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ARTICLE

Investigation of skin reactions in complex interventional radiology procedures

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Abstract – The aim of this study was to compare the radiation induced skin reactions, if any, on patients who underwent complex interventional radiology (IR) procedures and received cumulative air kerma (K_a) above 5 Gy, and experimentally validate the onset of skin reaction and estimate probable causes of such reactions. Six patients who underwent complex IR procedures and received K_a exceeding 5 Gy were followed up for a period of 2 years after the procedure to check for occurrence of skin reactions. Out of six patients, one patient reported with severe skin injury after a period of one month of IR procedure while another patient reported skin injury within 24 h after the IR procedure. The remaining 4 patients did not show any visible skin injury/reactions followed up for a period of two years after IR procedure. Reddening and peeling of patient skin reported within 24 h of the IR procedure were not concurring with exposed skin areas and this was validated by the phantom study. The follow up study of patients who received doses exceeding the threshold for skin reactions suggests that factors other than radiation dose may play a significant role in manifestation of radiation induced skin reactions. An intensive assessment and analysis of intrinsic and extrinsic factors related to radiation sensitivity of patients prior to complex IR procedures may help in preventing radiation induced skin reactions.

Keywords: interventional radiology / cumulative reference air kerma / skin reactions / anthropomorphic phantom

1 Introduction

The use of fluoroscopically guided interventional radiology (IR) procedures are rapidly increasing as it helps in avoiding complicated invasive surgery and reduces hospitalization time (Pantos *et al.*, 2009). Nevertheless, as the complexity of the IR procedures increases, so do procedure time and concomitant cumulative air kerma, and therefore, the risk of skin injury (McCabe *et al.*, 2011). Radiation-induced skin damage has been recognized as a rare complication of fluoroscopically guided interventional procedures (Valentin, 2000). The radiation doses in the complex procedures often exceed the threshold values for skin reactions in single or multiple procedures. Single procedure peak skin doses of the order of several tens of Gray (Gy) have also occurred during IR procedure as reported earlier (Koenig *et al.*, 2001a, 2001b; Balter *et al.*, 2010). Manifestations of radiation injury to the skin range from mild erythema at low doses to dermal necrosis or chronic ulceration at very high doses. Radiation skin reactions are not "burns"; but they occur as a result of damage to the basal cell layer of the skin and the resultant imbalance between the normal production of cells in this layer and the destruction of cells at the skin surface (Khanna *et al.*, 2013). Erythema occurs as a result of capillary dilatation and resultant increased vascularity in the dermis (Khanna *et al.*, 2013). The exposure of the subdermal lymphatics as a result of loss of the superficial epithelium leads to moist desquamation, or after higher doses, skin necrosis (Khanna *et al.*, 2013). It is essential that any damage is minimized, as far as possible, by ensuring that interventions are based upon best practice and supported by evidence-based guidelines (Porock and KristJanson, 2001).

During any interventional procedure, the dose delivered to the patient is distributed over different areas of the skin based on beam directions used in the procedure and hence, skin reactions are not observed in general. However, complex IR procedures may deliver doses which exceed the tissue reaction

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threshold to some areas of skin, causing skin injuries. Therefore, monitoring of patient doses in real-time would be helpful in predicting the occurrence of any tissue reactions. Thresholds for the nature and severity of radiation injury and period of its manifestation vary from patient to patient (Balter and Miller, 2014). Patient related factors that increase susceptibility to radiation injury include autoimmune and connective tissue disorders, hyperthyroidism, diabetes mellitus and compromised skin integrity among others (Miller *et al.*, 2010). National Council on Radiation Protection and Measurements (NCRP) recommends follow-up of patients who undergo IR procedures in which cumulative air kerma at reference point (K_a) exceeds 5 Gy in order to detect clinically relevant skin reactions (NCRP Report, 2010). The International Electrotechnical Commission (IEC) defines K_a as the air kerma accumulated at patient entrance reference point which lies on the central axis of the beam, 15 cm on the X-ray tube side of isocenter for isocentric IR equipment (IEC, 2010; Miller *et al.*, 2010). In this study, a comparative analysis was carried out for 6 patients who underwent complex IR procedures where K_a exceeded 5 Gy, to monitor the occurrence of skin reactions, if any. To the best of our knowledge, follow up studies of patients who received doses with potential to cause skin reactions in interventional radiology procedures are scarce. The objective of this study was to (a) compare the radiation induced skin reactions, if any, on 6 patients who underwent complex IR procedures and received K_a above 5 Gy and (b) experimentally validate the onset of skin reaction in one case and estimate probable causes of such reactions.

