

## Skin Injuries from Fluoroscopically Guided Procedures: Part 1, Characteristics of Radiation Injury

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**I**nterventional procedures in radiology and cardiology often involve high radiation doses to patients' skin. The potential for skin injury was discussed in 1994 [1]. More than 70 injuries have been reported in the referenced literature during the last decade or are known through other sources such as unpublished research and legal records [2–27] (Tables 1 and 2).

The incidence of radiation injuries is small compared with the number of procedures performed. More than 700,000 interventional cardiologic and other procedures are now performed each year [28, 29]. A serious injury can be debilitating, requiring a prolonged course of intense care that sometimes lasts for years [23, 24]. Severe skin injuries, like chronic ulceration and necrosis, are documented in 38 of the 73 cases that we reviewed [30]. Skin grafts were required in 18 patients, three of whom needed a repeated procedure after the first graft failed [23, 24] (Table 2, patient 14).

Interventionalists are often unaware of the magnitude of the radiation dose to the skin [30, 31]. Many are not aware that such injuries can even occur with modern equipment. Consequently, they, and other physicians, frequently do not recognize the injury as being related to the procedure. For this reason, an underreporting of the number of injuries from interventional work is suspected [29]. In this article we investigate the relationship be-

tween reported skin damage and known patterns of progression to assist physicians in the recognition of these injuries. We also identify factors that can help improve patient care.

### Fundamental Facts About Skin Injury

#### *Historical Background*

Within months after the discovery of X rays in 1895 by Wilhelm Konrad Roentgen, X-ray-induced effects in the skin became apparent [32, 33]. In 1898, Gassmann [34] described the histologic changes of chronic roentgen ulcers. One of the first reports ascribing malignant changes to chronic radiation damage of the skin appeared in 1902 [35]. Since then a vast literature on radiation damage has been published. Contemporary knowledge of biologic skin effects is based mainly on experience gained in radiotherapy and from animal studies [36–42].

#### *Mechanisms of X-Ray Injury*

Because of their neutrally charged subatomic property, X rays can penetrate cells, releasing kinetic electrons that create an ionization track across many cells. This focally concentrated deposition of a tiny amount of energy breaks molecular bonds, bringing about biochemical changes in the affected cells. No detectable temperature rise and, typically, no disturbance to the sensory system occurs. The

body's first response occurs as an internal biologic response in dysfunctional cells. This stimulated response goes unnoticed by the host when the biochemical changes are minor.

#### *Deterministic Versus Stochastic Effects*

Skin changes such as erythema, ulcers, telangiectasia, and dermal atrophy are deterministic effects. Such effects occur only when the radiation dose exceeds a certain threshold. Histologically, a minimum number of cells must be damaged to elicit a response, the probability and severity of which increases rapidly as the dose increases beyond the threshold. If the dose is sufficiently large, the effect will be seen in 100% of cases. Depending on dose, some effects may occur promptly (<24 hr); others may be delayed for years. Skin is the organ at greatest risk because it receives the greatest dose. The inflammatory changes after irradiation are often referred to as radiodermatitis.

Radiation-induced cancer is a stochastic effect that may be induced at any dose; that is, no threshold dose is involved. Its severity is independent of dose, although the probability of occurrence increases as dose increases. Some authors advocate regular follow-up to detect possible malignancies in patients with high radiation doses [22]. Though radiation-induced cancer is an important potential long-term sequela of a pro-

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**TABLE 1** Case Reports of Skin Injuries

Study	Date	No.
<b>Coronary Angiography and Intervention</b>		
Iyer [2]	1976	1
Wolff and Heinrich [3]	1993	2
Lichtenstein et al. [4]	1996	4
Shope [5]	1996	1
Søvik et al. [6]	1996	1
D'Incan and Roger [7]	1997	6
Poletti [8]	1997	1
Gironet et al. [9]	1998	1
Granel et al. [10]	1998	4
Stone et al. [11]	1998	1
Dandurand et al. [12]	1999	4
Dehen et al. [13]	1999	2
Miralbell et al. [14]	1999	1
Pezzano et al. [15]	1999	6
Sajben et al. [16]	1999	1
This article	2001	11
Total		47
<b>Cardiac Radiofrequency Catheter Ablation</b>		
Court documents <sup>a</sup>	1993	1
Shope [5]	1996	3
Rosenthal et al. [17]	1997	1
Nahass [18]	1997	2
Vañó et al. [19]	1998	4
Wagner et al. [20]	2000	1
Total		12
<b>TIPS Placement</b>		
Payne [21]	1995	1
Knautz et al. [22]	1997	1
Nahass and Cornelius [23]	1998	3
Wagner et al. [24]	1999	1
This article	2001	1
Total		7
<b>Neuroradiologic Intervention</b>		
Huda and Peters [25]	1994	1
Carstens et al. [26]	1996	1
Krasovec and Trueb [27]	1998	1
Total		3
<b>Other</b>		
Iyer [2]	1976	1
Shope [5]	1996	2
Dandurand et al. [12]	1999	1
Total		4

