

# Fluoroscopy: Radiation Protection of the Eye



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# Fluoroscopy: Radiation Protection of the Eye

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*Visual system tissues, particularly the lens of the eye, are extremely vulnerable to the harmful effects of ionizing radiation. There is no well-established “safe” level of radiation exposure for the eyes. With the expanding use of fluoroscopy and fluoroscopy-guided interventional procedures, radiation doses to patients have increased dramatically. Radiation dose management is crucial to protect the eyes of patients and health care personnel who perform fluoroscopic exams.*

*Dosimetric monitoring and dose minimization practices — including planning, careful selection of fluoroscopy imaging modes, the proper use of protective equipment and shielding, effective quality assurance and quality control programs, and adequate operator training — all play important roles in protecting the eyes of patients and health care personnel.*

## After completing this article, readers should be able to:

- Describe the functional anatomy of the eye.
- Explain how ionizing radiation can disrupt the structure, physiology and function of visual system tissues.
- Discuss different types of visual system diseases and disorders and their relation to ionizing radiation exposure.
- Discuss changing views about dose thresholds for radiation cataract formation.
- Identify how staff position with regard to the fluoroscopy unit and patient can affect dose.
- Describe strategies for minimizing patient and staff radiation doses during fluoroscopic procedures.
- Explain why fluoroscopic radiation dose to the eye lens is a major occupational exposure concern and how the threat of chronic exposure can be mitigated.
- Describe sentinel event thresholds requiring postfluoroscopic monitoring for radiation injury.

**F**luoroscopy and other imaging modalities have revolutionized modern medicine, providing physicians with invaluable anatomical and physiological information about their patients. The range of fluoroscopic examinations, particularly fluoroscopy-guided interventional procedures, has proliferated over the past 20 years. Because of prolonged examination times and other factors, patient radiation doses and the incidence of serious radiation injury from fluoroscopy also have increased.<sup>1</sup> For example, interventional fluoroscopy for transcatheter embolization involves patient radiation doses of up to 100 mSv, an amount that is 1,000 times the dose delivered by a typical chest radiograph.<sup>2</sup>

Visual system tissues, particularly the lenses, are very vulnerable to damage caused by ionizing radiation and, therefore,

are of particular concern to patients and health care personnel. Fluoroscopy not only can expose the eyes of patients to varying doses of ionizing radiation, but also the eyes of surgeons, radiologists, radiologist assistants (RAs), radiologic technologists and other personnel who are involved in these procedures. Fluoroscopic radiation doses are subject to the type of examination, target tissue, exam duration, and the radiation protection practices and specific equipment used.<sup>1</sup>

Ionizing radiation is not the only potential medical imaging hazard to the visual system. In fact, animal experiments suggest that ultrasound energy can cause free radical damage to the endothelial cells of the cornea.<sup>3</sup> However, ionizing radiation is a well-established threat to visual system integrity and health, and the higher radiation doses associated with

fluoroscopy must be considered when planning and performing procedures.

This article describes the anatomy and physiology of the eye, the biological effects of ionizing radiation on the eye and the implications of radiation pathobiology for radiation protection of the eyes. The article also discusses the risks posed by long-term exposure to low-dose scatter radiation to the eyes of health care professionals.

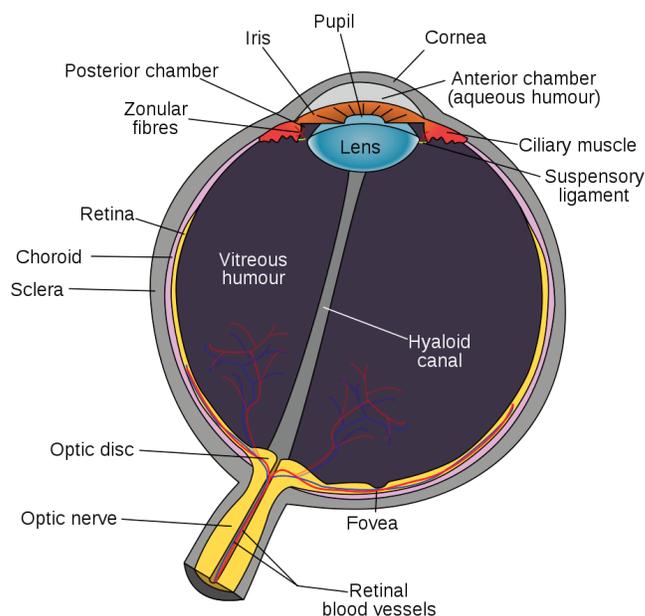
### History

Ophthalmology evolved over the centuries from folk cures and quackery to a systematic, scientific field of medicine and surgery. The first published description of eye anatomy, Benvenuto Grassi's *De Oculis*, appeared in 1474, at which time ophthalmology was a primitive medical endeavor. Eye medicine was the dubious province of barbers, who also practiced crude dentistry and general surgery.<sup>4</sup> Physician Leonhart Fuch's 1539 text *Alle Kranckheyt der Augen* (*All Illnesses of the Eyes*) was an early scientific text on ophthalmology; it systematically described the eye's anatomy, pathologies and treatments.<sup>4</sup>

Surgeon Jacques Daviel explained the surgical removal of cataracts in 1753, and by 1817 a 2-volume ophthalmology textbook was published, marking the early origins of ophthalmology as a distinct field of medicine.<sup>4</sup> In 1820, partly in response to an epidemic of trachoma bacterial infections of the eye, Benjamin Travers wrote the first English-language ophthalmology text, *A Synopsis of the Diseases of the Eye*. By 1900 ophthalmology was a well-established medical field.