2 Materials and methods

2.1 Patient case studies

In the present study, comparative analysis of onset of skin injury was carried out for 6 patients (hereafter referred to as Patients #1 to #6) who underwent complex IR procedures. The complexity of procedures is considered based on time of exposure (fluoroscopy/cine acquisition) and resultant radiation dose delivered. The six patients included in the study did not have any history of diabetes and none of them were obese. Out of six, five IR procedures were carried out by the same interventional radiologist. Two patients (#1 and #2) reported with suspected radiation-induced skin injury. Patient #1 developed skin reactions on the right mid forearm and gluteal region one month after embolization procedure for treatment of pelvic arteriovenous malformation (AVM). Dose records of patient #1 were not available in the system. The total fluoroscopy time for this patient was 90 minutes; and total skin dose was estimated to be approximately 8 Gy. The skin reactions were reported by the patient after a month of the procedure. Skin biopsy test and successive investigations carried out by the hospital showed that the patient has developed chronic radiation dermatitis (RD). Patient #2 reported skin reddening and desquamation within 24 h of the ventricular pacemaker implantation procedure. The total procedure time was 101 minutes and the cumulative air kerma recorded in the IR system was 5.7 Gy. This dose was delivered from three different angulations of the C-arm, namely postero-anterior (PA), 30° left anterior oblique (LAO) and 20° right anterior oblique (RAO). In this case, skin reactions were visible in the various areas of the patient skin, not consistent with the irradiated area. Patient #3 to Patient #6 who underwent complex IR procedures and received cumulative K_a exceeding 5 Gy were followed up for a period of 2 years after the procedure to check for occurrence of skin reactions.

2.2 Estimation of peak skin dose

2.2.1 Anthropomorphic phantom and radiochromic film

The skin reactions in case of patient #2 were not concurring with the skin areas subjected to radiation exposure. Anthropomorphic phantom based experimental simulation was performed to estimate the peak skin dose and identify the skin areas which might have received dose above the skin reaction threshold. The dosimetric measurements were carried out on C-arm mount monoplane digital angiography unit (Artis Zee, Siemens, Germany) which was used for conducting the clinical procedure on patient #2. An anthropomorphic thorax phantom (Alderson Lung/Chest Phantom RS-320, Radiology Support Devices, USA) which extends from the neck to below the diaphragm was used. The phantom is molded about a male skeleton, corresponding to the external body size of a patient, 5 feet and 9 inches (175 cm) tall and weighing 162 lbs (73.5 kg). The materials in the phantom cavity are equivalent to natural bone and soft tissues. Lungs are fixed in the inflated state and are molded to conform to the pleural cavities of the phantom. The pulmonary arteries are injected with a blood equivalent plastic to simulate patient anatomy.

Gafchromic XR-RV3 dosimetry film (Ashland Inc. Covington, Kentucky, USA) was used to record and measure patient skin dose during interventional procedure. The film was calibrated in terms of entrance surface air kerma in the range of 15–1000 cGy using 80 kV X-ray beam with 3 mm Al filtration. During calibration, film samples were placed on $20 \times 20 \times 30$ cm Perspex phantom to simulate patient-equivalent backscattering conditions (McCabe *et al.*, 2011). The irradiated film samples were scanned using Epson Expression 10000 XL flatbed scanner.

