Multicentre dose audit for clinical trials of radiation therapy in Asia

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ABSTRACT

A dose audit of 16 facilities in 11 countries has been performed within the framework of the Forum for Nuclear Cooperation in Asia (FNCA) quality assurance program. The quality of radiation dosimetry varies because of the large variation in radiation therapy among the participating countries. One of the most important aspects of international multicentre clinical trials is uniformity of absolute dose between centres. The National Institute of Radiological Sciences (NIRS) in Japan has conducted a dose audit of participating countries since 2006 by using radiophotoluminescent glass dosimeters (RGDs). RGDs have been successfully applied to a domestic postal dose audit in Japan. The authors used the same audit system to perform a dose audit of the FNCA countries. The average and standard deviation of the relative deviation between the measured and intended dose among 46 beams was 0.4% and 1.5% ($k = 1$), respectively. This is an excellent level of uniformity for the multicountry data. However, of the 46 beams measured, a single beam exceeded the permitted tolerance level of $\pm 5\%$. We investigated the cause for this and solved the problem. This event highlights the importance of external audits in radiation therapy.

KEYWORDS: dosimetry, dose audit, linac, forum for nuclear cooperation in Asia, radiophotoluminescent glass dosimeter

INTRODUCTION

Multicentre clinical trials have been conducted within the framework of the Forum for Nuclear Cooperation in Asia (FNCA) to develop and establish effective strategies of medical care for common malignant tumours (such as carcinoma of the uterine cervix and nasopharyngeal cancer) in Asian countries [1–6]. The FNCA is a framework of regional cooperation between Asian countries with the aim of promoting peaceful and safe application of nuclear science and technology. The FNCA medical project was launched in 1993 and has successfully continued its clinical trials. Today 11 countries are participating in this project: Bangladesh, China, Indonesia, Japan, Kazakhstan, Korea, Malaysia, Mongolia, Philippines, Thailand and Vietnam. One of the most important aspects of an international multicentre clinical trial is the uniformity of absolute dose between centres [7]. The quality of radiation dosimetry varies because of large variation in the conditions of radiation therapy among the participating countries. For instance, some countries do not have a Primary Standard Dosimetry Laboratory (PSDL) or a Secondary Standard Dosimetry Laboratory (SSDL) for calibrating the ionization dosimeters used in adjusting the linear accelerator (linac) output [8]. In addition, the absolute dosimetry protocols are different for each country, depending on the worldwide standard they are based on, such as IAEA TRS-398 or AAPM TG-51. The training level of the medical physicists can also affect the precision of the delivered doses [9]. Thus, a final output intercomparison using a linac beam should be performed. The National Institute of Radiological Sciences (NIRS) in Japan, which has played a role as a data centre for the multicentre clinical trials, has conducted a dose audit of participating countries since 2006 in order to ensure the quality of the irradiation doses used in these trials. NIRS has developed a dose audit system using a radiophotoluminescent glass dosimeter (RGD) [10, 11]. The RGD has superior characteristics (such as repeatable readouts, reduced fading, and an engraved ID number on elements) when compared with the thermoluminescent dosimeters (TLDs) that have been used worldwide for these types of dose audits [10, 12]. RGDs can be also used in small-field dosimetry [13–15]. The domestic dose audit in Japan has been successfully conducted using this system since 2007 [10, 11]. The same audit system was used for the audit of the FNCA participating countries. Here, the results of the audit are reported together with the necessary follow-up actions for the case where an error was detected by the audit.

METHODS
RGD

The RGD (DOSE ACE, Asahi Glass Co., Tokyo, Japan) is a silver-activated phosphate glass with the following weight composition: 11.0% Na, 31.55% P, 51.16% O, 6.12% Al and 0.17% Ag [16]. The RGD is 1.5 mm in diameter and 12 mm in length. The readout area for an RGD is 1 mm in diameter from its central axis and 6 mm in length for normal doses (up to 10 Gy). The effective readout centre for the longitudinal axis is offset from the geometrical centre by ~1.8 mm due to the design of the reading magazine. An ID number is engraved on each unit. The output precision is improved by performing sequential readings. The depletion of the signal caused by

reading is very small. The principles and practice of the signal reading have been described in detail in previously published papers [10, 15]. The reproducibility had a standard deviation (SD) of 0.8% [10]. Depending on the irradiated beam energy, an energy correction was applied to the RDG readings [10, 17].