### Functional Anatomy of the Eye

The human eye is frequently described as the "window to the soul" or, less poetically, compared with a simple camera with respect to its ability to capture images. Simply put, light enters the eye through a refracting cornea; the cornea redirects light to the retina, where photon energy is converted into an electrochemical signal that is transmitted to the brain. The components of the eye reduce light scatter, improve focus and control the aperture through which light enters the overall structure. In reality, the eye is a much more complex and dynamic structure than George Eastman's Kodak machine or even, arguably, contemporary magnetic resonance (MR) and computed tomography (CT) scanners.



**Fig. 1.** Gross anatomy of the eye. (Used with permission from Wiki Commons, <http://commons.wikimedia.org>).

We understand the gross anatomy and overall function of the eye reasonably well (see Figure 1); however, we know little about the biology, genetics and pathobiologies of the eye's protein structures and immunological defenses. The molecular biology of ocular surfaces, cell membranes and mucosal secretions, not to mention the intricate neurobiology of the visual pathway, also are not well known.<sup>5-8</sup>

In the most general terms, the eye consists of 3 primary tissue layers. The protective outer layer of the eyeball, or globe, is the tunica fibrosa, a tissue rich in collagen and elastins.<sup>9</sup> The tunica vasculosa, more commonly referred to as the uvea (from the Latin *uva*, or grape), is the middle layer of the eye orb. As the term "vasculosa" suggests, this layer contains the eye's vasculature, as well as its pigmented iris.<sup>9</sup> The innermost primary layer of the eye is the tunica nervosa, named for the optic nerve and the fact that it originates as an outgrowth of the developing fetal brain.

Early in prenatal development, the embryo's anterior neuroectodermal tissue layer folds into the optic cup and eventually the eyeball. Neuroectodermal tissue also forms the neural crest and tube, an early developmental phase of the central nervous system.<sup>9</sup> The tunica fibrosa

contains the corneal tissues and sclera, for example, and the tunica nervosa contains the retina and lens.

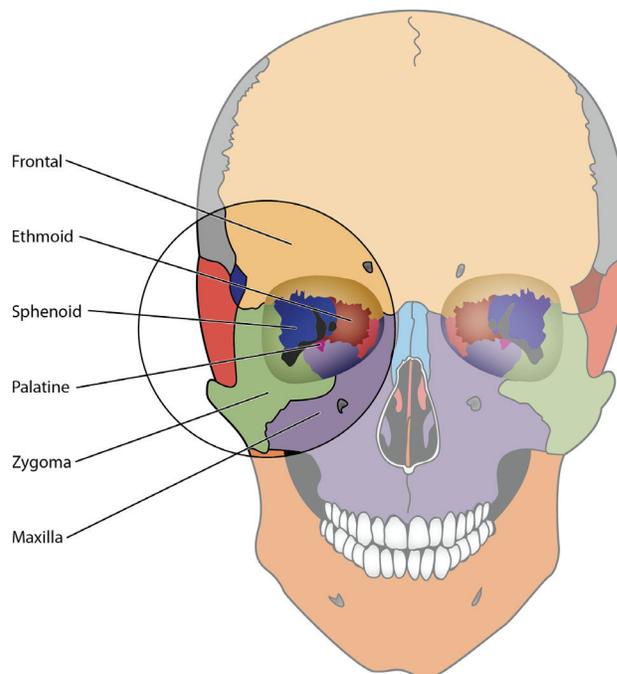
Radiologic imaging in and around the eyes, and even imaging of other parts of the body, can expose visual system tissues to ionizing radiation. Thus, it is important to understand the structure, physiology and function of the eye's major anatomical subsystems.

### **The Orbit and Eyelids**

The eyes do not function in isolation from adjacent tissues. The eyelids, for example, shield the eyes from particulate matter and intense light levels, but these complex flaps also are anatomically contiguous with, and functionally related to, adjacent skin, bone and muscular structures in the face.<sup>10</sup> A complex network of nerves and musculature known as the superficial musculoaponeurotic system coordinates muscular contractions of the eyelids, eyes, lips, nostrils and nose, and forehead.<sup>10</sup> This musculature attaches to larger muscle systems such as the zygomatic muscles, and to facial and orbital bone structures, including the zygomatic arch.