Note.—TIPS = transjugular intrahepatic portosystemic shunt. No. = number of cases.

<sup>a</sup>Third Circuit Court for Davidson County, Nashville, TN, No. 93C-1916, 2 July 1993.

longed interventional procedure, the focus of this article will be on the much-earlier-occurring deterministic effects.

#### *Dose Rate Delivery and Fractionation*

Repair of radiation damage occurs at molecular, cellular, and tissue levels. Enzymes repair radiation-induced DNA lesions within hours. Repopulation at the cellular level occurs within days after irradiation [41, 43]. As a result, the rate of dose deposition in tissue is critical to cellular repair.

Intermittent fluoroscopy and fluorography at different dose rates are often used in interventional procedures. Dose rates may vary over a wide range depending on a multitude of factors and can be between 0.01 and 1.0 Gy/min to the skin [20]. For low-dose-rate application or for fractionated delivery of high doses, sublethal cell injuries can be repaired and killed cells replaced during the entire process of dose accumulation [40–43]. For instantaneous delivery of high doses, no interim repair is possible. Protraction of the total dose, therefore, results in higher threshold doses (total cumulated dose) for both early and late deterministic effects [37].

Although intracellular repair is complete within a few hours, repopulation of the cells in the dermis and epidermis takes much longer. Animal models suggest that full recovery of the epidermis occurs by 6 weeks as long as permanent damage is not induced [37]. Skin damage responsible for early effects can be virtually eliminated in a few months [41]. However, it is uncertain whether damage responsible for late dermal effects will recover fully or whether a residual remembered injury remains, decreasing the tolerance for future irradiation [37, 41].

Fractionation of the total dose, as seen in patients undergoing several procedures separated by days or weeks, increases overall tissue tolerance, but tolerance for each subsequent individual session may decrease. For example, if the skin has not completely recovered from a previous intervention, then the dose required to produce injury from an additional future session will be lower than that for nonirradiated skin. Of 73 patients reviewed [30], 66% of the cardiology patients had more than one angioplasty in 3 years and 14% had more than two angioplasties in 3 years. This compares with 21% and 4% as reported by Pattee et al. [44] in a study of radiation risk to patients undergoing percutaneous transluminal coronary angioplasty. The greater percentage of multiple procedures involving injury suggests that previous

procedures may play a role in reducing skin tolerance, as suggested by Lichtenstein et al. [4] and Søvik et al. [6].

#### **Biology of Radiation Effects in the Skin**

##### *Latent Period Between Procedure and Clinical Injury*

The response of the skin to high levels of radiation generally follows a characteristic pattern determined by the radiosensitivity of various cell populations and by their temporal patterns of injury and repair. The time course may vary depending on dose delivery characteristics and the condition of the patient. The time between a fluoroscopic procedure and when a skin lesion becomes symptomatic is variable. In the reviewed case material [30], most lesions were apparent by about 2 weeks to 3 months after the procedure. However, intervals of less than 1 day for pain (Table 2, patient 2) and more than 3 years for dermal necrosis [12] have been reported.

##### *Threshold Doses*

The threshold doses for various types of skin injuries are summarized in Table 3. These doses represent skin entrance doses for single-dose irradiation. The temporal patterns in Table 3 and in the discussions to follow should be used as reasonable guidelines, not as absolute time frames.