2.2.2 Experimental set up

The performance of the IR equipment was tested using a calibrated mult-O-meter (Unfors RaySafe AB, Billdal, Sweden) before conducting the experiment. The tabletop dose rate of the IR equipment was measured and verified with system displayed data. Based on the dose report of patient #2 stored in the IR system and inputs of the interventional cardiologist who performed the procedure, phantom exposures were carried out. The phantom was placed on the patient table reproducing the patient position for IR procedure. Gafchromic XR-RV3 films are available in standard size of 14" × 17". A single sheet of film was cut into two sections, each of size 7" × 8.5" for better conformity to the phantom contours and was placed adjacent to each other on the anterior side of the chest. Film sections of size 7" × 8.5" were placed on lateral sides of the phantom and a single film sheet of size 14" × 17" was placed on the posterior side. The phantom was irradiated using same angulations as in the case of patient #2 and cumulative air kerma values delivered in each angulation was matched as closely as possible to the values recorded in the patient dose report. The irradiated films were scanned after 48 h and peak skin doses were determined using the calibration curve.

Table 1. Details of patients and IR procedures.

Patient	Age	Procedure	Total fluoroscopy time (minutes)	No. of cine acquisitions	Total cumulative air kerma (Gy)
Patient 1	55	Pelvic arterial embolization	90	–	8[a]
Patient 2	72	Ventricular pacemaker implantation	100.8	18	5.7
Patient 3	24	Uterine artery embolisation	36.6	38	5.2
Patient 4	58	Left colic artery embolisation	36.7	27	7.1
Patient 5	52	Endovascular embolization	34.3	24	5.4
Patient 6	65	Fenestrated endovascular aortic repair	322.9	60	19.9