Methodology of the dose audit

RGDs and a water-equivalent solid phantom (Tough Water Phantom, Kyoto Kagaku Co., Kyoto, Japan) were sent or taken to radiotherapy facilities, where the RGDs were irradiated with a 1 Gy dose in the reference condition of the X-ray beam. The phantom was a 30 cm × 30 cm slab with a thickness of 16 cm. The central region was modified to hold the glass dosimeters (Fig. 1). The three RGD elements were mounted perpendicular to the beam axis at 1 cm intervals and were mounted at 10 cm depth in the phantom on the isocentre plane for a single irradiation. For each irradiation, the averaged outputs of the three elements were used as the output of the beam. The RGD output was calibrated by six control elements, which were irradiated with a dose of 1 Gy by a ^{60}Co gamma-ray beam at NIRS (SSDL). The control elements were used to translate the RGD output to the absorbed dose to water and to calibrate the sensitivity of the reader. The absorbed dose to water was calculated from the measured RGD outputs using the following equation:

$$D = \sum_{i=1}^{3} (X_i \times I_i)/3 \times E_q \times P_q \times \frac{Dose_{^{60}\text{Co}}}{\sum_{i(c)=1}^{6} (X_{i(c)} \times I_{i(c)})/6},$$

where X_i is the raw output value of the glass element whose ID number is i.[or $i(c)$ for control elements]; I_i is the sensitivity
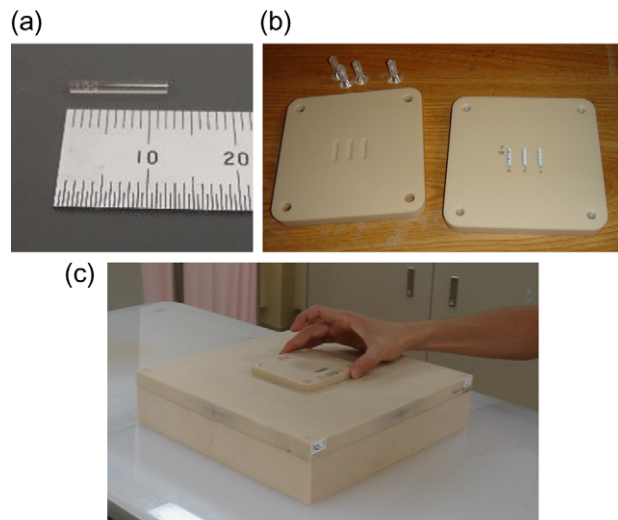

Fig. 1. (a) RGD element with ID number '100'. (b) Central part of a solid phantom containing 3 RGD elements. The interval between each element is 1 cm. (c) The central part of the solid phantom is inserted in the 30 × 30 cm solid phantom to irradiate the RGDs at reference conditions.

correction factor of the glass element whose ID number is I (derived by uniform irradiation using ^{60}Co-γ rays).

$$I_i = \frac{D_{^{60}Co}}{X_i}$$

E_q is the energy correction factor of beam quality 'q'. [The glass elements were irradiated by ^{60}Co-γ rays and 4–20 MV X-rays. The correction factor was derived by using the outputs of the ionization chamber (IC), D(^{60}Co) and D(q), which were measured at the same set-up as the glass dosimeter. The value of the correction factor was 1.007 for 4 MV and 1.013 for 20 MV.]

$$E_q = \left[\frac{\sum_i X_i(^{60}Co) \times I_i}{\sum_i X_i(q) \times I_i} \right]^{Glass} \times \left[\frac{D(q)}{D(^{60}Co)} \right]^{IC}.$$

P_q, Phantom correction factor of beam quality 'q.'

$$P_q = \frac{D_w}{D_T},$$

where D_w is the output of the ionization chamber irradiated by X-rays of beam quality 'q' in 10 cm deep water (reference condition);

D_T is the output of the ionization chamber irradiated by X-rays of beam quality 'q' at 10 cm deep in the tough water phantom (reference condition); *Dose* 60_{Co} is the output of the ionization chamber irradiated by ^{60}Co-γ rays just before the irradiation of control elements with the same set-up.

I_i was assigned to each element to increase the precision of the outputs. I_i, E_q and P_q were determined before the audit trial started. The accumulated uncertainty of each parameter was estimated to be 1.1% in one standard deviation [11].