##### *Responses Beginning Within Days of Irradiation*

Within a few hours after single doses in excess of about 2 Gy, an early transient erythema might occur in a well-defined area matching the entrance site of the X-ray beam. The area may look much like sunburn. This reaction peaks at about 24 hr and subsides after approximately 48 hr. It is thought to represent an early phase of inflammation, with hyperemia and increased permeability of the capillaries resulting from the release of proteolytic histamine-like enzymes [37, 45, 46]. The intensity of the erythema increases with the dose. However, the reaction is often faint, is only briefly present, and probably goes unnoticed in many cases because no particular attention is paid to it. If observed, this finding can serve as a warning that a certain threshold dose has been exceeded.

##### *Responses Beginning 1–2 Weeks After Irradiation*

A second hyperemic phase, the main erythematous reaction (main erythema), begins about 10 days after a dose of about 6 Gy and earlier when doses are very high. Its intensity, which is also dose-dependent, reaches a peak around the 14th day. The skin becomes warm

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<b>TABLE 2</b> Fourteen Patients with Radiation-Induced Skin Injuries				
Patient No.	Sex, Age	Procedure	Location of Skin Lesion	Clinical Features
1	Male, 54	Angiography, PTCA	Right scapula	At 14 da: erythema progressing to deep ulceration, no healing After 14 mo: skin graft
2	Male, 56	Angiography, PTCA	Below right axilla	At 24 hr: sharp pain After 3 da: erythema progressing to superficial ulceration At 2.5 mo: 12 × 6.5 cm pigmented plaque with hyperkeratosis
3	Male, 63	Angiography	Left scapula	At 13 mo: 2.5 × 1 cm depigmented plaque with telangiectasia
4	Male, 65	Angiography, PTCA, stent	Right scapula	At 7 mo: large asymptomatic pigmented plaque with telangiectasia
5	Female, 75	2 Angiographies, 1 PTCA	Below right axilla	At 2 wk: erythema with ulcer formation in subsequent weeks At 10 mo: 12 × 10 cm poikilodermic lesion
6	Male, 64	2 Angiographies, 2 PTCAs	Left scapula	At 16 mo: 8 × 5 cm area of dyspigmentation and telangiectasia
7	Male, 83	Angiography, 2 PTCAs	Right scapula	At 35 mo: 4 × 5 cm hyperpigmented plaque
8	Male, 57	Angiography, 2 PTCAs, atherectomy, stents	Right scapula	At 5 mo: prolonged erythema, progressing to ulcer formation necessitating skin graft
		Angiography, PTCA, atherectomy, stent	Right mid back	Prolonged erythema
9	Male, 69	Angiography, 2 PTCAs	Mid back	At 3 wk: erythema progressing into moist desquamation At 3 mo: ulceration that continued for 17 months
10	Male, 67	Angiography, stent	Left scapula	At 5 wk: erythema At 6 wk: moist desquamation At 24 wk: ulceration
11	Male, 62	Angiography, stents	Mid back	At 8 mo: deep ulceration
12	Male, 53	3 Angiographies, stents	Right mid back	At about 1 mo: erythema and pain At 3–4 mo: full thickness ulcer At 7 mo: excision and grafting
13	Male, 48	2 Angiographies, 1 PTCA	Mid back	At <2 wk: erythema progressing to moist desquamation At 7 mo: deep ulceration and necrosis At 8.5 mo: débridement and skin graft
14	Male, 49	2 TIPS + 1 TIPS attempt	Mid back	At 4 wk: 13 × 18 cm discoloration with pain At 5 wk: desquamation progressing to nonhealing chronic ulceration with secondary infection After 22 mo: two skin graft procedures After 26 mo: complete healing

Note.—PTCA = percutaneous transluminal coronary angioplasty, TIPS = transjugular intrahepatic portosystemic shunt.

and edematous. The patient may complain of burning, tenderness, and itching. The main erythema represents a secondary inflammatory reaction to damage to the proliferating cells at the basal cell layer of the epidermis. If the dose is not much greater than the threshold, the erythema fades after 4 weeks. Figure 1A is an example of an erythema, shown at 3 weeks after radiofrequency cardiac catheter ablation. The patient was exposed to about 20 min of fluoroscopy with her elbow about 20–25 cm from the X-ray source. The circular port of the X-ray system defined the sharply demarcated border of the injury.