The eyelids protect the ocular surfaces, and even seemingly small problems in the development of these muscular flaps can cause corneal disorders.<sup>10</sup> Blinking, or the rapid opening and closing of the eyelids, is categorized into spontaneous, reflexive and voluntary behaviors. Reflexive blinking is controlled by relatively simple, local nerve pathways and is triggered by touch, sound, bright light or irritation of the ocular surface.<sup>10</sup>

Eyelid width grows by 10% during adolescence and early adulthood, and then contracts by 10% after the mid-30s, so that the eyes appear larger or wider during reproductive years than they do in childhood or late adulthood.<sup>10</sup> The eyelid margin is home to musculature, conjunctiva and glands. Although eyelids basically open and close, the force, speed and frequency of these movements are under both autonomic and voluntary control. The eyelids close and blink chiefly through contraction of the orbicularis oculi muscle, which also contributes to facial expressions. In addition, eyelid closure involves contraction of the levator palpebrae superioris muscle, also known as the upper lid's "chief reactor" muscle.<sup>10</sup> The upper eyelids and eyeball share attachments to the superior rectus muscle, so that movement of the upper eyelid and globe are coordinated, particularly when looking upward.<sup>10</sup>



**Fig. 2.** *The bony orbit.*

The bony orbit, which supports and protects the soft tissues of the globe, is composed of 7 bones — the sphenoid, frontal, ethmoid, maxillary, zygomatic, palatine and lacrimal bones. These bones articulate to create a roughly pyramidal orbit structure with gaps to accommodate nerve bundles and vasculature (see Figure 2).<sup>11</sup> Bone composing the anterior (frontal) orbital rim is thicker to protect the eye from traumatic blows. The zygomatic (cheek) bone, which constitutes roughly the lower and outer quarter of the anterior orbital rim, is thicker than the rest of the orbit and is the orbit circumference's strongest component.<sup>11</sup> The maxilla represents the inner and lower quarter of the anterior orbital rim and much of the triangular orbital floor, which is thin, poorly supported, and more prone to fracture than the rest of the orbit.<sup>11</sup> Blows to the lower anterior orbital rim can fracture the orbital floor, causing the eye to sink or recess into the orbit. This type of trauma may be accompanied by cheek neuropathy (numbness) and affected eyesight (double vision and, in some cases, blindness).<sup>11,12</sup> The optic canals carry the optic nerves and arterial vasculature. They meet behind the bony orbits, where the optic nerves cross contralaterally to the brain's visual cortex.<sup>11</sup>

An intact bony orbit cannot accommodate displacement of the eyeball back toward the skull, so dislocation of the eye within the orbit results in exophthalmos, or pushing of the eye forward through the anterior orbit.<sup>11</sup> This protrusion can cause severe myopia and can be the result of inflammation, such as that associated with adult thyroid eye disease, or tumors, either benign or malignant. Postsurgical or radiation therapy-related exophthalmos involves the eye contralateral to the tissue that has undergone treatment.<sup>11</sup>

The extent of protrusion can be measured using an exophthalmometer, but the underlying cause of a protrusion cannot. Asymmetrical protrusion of the eyes, especially asymmetries exceeding 2 mm of difference, indicate orbital disease and globe displacement, and should be evaluated with diagnostic imaging examinations.<sup>11</sup>

Orbital connective tissue is nearly devoid of elastin, but spaces within this tissue are filled with adipose (fat) deposits and fatty acids.<sup>11</sup> The carotenoid content of fat in these tissues is up to 4 times that found in other body tissues, but the reason for this excess is not known. Yellow-pigment, fat-soluble carotenoids such as beta-carotene bind free radical molecules that would otherwise damage cellular proteins and DNA. Free radicals are highly reactive molecules that can disrupt chemical bonds within proteins and DNA, causing mutations and structural abnormalities.<sup>11</sup>

The orbital blood system consists of complexly branching vascular trees. The ophthalmic arteries, which supply the globe and orbital tissues, arise from the internal carotid arteries.<sup>11</sup> Each ophthalmic artery has a dozen major arterial branches, although there is considerable variation in arterial branching patterns and the precise course of arterial branches. Damage to retinal or choroidal vessels within the globe can cause ischemia and loss of sight.<sup>11</sup>

Orbital defenses against infection include the shielding provided by eyelids and the lubricating and cleansing effects of blinking. Because early dye studies failed to identify lymphatic vessels within the orbit, it was long assumed the eye lacked a lymphatic immune system defense. But enzyme histochemical studies in the 1990s revealed the presence of lymphatic capillaries within the optic nerve and lacrimal gland, strongly suggesting the existence of an orbital lymphatic pathway.<sup>13-15</sup>

### **The Ocular Surface**

The transparent ocular surface broadly comprises 2 tissues: the corneal epithelium, composed largely of collagen fibers, and a clear mucous membrane covering the sclera (the white outer wall of the eyes).<sup>16</sup> The cornea serves 2 important functions for the visual system. First, corneal and scleral tissues encase and protect the globe of the eye; the cornea acts as a physical barrier, blocking potentially harmful particulate matter and pathogens that are not stopped by the eyelids. Second, the oval-shaped cornea refracts light and focuses it to the retina, a key first step in the visual pathway.

Thanks to its complex molecular structure, the cornea is extraordinarily efficient at transmitting and refracting light, a crucially important factor in maintaining eyesight. Corneal tissues transmit more than 99% of visible light waves hitting the ocular surface.<sup>16</sup> The cornea contains no blood vessels that could potentially compromise the passage of light.

The cellular arrangement of corneal tissues also maintains transparency. An outer epithelium and inner endothelial cell layer sandwich membranes and stromal cells. Collagen fibers strengthen the extracellular matrix without scattering light.<sup>16</sup> The ocular surface sustains continual damage; therefore, the surfaces of the corneal epithelium and conjunctiva undergo constant cellular turnover. Supplied by stem cells, the cells of the corneal epithelium are entirely repopulated every 1 to 2 weeks.<sup>10</sup>

The following sections describe the layers of the ocular surface from the outer epithelial layer to the inner endothelium.