[a] Estimated value

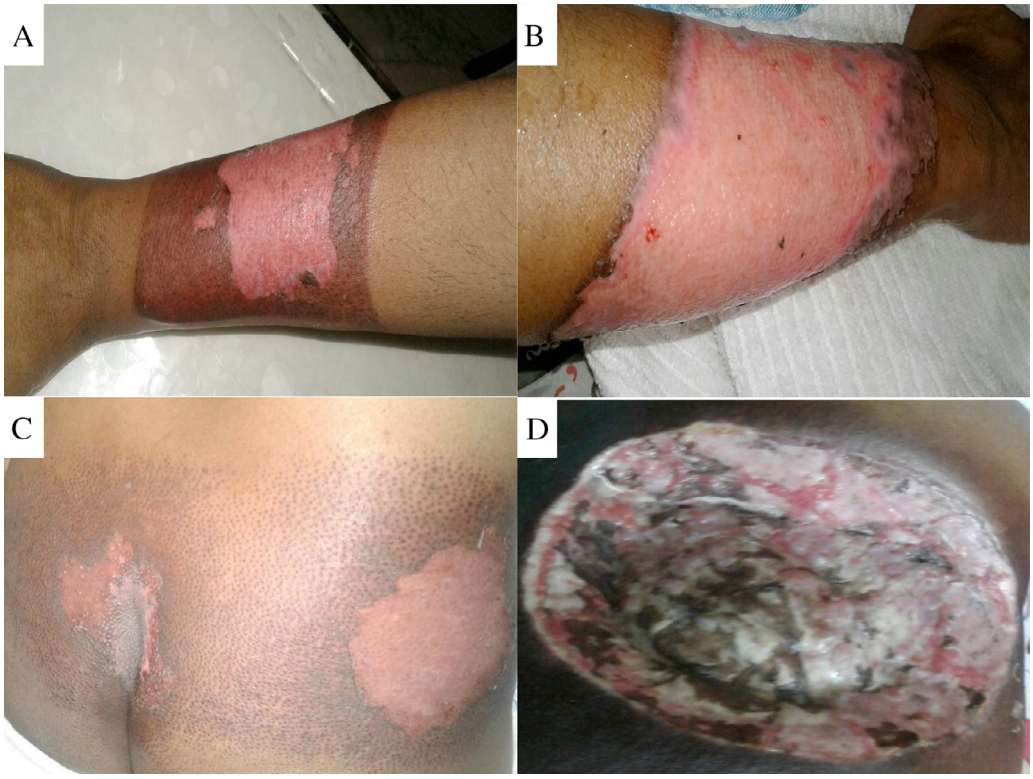

Fig. 1. Skin reactions in patient #1 who underwent embolization procedure for pelvic AVM.
A: Skin reaction on right arm after a month of the IR procedure; B: Skin reaction in the right arm progresses after 3 months of the procedure; C: Skin reactions in the posterior and right lateral gluteal region after a month; D: Skin reactions in the right gluteal region progresses to a non-healing ulcer in a period of 6 months after the procedure.

3 Results

Table 1 shows the patient age, type of interventional procedure, total fluoroscopy time and cumulative air kerma at reference point of the 6 patients included in the present study. Patient #1 developed radiation dermatitis which initially presented as mild form of skin damage and eventually became ulcer within a period of four months after the embolization procedure (Fig. 1). Exposure parameters of experimental simulation performed to estimate the peak skin dose and identify the skin areas which received maximum skin dose in case of patient #2 are presented in Table 2. The analysis of exposed Gafchromic films showed that the lower right area of the back where radiation fields from all the three angles overlapped received maximum dose. The value of peak skin dose measured by Gafchromic film was 5.8 Gy. Even though this dose is higher than the threshold dose for skin reactions, no specific injuries were observed in the area of skin which received maximum dose. Reddening and peeling of skin of patient #2 were not specific to the area of radiation exposure but were noticed in other parts of the body. Patient #2 also had predisposed skin condition. Patient #3 to patient #6 did not report any skin reactions after the procedure (followed up for 2 years).

Table 2. Operating parameters and recorded cumulative air kerma in anthropomorphic phantom study performed to determine peak skin dose in case of patient #2.

Projection	Fluoroscopy		Cine acquisition		Cumulative air kerma (mGy)
	kV	mA	kV	mA	
PA	65	4	81	178	3990
LAO	68	3.8	81	130	684
RAO	70	3.6	87	116	1026

4 Discussion

Fluoroscopically guided interventional procedures are associated with a risk of radiation injury to the skin. Many a times, complex procedures require long fluoroscopy times which may cause significant increase in patient skin dose. The skin dose in such cases might exceed the threshold limits for skin reactions. The threshold dose for transient skin erythema is 2 Gy (Miller *et al.*, 2003). In the present study, 6 patients who received cumulative air kerma exceeding 5 Gy were followed up for a period of 2 years after the completion of IR procedure. These cases were selected to compare the radiation induced skin reactions, if any, in these patients. The cumulative air kerma to the reference point is the best immediate estimate of the patient skin dose during a procedure (Weinberg *et al.*, 2015). The cumulative air kerma values are used in this study for comparison between the patients and as qualitative indication to identify the area where the dose reaches its maximum value. Out of six, only two patients reported suspected radiation induced skin injury. The skin injury of patient #1 was diagnosed as chronic RD through biopsy test. The biopsy report describes the injury shown in Figure 1D as "Sections from the blocks show skin with necrosis of epidermis and superficial dermis with ulceration, ulcer bed contain granular debris. The deep dermis and subcutis show homogenous sclerosed collagen, inflammatory cell infiltrate of histiocytes and neutrophils, and fibrinoid necrosis of some of the small caliber vascular channels". The initial symptom of skin injury in the case of patient #1 was erythema in the upper mid line and right lateral gluteal region. The right arm of patient #1 was also exposed during the procedure to radiation and skin reactions were observed on the arm as well (Fig. 1). The radiation induced erythema in the right gluteal region progressed to a non healing ulcer and hence, skin grafting had to be performed. The initial skin grafting was unsuccessful and hence, the patient underwent repeated skin grafting. The skin reaction on patient arm could have been avoided, if it would have been placed out of the primary beam.

