in the experimental phantom study, and the read-out data of the TLDs were corrected with the calibration factor. The possible variance for sensitivity of the individual TLD pellet was minimized by using multiple (three) TLD pellets at each position. The real-time dosimeter made it possible to assess the patient’s skin dose from fluoroscopy and each DSA acquisition separately. The mean entrance surface (skin) doses of the patient during interventional radiological procedures have been reported; 40 mGy by fallopian tube recanalization (13), 80 mGy by interventional endoscopic retrograde cholangiopancreatography (ERCP) (10), 260-270 mGy by lower-limb angioplasty (14), 1600 mGy by uterine artery embolization for leiomyomas (11), 1000 mGy by percutaneous coronary angioplasty (PTCA), 1500 mGy by single coronary stent placement, and 2500 mGy by rotational atherectomy with double stents placement (15). In the present study, the mean effective skin dose at the patient’s back was 973 mSv, which was comparable to the dose by PTCA (15). The 2000 mSv, the threshold for early transient erythema (16) was exceeded in 2 cases associated with extended fluoroscopic time and frequent DSA acquisitions. Real-time skin dose monitoring demonstrated that 56% of the total skin dose was exposed by DSA and 44% by fluoroscopy. It is evident that attention should be equally paid for both fluoroscopy and DSA in order to decrease a total radiation of the patient.

Real-time skin dose measurement at the 6 institutions demonstrated that there was a considerable variance in the mean dose rates by fluoroscopy and DSA. The dose rate by fluoroscopy is determined by various factors including the patient’s body thickness, tube voltage and current, and mode of exposure (e.g., continuous or pulsed exposure and the pulse rate). Use of magnified fluoroscopy increases exposure in relation to the selected size of effective field-of-view of the image intensifier. The dose by DSA is determined by the above listed conditions and, because the DSA images are obtained by pulsed exposures, it increases in relation to the number of image frames acquired. The operator-dependent parameters should be appropriately set at each stage of diagnostic and interventional procedures in order to decrease radiation exposure by avoiding use of unnecessarily high magnification fluoroscopy and limiting the frame number of DSA acquisition.

The skin dose at the patient’s lower abdominal surface was 0.98 mSv. This area is apart from the working field of TAE and radiation exposure is caused by fluoroscopy (exit surface) during the initial femoral arterial puncture and by scattered radiation from the hepatic portion during TAE. The local dose is considered to be within the usual range of exposure for diagnostic procedures such as excretory urogram (17).

The dose at the operator’s forehead was relatively small (mean, 0.04 mSv). It is reported that manual-injection DSA is the largest contributor to radiation exposure received by the interventional radiologist, therefore, the use of a power injector is always recommended when performing DSA (5). In the present study, 77% of DSA was performed using power injectors. Manual-injection DSA was performed in 23% at small arteries to prevent reflux or extravasation of contrast material. When manual-injection DSA is necessary, it is recommended for radiologists to position themselves as far away from the patient as possible.

Radiation exposure to the radiologist’s abdomen was effectively shielded by the lead apron. The mean dose over the apron of 0.15 mSv was decreased to 0.005 mSv under the apron by a factor of 30. The maximum dose recorded under the apron was 0.05 mSv in a procedure with a long fluoroscopic time (38 minutes) without a manual-injection DSA. International Commission on Radiological Protection (ICRP) recommends the annual dose limits for occupational radiation exposure as 20 mSv for the body and 150 mSv for the lens (18). Our results from the present study indicated that the maximum dose to the radiologist’s abdomen under the apron and to the lens (forehead) was 1/400 (0.05mSv) and 1/1000 (0.15 mSv), respectively, of the ICRP annual dose limits. We believe the standard TAE procedure is safe from a viewpoint of personnel radiation exposure, however, the radiation in each procedure should be remained as low as possible because it is not uncommon for an interventional radiologist to perform hundreds of TAE a year including complicated cases.

In conclusion, radiation exposure to the patients and the interventional radiologists during TAE for hepatocellular carcinoma is thought to be acceptable when proper techniques are used. Further effort to reduce radiation doses during the procedure will be directed toward both digital angiographic and fluoroscopic techniques.

REFERENCES

3. H.Nakamura, T.Hashimoto, H.Oi, S.Sawada, Transcatheter oily chemoembolization of hepatocellular