The dose audit implementation

The dose audit of the FNCA participating countries has been conducted since 2006. By 2014, 11 countries had participated in this audit. The countries are Bangladesh, China, Indonesia, Japan, Kazakhstan, Korea, Malaysia, Philippine, Pakistan, Thailand and Vietnam. Pakistan is not an official member of FNCA, but participated in this activity as an observer member. Mongolia is an official member of FNCA but could not participate in this activity because it does not have a linac. The names of the facilities, irradiation dates, and the number of beams audited are listed in Table 1. One facility received the audit twice, but the linac was different. The linacs used during this audit were Siemens (Mevatron, Primus, ONCOR

Table 1. List of countries, facilities, and number of beams that received the FNCA dose audit

Country	Facility	Date	Beams
China	Changzhou Tumor Hospital	Nov. 2006	4
	The First Affiliated Hospital of Su Zhou University	Nov. 2006	2
Korea	Korea Institute of Radiological and Medical Sciences	Feb. 2007	4
	Samsung Medical Center	Mar. 2007	2
Indonesia	Dr. Cipto Mangunkusumo Hospital	Oct. 2007	2
	Dharmais Cancer Hospital	Oct. 2007	2
Vietnam	Ho Chi Minh City Oncology Hospital	Feb. 2007	4
Philippines	St. Luke's Medical Center	Jan. 2009	4
Japan	National Institute of Radiological Sciences	Jun. 2009	2
Malaysia	Sarawak General Hospital	Oct. 2009	4
Thailand	Siriraj Hospital	Nov. 2009	4
Bangladesh	Delta Hospital Ltd	Oct. 2010	2
Pakistan	INMOL Hospital, Lahore	Dec. 2011	2
Vietnam	National Cancer Hospital	May. 2012	2
	National Cancer Hospital K2	May. 2012	2
Kazakhstan	Kazakh Research Institute of Oncology and Radiology	Aug. 2013	2
Thailand	Siriraj Hospital	Aug. 2014	2
	Total		46

Impression Plus), Varian (Clinac 2100 C, 2100 C/D, 2300, 21EX, 23EX, iX) and Elekta (Precise Treatment System). The energies of the beams were 4, 6, 10, 15 and 18 MV. We performed either on-site or off-site audits depending on the auditor manpower/budget situation. The method used to irradiate the RGDs was the same as that previously set for on/off-site audits.

RESULTS AND DISCUSSION

The results of the dose audit are summarized in Table 2. The averages of the relative deviations for beam energies of 4, 6, 10, 15 and 18 MV were −1.2%, +0.4%, +1.0%, −0.1% and +1.0% respectively. The definition of the relative deviation is ($D_{measured}$ − $D_{intended}$)/$D_{intended}$. No systematical energy dependence was observed, and thus the energy correction of the RGDs was valid. The majority of the beam energies were between 6 and 15 MV, and the deviations were within ±1% for these energies. For other energies, the deviation was around or slightly higher than ±1%, but these are limited statistics because the number of 4 MV and 18 MV beams tested was only 1 and 3, respectively. The average and standard deviations of the relative deviation between the measured and intended dose among 46 beams was 0.4% and 1.5% ($k = 1$), respectively. Taking into account the uncertainty value of RGD, 1.1%, the deviation is excellent from the point of view of the uniformity of the multicountry data. The intended dose, 1 Gy was derived using a simple tissue phantom ratio (TPR) calculation. Figure 2 shows the histogram of the relative deviation. More than 90% of the beams (43 beams) were within ±3%. Only one beam exceeded the tolerance level of ±5% [11]. The exact value of this 10 MV beam was +6.1%. The result for the 6 MV beam at the same facility was +3.5%, which was a high value but still within the tolerance level.

A thorough and lengthy investigation was performed to identify the cause of this deviation. The weekly monitor check dosimetry datasheets that were performed around our dose audit date for the 10 MV beam were reviewed according to the national dosimetry standards. The methodology was fine, but we found one irregular value of the temperature and pressure correction factor, k_{TP}. On the datasheet, $k_{TP} = 0.948$ was used as the correction factor. This was an irregularly small value. To derive this factor, a pressure value of 106 kPa was used. This was an unfeasible value from our experience of radiation dosimetry in Asian countries. However, on the datasheet for the 6 MV beam measured on the same date, the pressure recorded was 100.6 kPa, which resulted in $k_{TP} = 0.998$. We concluded that the operator miswrote the pressure value as '106' instead of the true value '100.6' in the Excel-based datasheet. This difference corresponded to a 5.3% underestimate of k_{TP}, leading to an overdose of exactly the same percentage. As a result, the +6.1% overdose measured by our dose audit could be attributed to this mistype. The information was immediately sent as feedback to the hospital together with a message stating the importance of accurate typing and double checking of parameters.