#### The Epithelium

The cornea's outermost layer is organized more precisely than epithelia in other organs, reflecting the need to maintain transparency and provide a physical barrier.<sup>16</sup> The epithelium is composed of up to 7 well-ordered cell layers, with only the basement layer producing new cells through mitotic division.<sup>16</sup> The basal cells are anchored by collagen fibrils to the stroma below.<sup>16</sup>

New cells migrate toward the corneal surface to repopulate the upper layers along a maturational escalator. As the cells mature into intermediate "wing" and superficial cells and progress up through the epithelial layer, their external structure changes. Cell wall adhesion mechanisms ensure overall order and stability.

Impaired cell-cell adhesion appears to leave some individuals more vulnerable to infection and more prone to edema. In addition, epithelial adhesion is impaired in patients with diabetes, causing loss of epithelium.<sup>16</sup> Older, damaged cells eventually detach and are shed from the surface of the eye during blinking and tearing. This process is remarkably dynamic, with the epithelial cell layer regenerating very quickly.<sup>10,16</sup>

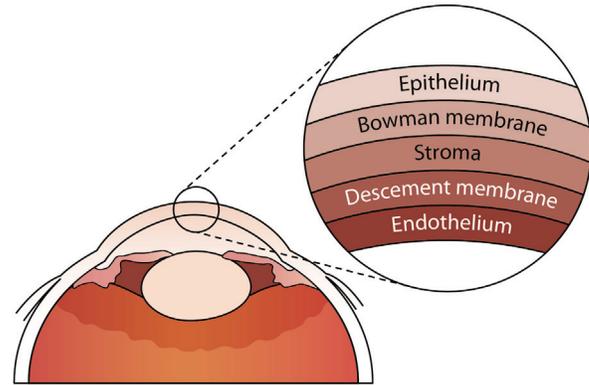
The corneal epithelium remains transparent in part because it does not become keratinized, a process by which epithelial cells lose their moisture and are replaced by horny tissue. Vitamin A malnutrition can cause keratinization and impede cellular turnover.<sup>16</sup> Relatively low levels of RNA and chromatin in the nuclei of the upper-layer corneal cells also help sustain transparency.<sup>16</sup> Chromatin is composed of dark, tightly coiled DNA.

#### The Corneal Interior

The cornea contains 3 layers between the outer epithelial layer and the inner endothelium: the Bowman membrane, stroma and Descemet membrane. The Bowman membrane is an unusual visual cell structure with unknown functions. It is found only among primate species.<sup>16</sup> Unlike the highly ordered cell layers described above, the Bowman membrane is composed of disordered collagen. Some authors consider the Bowman membrane to be a modified, anterior component of the stroma, the layer that occurs immediately below (see Figure 3).<sup>16</sup>

Figure 3 depicts the order but not the relative thickness of corneal components. In reality, the central layer of stroma represents 90% of the cornea's thickness.<sup>16</sup> Thus, the stroma is an important influence on the cornea's structure and refractory function. This layer is composed primarily of collagen fibrils (forming an extracellular matrix representing 90% of stromal volume) and a support network of cells called keratocytes.<sup>16</sup> Keratocytes become more active when healing or replacing damaged stroma.<sup>16</sup>

The molecular arrangement of the stroma is well ordered, minimizing the light lost to scattering and playing an important role in the overall shape and function of the cornea; damage to stromal structures during cataract surgery can impair visual focus.<sup>16</sup> Between the stroma and endothelium is the Descemet membrane, a thin layer of collagen produced by adjacent epithelial cells. The Descemet membrane thickens with age.<sup>17</sup>



**Fig. 3.** Structure of the corneal tissue layers.

#### The Endothelium

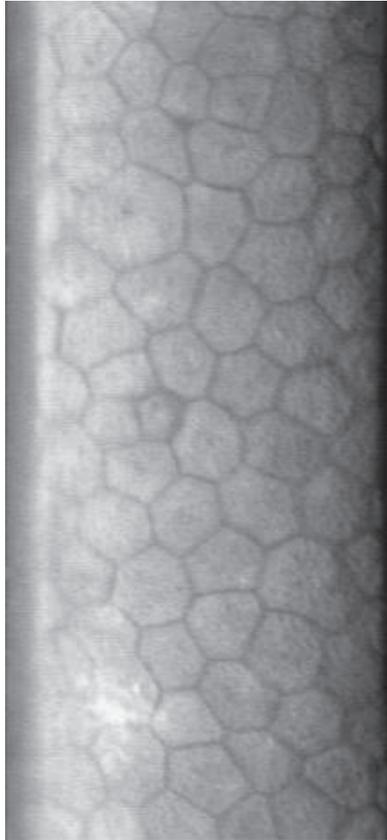
The posterior cornea is covered by a 1-cell-thick layer made up of uniform, tightly packed, hexagonal cells.<sup>16</sup> These cells are very metabolically active, as shown by their high levels of mitochondria (the primary source of cellular energy).<sup>9</sup> Heterogeneous cell size is an indicator of endothelial stress or disease and advancing age; endothelial stress also is associated with less uniformity in the hexagonal shape of cells (see Figure 4).<sup>16</sup> Prolonged contact lens use can deprive the endothelial layer of oxygen, causing hypoxia and cell death.<sup>18</sup>

#### The Uveal Layer

The uvea is a darkly pigmented, well-vascularized layer of fibrous tissues and optic nerve situated between the optic surface and the retinal tissues at the rear of the eye (see Figure 1).<sup>19</sup> The uveal tract contains white blood cells (lymphocytes), and uveal tissues can become inflamed as a result of immune and autoimmune processes.<sup>19</sup>

The uvea is subdivided into distinct tissue regions: the iris, ciliary processes and body, pars plana and choroid (or posterior uvea), a layer of connective tissue and vasculature situated between the retina and sclera.<sup>19</sup> The anterior uvea is a clinical term that refers to the iris and ciliary body; the use of this term reflects the frequency with which diseases affect more than 1 region of uveal anatomy.