Patient #2 reported with reddening and peeling off skin in areas exposed to radiation as well as unexposed areas within 24 h of the IR procedure. An anthropomorphic phantom based study was performed to simulate the exposures performed in the case of patient #2. The results of the experimental study using phantom and XR-RV3 Gafchromic films enabled to identify the area exposed to maximum radiation dose due to overlapping fields. Reported skin condition of patient #2 was not consistent with areas exposed to radiation during the procedure. The dermatological tests confirmed that the patient has epidermal necrosis which appeared within 7 days after procedure which may be due to allergic drug reaction. Hence, in the case of patient #2, it was concluded that the skin reactions were not radiation induced. Patient #3 to patient #6 received cumulative air kerma in the range of 5.2–19.9 Gy and there was no reportable radiation induced skin reaction. In the case of patient #6, cumulative air kerma value was much higher compared to other patients included in the study. However, no skin reactions were observed in this patient. This may be attributed to the distribution of radiation dose in different areas of the body without overlapping the separate radiation fields, thus reducing peak skin dose (Balter and Miller, 2014).

The comparative analysis of 6 patients suggests that the effect of radiation on patients undergoing complex fluoroscopically guided interventional radiology procedures delivering doses exceeding the threshold values for skin reactions is widely varying. The follow up study in patients who received doses exceeding the threshold for skin reactions indicates that factors other than radiation dose may play a significant role in manifestation of radiation induced injuries. Obesity, diabetes, nicotine abuse, compromised skin integrity, skin type, autoimmune/connective tissue disease, hyperthyroidism and certain drugs are among many factors which affect the expression and severity of the radiation injuries (Jaschke *et al.*, 2017). Individual differences in radiosensitivity exist in human populations, which could be caused by nucleotide variants of DNA repair genes (Matsuura *et al.*, 2016). As radiation produces DNA damage, patients with impaired cellular DNA repair capabilities are at increased risk. Patients suffering from ataxia teleangiectasia, a rare autosomal-recessive disorder resulting from mutations in both copies of ATM (ataxia teleangiectasia mutated) gene, are predisposed to develop severe cutaneous complications after radiation exposure. It has been suggested that many patients with serious and unanticipated radiation injuries may be heterozygous for the ATM gene or possess some other ATM abnormality (Balter *et al.*, 2010). ATM heterozygocity occurs in approximately 1% of the general population (Hymes *et al.*, 2006; Balter *et al.*, 2010).

The present study had a few limitations. The first one is the limited number of patients included in this study that cannot allow firm conclusions about the dose response of the patients nor on the frequency and severity of skin reactions. The study is, in fact, limited to the presentation of 6 clinical cases. Moreover, in the absence of dose records for patient #1, estimate of entrance skin dose was made from system technique factors, exposure rate during fluoroscopy and total fluoroscopy time. Cumulative air kerma values were used as surrogate for patient entrance surface dose for all the other cases. Since cumulative air kerma does not include corrections

for scatter contribution, C-arm angulations, rotation or table movements, it may overestimate the skin dose. The exact cause of radiation injury induction in one patient out of 6 patients who received similar values of radiation dose could not be verified.

5 Conclusion

The present study of comparison of onset of skin reactions, if any, of 6 patients who underwent complex IR procedures, suggests that individual-specific factors may play a significant role in the onset/occurrence of skin reactions. Therefore, an intensive assessment and analysis of intrinsic and extrinsic factors related to radiation sensitivity of patients prior to complex IR procedures may help in preventing radiation induced skin injuries. The study also emphasize the significance of patient positioning during IR procedures so that extraneous body parts like arms would not be exposed in primary X-ray beam. Method of in-phantom dose measurement simulating the clinical conditions may be used in investigation of skin injury cases reported after complex interventional radiology procedure to identify the skin areas exposed and determine the dose delivered.

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