#### *Responses Beginning About 3 Weeks After Irradiation*

Epilation (hair loss) results from depletion of the germinal layers of hair follicles. Single doses of 3–6 Gy might result in temporary loss of hair after about 3 weeks [37]. Regrowth oc-

curs after approximately 8–12 weeks [37, 47]. New hair may be thinner and more sparse and can occasionally show a different degree of pigmentation [41]. Doses in excess of 7 Gy may irreversibly damage the hair follicle, and permanent epilation of the affected follicles ensues. Huda and Peters [25] describe such hair loss after a neurointerventional procedure.

Sebaceous glands are as sensitive to radiation as hair follicles, whereas sweat glands are somewhat more resistant. Because of the lack of secretions from these glands, the patient may complain of dry and scaly skin [41, 48].

Radiation doses below the threshold that is lethal to epidermal cells may stimulate melanocytes to produce more pigment. After single doses of greater than 10 Gy, a prolonged hyperpigmentation lasting weeks to months may occur (Fig. 2). The hyperpigmentation gradually fades during the following months

but sometimes persists indefinitely. At higher doses, melanocytes will be killed, and an area of hypo- or depigmentation will result. Often, hyper- and hypopigmentation can be observed in the same lesion. For example, an irradiated field can have a central area of hypopigmentation with margins of hyperpigmented skin. This pattern is also seen after healing of an area of dermal ulceration [39, 41] (Fig. 3).

#### *Responses Beginning About 1 Month After Irradiation*

If the radiation dose exceeds about 14 Gy, the main erythema may progress to dry desquamation of the skin. The erythematous skin is then covered with scales and flakes of corneum, similar to the aftereffects of a sunburn. If the radiation dose is even higher (≈18 Gy), blistering and sloughing of the superficial skin (moist desquamation) occurs (Fig. 4). There is continuous weeping of serum from



A



B



C

TABLE 3 Threshold Skin Entrance Doses for Various Skin Injuries		
Effect	Dose (Gy)	Onset
Early transient erythema	2	Hours
Main erythema	6	~10 days
Temporary epilation	3	~3 wk
Permanent epilation	7	~3 wk
Dry desquamation	14	~4 wk
Moist desquamation	18	~4 wk
Secondary ulceration	24	>6 wk
Late erythema	15	~8–10 wk
Ischemic dermal necrosis	18	>10 wk
Dermal atrophy (1st phase)	10	>12 wk
Dermal atrophy (2nd phase)	10	>1 yr
Induration (invasive fibrosis)	10	
Telangiectasia	10	>1 yr
Late dermal necrosis	>12?	>1 yr
Skin cancer	—	>5 yr

Note.—Data are taken from [1] and updated from Hopewell J, personal communication, 1999. Dash (—) indicates not known.

**Fig. 1.**—49-year-old woman with 8-year history of refractory supraventricular tachycardia. (Reprinted with permission from [20])

**A–C,** Photographs show sharply demarcated erythema above right elbow at 3 weeks after radiofrequency cardiac catheter ablation (A), tissue necrosis 5 months after procedure (B), and deep ulceration with exposure of the humerus at 6.5 months (C).



**Fig. 2.**—56-year-old man with obstructing lesion of right coronary artery. Photograph of right posterolateral chest wall at 10 weeks after percutaneous transluminal coronary angioplasty shows 12 × 6.5 cm hyperpigmented plaque with hyperkeratosis below right axilla (Table 2, patient 2).



**Fig. 3.**—75-year-old woman with 90% stenosis of right coronary artery. Photograph of right lateral chest obtained 10 months after percutaneous transluminal coronary angioplasty shows area of hyper- and hypopigmentation, skin atrophy, and telangiectasia (poikiloderma) (Table 2, patient 5).

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**Fig. 4.**—48-year-old woman with history of diabetes mellitus and severe coronary artery disease who underwent two percutaneous transluminal coronary angioplasties and stent placements within a month. Photograph of left mid back 2 months after last procedure shows well-margined focal erythema and desquamation. (Reprinted with permission from [11])



**Fig. 5.**—69-year-old man with history of angina who underwent two angioplasties of left coronary artery within 30 hr. Photograph taken 1–2 months after last procedure shows secondary ulceration over left scapula. (Reprinted with permission from [10])

the deep cutaneous layers. This weeping is associated with considerable pain and discomfort and exposes the skin to infection. Topical antibiotics and sterile dressings are required prophylactically [49]. Histologically, the proliferative cells in the basal layer of the epidermis are damaged and their number is reduced. The time delay to observe skin desquamation is approximately the same time that differentiating basal cells take to migrate to the stratum corneum epidermis [46].