The uvea minimizes the reflection of light once it enters the eye, enhancing image contrast at the retina. Because the cornea and lens lack a blood supply, the uveal tract also provides nutrients to these structures via diffusion. The



**Fig. 4.** Hexagonal endothelial cells of the cornea. (Used with permission from Philippe Gain, PhD, Bellevue Hospital of Saint-Etienne, France. [http://commons.wikimedia.org/wiki/File:Cornea\\_endothelium\\_specular.jpg](http://commons.wikimedia.org/wiki/File:Cornea_endothelium_specular.jpg). Accessed October 3, 2010.)

ciliary process produces vitreous (or aqueous) humor that fills much of the globe of the eye. The ciliary body is a muscle that helps the lens to focus light, and the iris controls the amount of light hitting the retina.<sup>19</sup>

### The Lens

The function of the lens is to focus light on the retina. The structure is precisely curved for light refraction and can be adjusted to focus on objects at a distance or in the near visual field, a process known as accommodation.<sup>20</sup> The lens also protects other visual system tissues from harmful light radiation.

The lens contains chromophores that intercept the shortest and most energetic wavelengths of visible light to prevent damage to the retina.<sup>20</sup> Infants have higher chromophore concentrations than adults, sometimes causing the lenses of newborns to appear slightly yellow. The lens develops most rapidly in utero and during the first year of life, gradually slowing thereafter and throughout the life span.

The transparency of the lens depends on the precise arrangement, distribution and concentration of numerous cells and molecules. The lens is composed of several layers of transparent tissues: the anterior lens surface epithelium, crystallin-producing fiber cells beneath the lens epithelium and an elastic capsule surrounding the lens.<sup>20</sup> Epithelial cell division produces new cells that move into place as they mature into fiber cells, attaching to the capsule. The epithelial cells of the lens also move glucose and other nutrients from the aqueous humor into fiber cells.<sup>21</sup>

Fiber cells are unusual structures, with plasma membranes containing more cholesterol than any other cell in the human body, a factor believed to contribute to the membranes' unusual rigidity.<sup>20</sup> The fiber cells are tethered by a complex network of protein microtubules and microfilaments that serve as a supportive "submembrane scaffold."<sup>20</sup> Mature fiber cells are terminally differentiated cells, meaning they have stopped dividing.<sup>20</sup>

Lens fiber cell cytoplasm, crystallin proteins and the degree of lens curvature determine how well the lens refracts light to the retina. The elasticity of the capsule helps muscle-controlled adjustment of the lens curvature, and the high concentration of crystallins in fiber cells dramatically improves the refractive power of the lens tissue.<sup>20</sup>

Crystallin proteins are specialized members of the heat shock protein family and constitute up to 40% of lens fiber cell mass. Young, immature fiber cells are highly mitotic, dividing at a rapid rate.<sup>21</sup> The concentration of crystallin varies, with fiber cells in the anterior lens containing lower concentrations than posterior fiber cells. The difference in crystallin levels appears to correct for the distortion of light traveling through a sphere.<sup>21</sup>

Mature fiber cells are essentially elongated crystallin-producing machines. During terminal maturation, fiber cells destroy their own internal cell organelles, enhancing cell transparency. Crystallin density is positively and causally correlated with lens refractivity.<sup>20</sup>

Layers of fiber cells accumulate throughout the life span, causing the lens mass and width to increase with advancing age. Older fiber cells are found in the middle of the lens, and the newest fiber cells are found on the lens surface. Some researchers have compared the layers of the lens to tree rings or time capsules, documenting the structural and chemical changes to the lens over time.<sup>20</sup>

The disruption of crystallin organization and the loss of crystallin-producing fiber cells contribute to the

loss of lens transparency and formation of lens opacities known as cataracts.<sup>20</sup> Cataracts are a leading cause of visual impairment and blindness, and cataract removal surgery is the single most common surgical intervention among elderly Americans (see Figure 5).<sup>20</sup>

One form of crystallin,  $\alpha$ -crystallin chaperone protein, binds to damaged lens crystallins to hold them in place and prevent them from accumulating and affecting lens transparency. The concentration of unbound lens  $\alpha$ -crystallin correlates positively with lens opacity and is therefore a useful early indicator of cataract risk and formation.<sup>22</sup>