The International Organization for Medical Physics (IOMP) is collaborating with professional organizations on the development of a professional certification system for medical physicists that can be implemented globally. The International Medical Physics

Table 2. Summary of the results of the dose audit

Beam energy	Number of beams	Average deviation	S.D. of the deviation
4 MV	1	−1.2%	
6 MV	22	+ 0.4% (−1.6 to +3.5%)	1.4%
10 MV	11	+ 1.0%* (−1.4% to +6.1%)	2.0%
15 MV	9	−0.1% (−1.0 to +1.4%)	0.8%
18 MV	3	+ 1.0% (+0.1 to +1.5%)	0.8%
Total	46	+0.4%	1.5%

*The average deviation of the 10 MV beams is reduced to +0.4% if the beam with the largest deviation (+6.1%) is excluded. The results were categorized according to their beam energies.
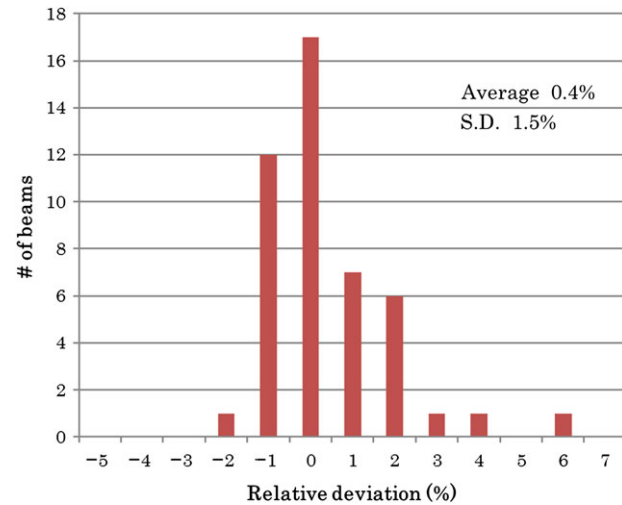

Fig. 2. Relative deviations of the results of the dose audit. Relative deviation is the percentage difference of the measured dose compared with the intended dose.

Certification Board (IMPCB) has started to build models to develop international certification programs, established requirements for the successful completion of the certification process, and is working on collaborations with the IOMP and IAEA. The Asia–Oceania Federation of Organizations for Medical Physics (AFOMP) has also developed a policy to provide guidance when developing medical physicist education and training programs. In this regard, we conducted a survey of the status of medical physicists within the FNCA participating countries. The survey was performed by interviewing the participants of FNCA workshops during 2009 and 2010. The participants answered each question in cooperation with their colleagues or related people in their countries. The results are summarized in Table 3. There were many variations in the certification system, education and number of physicists. Through the standardization of these systems, human errors should decrease, and the quality of multicountry international clinical studies should increase.

Table 3. Survey results of the status of medical physicists within FNCA participating countries

Questions	MY	ID	TH	BD	JP	CN	VN	PH	KR
What is the status of medical physicists in your country?									
(a) Certified by the Government									
(b) Certified by a professional society		x			x	x		x	x
(c) No official certification and given the position by each hospital	x		x	x			x		
Do they have contact with patients?									
Yes	x	x	x	x					
No					x	x	x	x	x
What is the average background education of medical physicists in your country?									
(a) Ph.D. in related field		x				x			x
(b) Masters Degree	x	x	x	x	x	x			
(c) Bachelor degree	x	x				x	x	x	
What is the minimum number of years of education and training required to become a medical physicist after graduation from high school?									
Years	4	4	8	6	8	5	4	4	5
How many medical physicists are working in radiation therapy departments in your country?									*Unanswered
Number	50	40	74	20	100–200	1181	28	*	84
In your country, is foreign certification of medical physicists valid?									
Yes				x					
No			x		x	x	x		
Decided on a case-by-case basis	x	x						x	x

MY = Malaysia, ID = Indonesia, TH = Thailand, BD = Bangladesh, JP = Japan, CN = China, VN = Vietnam, PH = Philippines, KR = Korea.

CONCLUSION

A dose audit of 16 facilities in 11 countries was performed (using glass dosimeters) within the framework of the FNCA quality assurance program. Of the 46 beams measured, only 1 beam exceeded the tolerance level of ±5%. We investigated the cause for this and solved the problem. This event shows the importance of external audits in radiation therapy.

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