### *Responses Beginning About 6 Weeks After Irradiation*

One or two weeks after the onset of desquamation, epithelial regeneration occurs from the margins of the lesion and from surviving basal cells. Size of the radiation field, and thus the size of the injury, is a factor. For all but very small fields, regeneration is prolonged, exposing tissues to the risk of secondary ulceration [40]. Endothelial swelling and proliferation result in arteriolar obstruction and compromise the microcirculation. The microvascular damage causes a relative ischemia in the irradiated area. Healing is delayed, and the developing epidermis is typically reduced in thickness [41]. When skin desquamation is severe and protracted, dehydration and infection can easily

complicate healing. Secondary ulceration (Fig. 5) may also be precipitated by trivial injury to the healed but fragile skin. Infection leads to additional skin breakdown, which further complicates healing.

### *Responses Beginning About 8–10 Weeks After Irradiation*

A third, late phase of erythema may develop 8–10 weeks after irradiation. The threshold for a single dose has been estimated as 15 Gy or greater for this effect to occur. This phase of erythema is associated with a dusky or mauve skin discoloration [37].

### *Responses Beginning About 10–16 Weeks After Irradiation*

Microvascular damage and an overall reduction in capillary density lead to progressive vascular insufficiency of the dermis. As a result, ischemic dermal necrosis (Fig. 1B) may ensue at 10–16 weeks after exposure with a suggested threshold dose of 18 Gy. The damage becomes more extensive with higher doses.

### *Prolonged Ulceration*

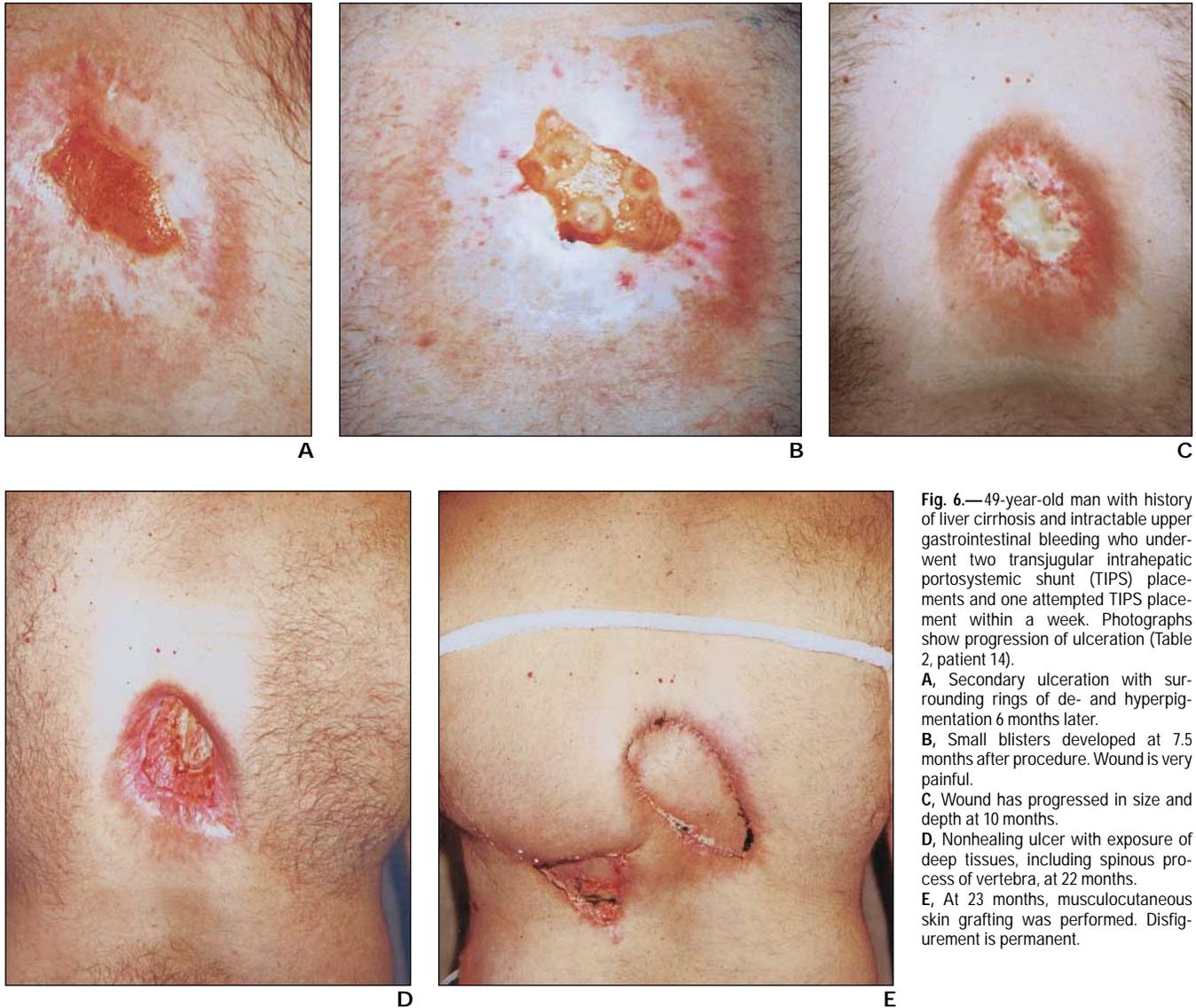
Radiation ulcers that have healed over prior weeks recur even without infection, often precipitated by trivial trauma, thermal in-