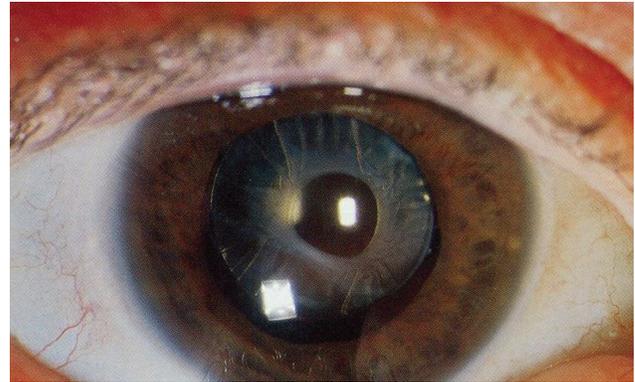
The full extent of ionizing radiation's effect on crystallin organization and fiber cell death is largely unknown. However, studies of genetic mutations of specific proteins provide insight into the potential ways irradiation can cause pathologies. For example, a heritable mutation at the  $\alpha$ B-crystallin gene (the loci coding for 1 particular form of  $\alpha$ -crystallin) causes structural abnormalities in crystallin proteins, leading to cataracts and myopathy even in the absence of environmental injury such as irradiation.<sup>20</sup> It is possible that subtle variations in crystallin genetics make certain individuals more or less vulnerable to radiation and other environmental triggers.

In addition to genetic studies, research using various lab animals has contributed to understanding the biological effects of ionizing radiation on the lens. Although some vertebrates have species-specific forms of crystallin proteins, humans appear to possess "classical" or generic crystallins, so it is possible to draw strong inferences from animal studies of environmental triggers.<sup>20</sup>

For example, lens fiber cells' intercellular gap junctions (connections) are largely composed of connexins, which manage intercellular movement of nutrients without compromising lens transparency. Fiber cells contain more connexins than any other cellular populations in the human body. In genetically engineered mice that lack a connexin gene, nuclear cataracts appear in juvenile animals.<sup>20</sup>

### The Lacrimal System

The production of tears is crucial for the health and function of the eyes; tears lubricate the eyelids, supply the cornea with oxygen and act as an important defense mechanism, clearing the ocular surface of particulate matter, dead cells and pathogens.<sup>23</sup> Tears also may contribute to the optical properties of the cornea.<sup>23</sup>



**Fig. 5.** Cataract showing lens opacities. (Public domain photo used with permission from Rakesh Ahuja, MD. [http://commons.wikimedia.org/wiki/File:Cataract\\_in\\_human\\_eye.png](http://commons.wikimedia.org/wiki/File:Cataract_in_human_eye.png). Accessed October 3, 2010.)

Glandular secretions make up a chemically complex tear film that contains proteins, immunoglobulins, hormones (growth factors), electrolytes, antimicrobial proteins and water. The tear film forms a 3-layer liquid barrier over the corneal surface<sup>23</sup>:

- Mucoid layer, which ensures even distribution of the tear film over the ocular surface.
- Middle aqueous layer, which delivers nutrients and oxygen to the cornea.
- Anterior lipid (fatty) layer, which reduces evaporation and gives the tear film structural integrity and stability. This layer is believed to play an important, but little understood, role in reducing the rate of evaporation from the ocular surface.<sup>24</sup>

Conjunctival goblet cells produce the mucoid layer, and lacrimal glands secrete aqueous tear fluid. These glands are located along the upper, outer region of the orbit. A small bulb of the gland lies adjacent to the globe, so that when the upper eyelids are inverted, the bulb portion of the gland can be seen.<sup>23</sup> The lacrimal gland contains 6 to 12 ducts that supply the upper eyelids' fornix conjunctiva.<sup>23</sup> From there, tears pass over the ocular surface to the lacrimal puncta, which is situated in the inner corner of each eyelid. When copious tearing occurs, fluid spills out onto the face via the nasolacrimal duct. The upper eyelid also contains up to 40 accessory glands of Krause that produce tear fluid.<sup>23</sup> Tear production is a normal, constant process, but the streaming of excess fluid from the nasolacrimal duct onto the face is linked to eye trauma, irritation or extreme emotional distress.

Specialized sebaceous glands called meibomian glands line the eyelids and exude the lipid components into the corneal tear film. Meibomian secretions include cholesterol and other sterols, fatty acids, phospholipids such as those found in cell membranes, and other waxy and hydrocarbon molecules.<sup>23</sup> Blinking triggers meibomian fluid secretion, and male (androgen) sex steroid hormones may control the amount of meibomian exudates produced.<sup>23</sup>

### The Retina

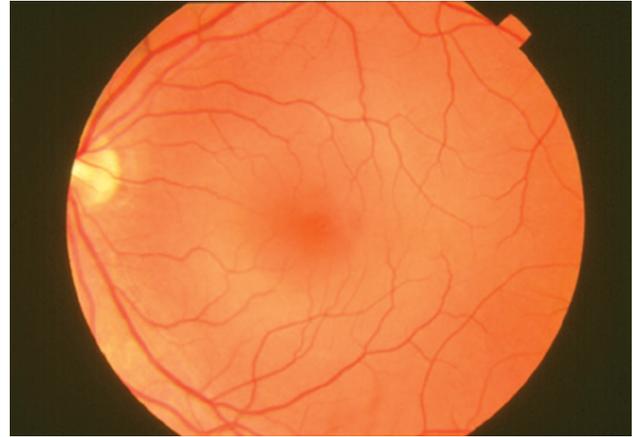
A heavily innervated, light-sensitive tissue called the retina lines the inner surface of the globe (see Figure 6). Light passing through the cornea and lens is refracted onto the retinal surface, triggering nerve signals that pass via the optic nerves to the cortical visual regions of the brain for processing.<sup>25</sup> Developmentally and anatomically, the retina and the optic nerve are extracranial projections of the brain.