jury, or exposure to ultraviolet light. These ulcers have a tendency to recur multiple times in the following months or years and may heal over a long, protracted course. Rosenthal et al. [17] report such healing characteristics in a woman who underwent radiofrequency catheter ablation.

Some radiation ulcers never heal completely but break down intermittently instead [47]. Progression of the ulcer may ensue and can be extensive, exposing deep tissues such as tendons, muscles, or bones (Figs. 1C and 6D). A number of radiation-induced ulcers, lasting more than 6 months to years after the interventional procedure, are described in the literature. Figures 6A–6D (Table 2, patient 14) show the progression of an injury from superficial ulceration to deep tissue necrosis over a period of 22 months after a series of transjugular intrahepatic portosystemic shunt procedures. Injuries that are advanced to this stage require surgical excision and grafting [49] (Fig. 6E).

### *Responses Beginning About 12 Weeks After Irradiation*

A common late consequence after a pronounced main erythema, especially when the erythema is associated with moist desquamation, is dermal atrophy (Fig. 7), which may



**Fig. 6.**—49-year-old man with history of liver cirrhosis and intractable upper gastrointestinal bleeding who underwent two transjugular intrahepatic portosystemic shunt (TIPS) placements and one attempted TIPS placement within a week. Photographs show progression of ulceration (Table 2, patient 14).

**A,** Secondary ulceration with surrounding rings of de- and hyperpigmentation 6 months later.  
**B,** Small blisters developed at 7.5 months after procedure. Wound is very painful.  
**C,** Wound has progressed in size and depth at 10 months.  
**D,** Nonhealing ulcer with exposure of deep tissues, including spinous process of vertebra, at 22 months.  
**E,** At 23 months, musculocutaneous skin grafting was performed. Disfigurement is permanent.

develop as early as 3 months after the injury and is seen in animal experiments to progress in two phases [40]. In the first phase, the dermis becomes hypoplastic and the epidermis is reduced to a few cell layers. Hair follicles disappear. Scattered focal deposition of melanin may give the skin a discolored, poikilodermic appearance [41] (Fig. 3).

Subcutaneous induration is seen in the late phase of radiodermatitis. The induration commonly progresses with time (Fig. 8). The loose stromal net of the epidermis and the adipose tissues of the subcutis are gradually replaced by dense and fibrous tissue. The skin and subcutaneous fat feel wooden on palpation and are tender. The patient tries to avoid movement that might stress the area [41]. If subcutaneous indu-

ration develops in the vicinity of a joint, permanent restriction of movement can result (Fig. 8).

#### *Responses Beginning About 1 Year After Irradiation*

Late skin changes result from damage to deeper layers of the skin, mainly to the dermis. A second phase of dermal atrophy may be observed [40]. Atrophy gradually progressing for about 4 years has been described [46].

After doses greater than about 10 Gy, an atypical dilatation of superficial dermal capillaries (telangiectasia) develops (Figs. 3 and 8). The delay between exposure and occurrence is often cited as 1 year but has been noted a few months after some interventional procedures. Telangiectasias often increase as time progresses, sometimes for more than 10

years. A clear dose-effect relationship has been shown [50, 51].

When the relatively fibrous, avascular dermis cannot support the atrophic epidermis, late dermal necrosis may ensue [46]. Late dermal necrosis can occur after a long latent period of more than a year without any history of exudative dermatitis [41] (Fig. 9). The presumed threshold dose of 12 Gy is less than the threshold dose for the earlier-occurring moist desquamation, secondary ulceration, or ischemic dermal necrosis. The incidence of necrosis is thought to reach a peak in the third or fourth year [52].

#### **Histology of Radiation Injury**

Histologic findings are not pathognomonic for exposure to ionizing radiation [36]. Diagno-

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**Fig. 7.**—54-year-old man with stenosis of left circumflex artery. Photograph of right shoulder at 5.5 months after percutaneous transluminal coronary angioplasty shows area of depigmentation and atrophy (Table 2, patient 1). Injury progressed to deep ulceration, requiring skin grafting.



**Fig. 8.**—17-year-old girl with history of cardiac arrhythmia underwent two cardiac ablation procedures in 13 months. Photograph taken 2 years after last intervention shows atrophic indurated plaque with skin telangiectasia at right lateral chest wall involving posterolateral aspect of breast. Induration resulted in limited movement of right arm. Risk of breast cancer is increased. (Reprinted with permission from [19])



**Fig. 9.**—69-year-old man with history of angina who underwent three coronary angiograms followed by three angioplasties within 8 months. Photograph 3 years after last procedure shows skin necrosis with surrounding erythema and hyperpigmentation in right subscapular region. (Reprinted with permission from [12])

sis essentially relies on clinical findings and an appropriate history of radiation exposure to the area of concern [13]. A skin biopsy may not be necessary if the presentation is very suggestive. Characteristic signs include erythema matching the position of the radiation port, and skin reaction evolving in typical temporal patterns. The histologic appearance of radiation dermatitis depends on the clinical presentation and on the phase of injury, and is too extensive to be dealt

with in detail [37, 39, 41, 45, 53]. The main changes in the early phase are marked edema, degeneration of the basal cell layer, and inflammatory reaction. These changes are associated with progressive pyknosis of nuclei and cell death. Dilated blood vessels with endothelial proliferation, arteriolar thrombosis, and extravasation of RBCs can be seen. Hyperkeratosis is observed in dry desquamation. Intraepidermal blisters and loss of corneum are features of

moist desquamation. In the late phase, the epidermis is irregular, with areas of atrophy and relative hyperplasia [39]. Dermal thinning with atrophy of the adnexal structures and dilatation of blood vessels is observed. Thickened, hyalinized collagen bundles and relative increase of elastic fibers are signs of dermal fibrosis that can lead to palpable induration of the skin. Atypical large stellate fibroblasts with enlarged hyperchromatic nuclei may be found at random

in the dermis. These cells are a sign of radiation damage and usually are not observed in other skin diseases that also lead to end-stage dermal fibrosis [36, 39, 41, 47, 53].

### Radiation Sensitivity

The degree of skin response to radiation varies for different body sites. Kalz [54] found that skin sensitivity for acute reactions, from most to least sensitive, is as follows: anterior aspect of the neck, antecubital, and popliteal spaces; flexor surfaces of the extremities, chest, and abdomen; the face; the back and extensor surfaces of the extremities; the nape of the neck; the scalp; and the palms and soles. Hair follicles of the scalp appear to be more radiosensitive than those in other parts of the body [41].

A variety of reports have been published that suggest a correlation between exaggerated reactions after radiotherapy and connective tissue diseases, especially scleroderma, systemic and discoid lupus erythematosus, and mixed connective tissue disease [24]. Although a causative relationship for these rare observations is assumed, definite evidence is lacking. Diabetes mellitus and hyperthyroidism have also been associated with increased skin response to irradiation [36, 41, 55]. Wagner et al. [24] describe a patient with multiple health problems, including mixed connective tissue disease and diabetes mellitus, who underwent a transjugular intrahepatic portosystemic shunt procedure and later developed a severe necrotic ulceration. Patients carrying the homozygous form of the ataxia telangiectasia gene are also known to exhibit significant hypersensitivity to radiation [36, 42].