Light-sensitive photoreceptor neurons within the retina occur in 3 forms: rods, cones and the much less common photosensitive ganglia. The photoreceptor neurons are electrochemical relay systems. Each neuron has a cell body and tentacle-like dendrites and axons, along which the cell receives and sends nerve impulses to adjacent nerve cells. At each interneuronal gap, called the synapse, electrical signals are transformed into extremely short-lived chemical signals. The chemical messages travel almost instantaneously across the synapse gap to trigger another electrical nerve impulse at the receiving cell.

Specific wavelengths of light trigger nerve impulses in rods and cones, which are carried across nerve axons to optic nerve fibers. Rods allow black-and-white vision; cones permit color vision. The neuron ganglia trigger aversion reflexes when potentially dangerous intense light hits the retina.<sup>25,26</sup>

The retina is composed of 10 distinct, but in some cases overlapping, tissue layers. From the innermost retina to the retinal surface, these layers are:

1. Inner limiting membrane, which separates the retina from the vitreous body of the globe.
2. Nerve fiber layer (stratum opticum), representing optic nerve fibers.
3. Ganglion nuclei layer, consisting of ganglion cell nuclei and optic nerve fibers.
4. Inner plexiform layer, composed largely of densely packed ganglion neuron dendrites (the tentacled, communicating ends of nerve cells).



**Fig. 6.** Normal retina. (Used with permission from the National Eye Institute, National Institutes of Health. [www.nei.nih.gov](http://www.nei.nih.gov). Accessed September 28, 2010.)

5. Inner nuclear layer, composed of tightly packed, elongated rod and cone bipolar, horizontal and amacrine cells. The axons of bipolar cells connect with ganglion cells via the inner plexiform layer; the other end of the rod bipolar cells reach into the outer plexiform layer. The horizontal cells sit at the periphery of the inner nuclear layer and communicate via their dendrites with the outer plexiform.
6. Outer plexiform layer, a densely interconnected layer of dendrites and axons from adjacent retinal layers acting as a communications hub for inner nuclear horizontal cells and the photoreceptor cells (rods and cones).
7. Outer nuclear layer, a layer of photoreceptor cells' nuclear bodies, sometimes called granules.
8. External limiting membrane, which separates the nucleus of rod and cone cells from the photosensitive anterior portion of those cells. The membrane anchors the photoreceptor cells within the retina.
9. Photoreceptor neuroepithelium contains the rods and cones, which represent the linchpin neurons of the visual system. Their function is to transform visible light into electrochemical nerve impulses that are carried by the bipolar cells to the brain's visual cortex.
10. Retinal pigmented epithelium, a layer of elongated hexagonal cells that fills both the anterior retina and the posterior iris, lending eyes their

characteristic colors. This layer supplies the retina with critical nutrients.

#### Photoreceptor Transduction

The photoreceptor and photosensitive ganglion cells of the retina are crucial to the human sense of sight. The role of the rod and cone cells is to transform light energy into nerve impulses, a process known as photoreceptor transduction. The ganglion cells contribute to important biological processes, such as reflexive pupil contraction against bright light and the regulation of circadian rhythms.<sup>27</sup>

An average adult retina contains 120 million rod photoreceptor cells, which are adapted to the low light levels commonly described as black-and-white conditions. There are far fewer — approximately 6 million — cone cells, the retina's brightness and color-detection transducers. The cones are adapted to functioning in bright daylight. Photoreceptors respond both to the intensity and color spectrum of light. Cone cells occur in 3 specialized forms that are sensitive to the blue, green and yellow-red segments of the visible light spectrum.<sup>25,26</sup>

When photoreceptor cells are not stimulated by light, they continuously release a neurotransmitter called glutamate, which controls the physiology of downstream neurons. This process is sometimes called a “dark current,” because it is an example of a biologically unusual case in which the *absence* of a neurotransmitter causes sensory neuron signaling. In other words, light-stimulated rods and cones release *less* chemical neurotransmitter to adjacent nerve cells.

The continuous release of glutamate is interrupted when light photons strike the photoreceptor cells, however. The light energy instantly changes the rods and cones, causing the cell membranes to become electrically polarized. Hyperpolarization refers to the cell membranes of the neurons becoming increasingly negatively charged, a disruption of electrochemical homeostasis.

Photoreceptor proteins, called opsins, are found in the outer segment of the rods and cones. These proteins combine with retinal pigment in the rod cells to form rhodopsin, or with other types of opsins in the cone cells to form photopsins. The ganglion cells produce a distinct opsin called melanopsin.<sup>27</sup>

Opsins absorb light photons, and the absorbed energy changes the opsins' protein structures. The

change triggers a cascade of temporary, chemically unstable protein configurations, culminating in the release of hundreds of cell proteins called transducins. The transducins short-circuit glutamate release and initiate the enzymatic pathway leading to hyperpolarization.