Skin sensitivity to radiation can be increased by various chemotherapeutic agents, such as actinomycin D, adriamycin, bleomycin, 5-fluorouracil, and methotrexate [36, 41, 56]. An early reaction that has healed over time can even manifest itself again in the same skin area when actinomycin D is given some weeks or months after the irradiation. This effect is known as a recall reaction. A similar reaction has been described in one patient after simvastatin administration [57]. Ciprofibrate, a fibric acid derivative used for the treatment of hyperlipidemia (not available in the United States), has been recently suggested to play a role in radiation-induced skin injury [9]. The patient in this case, however, also had lupus erythematosus, which may have contributed to the event, although the authors of the report noted that the disease could not be stimulated by ultraviolet radiation at that time.

### Diagnosis of Radiation-Induced Skin Injury

Some patients discussed in this review did not seek the attention of their physician for radiation-induced changes. In our series [30] (Table 2, patients 1–7), we found that four of seven patients with chronic lesions were not aware of them at the time of discovery by physical examination. The skin lesions are frequently on the back and not directly visible to the patient. Moreover, many patients have limited mobility and may be less likely to notice skin changes. When lesions are minor, they may go unnoticed. A number of patients have had skin lesions that were visible but did not cause any pain. These patients disregarded the finding until the lesion became painful.

Patients usually do not return to the physician who initially performed the procedure when they seek medical advice for their skin problem [30]. Usually they present at some stage to a dermatologist but do not give a history of prior fluoroscopy because they assume it is irrelevant for the complaint or have forgotten about it. This fact is especially true when there is a significant latent period. The physician will not be given the correct history indicating the cause of the lesion unless the physician specifically asks. In some cases, even if the patient mentions prior fluoroscopy, the dermatologist has disregarded fluoroscopy as a possible cause because of lack of experience with the high doses from these procedures. In our review of 73 patients [30], an initial diagnosis of a fixed drug eruption, morphea (circumscribed cutaneous scleroderma), contact dermatitis, viral or bacterial infection, or a spider bite was made, [7, 11, 12, 24], including four from this report. Consequently, the correct diagnosis was delayed. In some cases the correct diagnosis was made after a delay of 2 years [13] (Table 2, patient 14) and 5–6 years [4] after the first appearance of the lesion.

A skin biopsy was taken in 27 patients to confirm the diagnosis [30]. However, as previously stated, the diagnosis can be made from a careful medical history and the appearance of the lesion. A biopsy may be helpful if other skin conditions must be considered; however, biopsy is not always necessary. Pezzano et al. [15] discourage skin biopsies because they leave a defect that heals poorly and that can result in a chronic ulcer. We concur with this advice.

### Conclusions and Recommendations

In general, physicians have difficulty recognizing the cause of fluoroscopy-induced skin injuries because such injuries are rare,

and modern fluoroscopy typically has not been associated with such injuries. Inability of physicians to recognize radiation-induced skin changes has led to misdiagnoses and prolonged and uncertain courses of treatment. Dermatologists and interventionalists must be aware of the potential for skin injuries and recognize the characteristics of such injuries to avoid misdiagnosis.

Biopsy is frequently performed. However, the results are not pathognomonic for radiation changes. Fluoroscopy-induced injuries can be recognized by the location of the injury as being congruent to the entrance of the X-ray beam and by the temporal pattern of the injury in relation to the fluoroscopy. Additionally, the injury often shows well-defined borders, which occur when the beam is not moved or resized during prolonged fluoroscopy over one site. A biopsy is usually not necessary and is not recommended because it may result in a nonhealing ulcer.

Some patients may be at greater risk for injury because of preexisting health conditions such as collagen vascular disease, diabetes mellitus, or ataxia telangiectasia, or because of a high radiation dose from a previous procedure. Good communication with the patient is essential. Interviewing the patient for potential high-risk conditions before a procedure is recommended, as is appropriate counseling. A short skin examination should be considered for patients who have had previous procedures. Further irradiation of any previous injury should be kept to a practical minimum and the patient counseled appropriately.

If a procedure is prolonged or the dose to the skin is known to be high, the patient should be advised to examine him- or herself about 2–3 weeks after the procedure to look for skin changes and to contact the interventionalist if any are observed. This information is not only good for patient care, it also assists in quality control because it indicates when dose levels have reached certain thresholds.

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