### Biological Effects of Radiation

Ionization is the process by which an atom or molecule gains or loses electrons, changing its net electrical charge. Ionizing radiation delivers energy to atoms via electromagnetic x-rays or gamma ( $\gamma$ ) rays, or via particulate radiation, such as neutrons and radioactive alpha ( $\alpha$ ) or beta ( $\beta$ ) particles. The ability of ionizing radiation to disrupt DNA and damage tissue is related to the linear energy transfer, or energy deposition per unit length of target tissue. Neutrons and alpha particles have higher linear energy transfer values than x-rays and gamma rays, and therefore are more damaging to tissue and DNA molecules.<sup>28</sup>

Radiation refers to the energy emitted by an ionizing radiation source, and radiation dose is the quantity of the ionizing radiation energy delivered to a given volume of tissue. Several quantification systems or units are used to describe radiation levels.

The unit of absorbed radiation dose is the gray (Gy), which is the delivery of 1 joule of energy to 1 kg of mass.<sup>29</sup> The gray replaced an older unit of measure, the radiation absorbed dose, or rad (1 Gy = 100 rad). The effective dose is an estimate of the total amount of radiation absorbed by heterogeneous tissues, calculated as the tissue-weighted sum of the dose to irradiated organs and tissues.<sup>29</sup> Effective dose, once expressed as roentgen equivalent man (rem), now is given in sievert (Sv) or millisievert (mSv) units.

Cosmic and other natural sources of ionizing radiation have been present throughout history. Living organisms have normal cellular repair mechanisms that usually prevent biological damage from natural, background levels of radiation, although no exposure to ionizing radiation is truly safe. However, elevated radiation doses from unusual geological or human-made sources, or excessive exposure to cosmic radiation during space travel or frequent air travel, appear to increase the likelihood of damage to the eye tissue.<sup>30-32</sup> For example, according to data from NASA's Longitudinal Study of Astronaut Health, 8 mSv of space radiation appears to be sufficient to induce cataract formation in astronauts.<sup>32</sup>

Energy from ionizing radiation can disrupt the chemical structure of DNA and proteins (particularly those found in the eye lens), either directly, by disturbing vulnerable chemical bonds, or indirectly, by creating free radicals from cellular water molecules. The body has enzymatic defenses that transform free radicals such as hydrogen peroxide ( $H_2O_2$ ), hydronium and hydroxyls into biologically inert or less harmful compounds; however, these defenses are not 100% effective at preventing harm, particularly when tissues are exposed repeatedly to large numbers of free radicals. The harmful effects of ionizing radiation range from acute skin burns and hair loss to cataracts and delayed carcinogenesis (tumor formation).

DNA damage or errors in cellular repair can lead to mutations that cause improper regulation of the cell division cycle. A cell's DNA is most vulnerable during mitosis, when the DNA molecules uncoil from tightly wound chromosomes to replicate in preparation for cellular division. Most of the time, the cells die, but in some cases, cellular division can accelerate and tumors can form. Although the eye lens has epithelial cell repair enzymes, their concentrations appear to decline with age.<sup>33,34</sup>

DNA damage from ionizing radiation can take several forms, including point mutations, single- or double-DNA strand breaks and inversions, and DNA cross-links, any of which can contribute to carcinogenesis.<sup>28</sup> When DNA is damaged and unable to faithfully replicate new copies of genetic material, genomic instability results — a hallmark and potential predisposing factor for tumor growth.<sup>35</sup>

Genetic mutations in the ova or sperm can be passed on to future generations. Nonheritable mutations and tissue damage can result in somatic disorders such as congenital developmental defects or functional impairment of visual system tissues.<sup>35</sup>

Genetic damage, genomic instability and carcinogenesis are stochastic (probabilistic) effects of ionizing radiation exposure. With stochastic effects, a given exposure may or may not damage genes, and increasing a radiation dose adds to the overall probability that an adverse effect will occur. Although the probability of a stochastic effect increases with cumulative dose, the severity of the effect does not; for example, tumors caused by exposure to 1 Gy are not more aggressive than those caused by half that dose.<sup>1</sup>

In contrast, tissue damage such as hair loss and skin burns generally are considered deterministic effects,

resulting from direct harm to cellular populations. A specific radiation dose to a given tissue will predictably harm proteins, kill cells and impair tissue function. The severity of deterministic damage is dose dependent, and a dose threshold exists such that the probability of damage from low doses is negligible (zero or close to zero). Deterministic effects generally appear relatively soon (days or weeks) after exposure, but stochastic effects tend to be delayed, appearing years or even decades after exposure.

Radiation-induced cataracts fall between stochastic and deterministic categories. In most regards, cataracts are deterministic effects and have long been defined as such.<sup>36,37</sup> The latency period for radiation cataract formation is incompletely understood but appears to be broadly dose dependent. Epidemiological studies of atomic bomb survivors show dose-dependent latency periods for cataracts as short as 2 years, but lower radiation doses are associated with 3- to 4-decade latency periods, similar to those for radiation-induced cancers.<sup>38,39</sup> Curiously, however, recent research suggests there is no lower threshold dose for radiation-induced cataract formation, leading some authors to suggest that cataracts may be a stochastic effect, resulting from genomic damage in normal cell division and differentiation.<sup>40-42</sup> If no lower dose threshold exists for cataracts, occupational exposure regulations and diagnostic and interventional radiology practice might need to be revised to reflect the previously unrecognized risk of low-dose radiation to the lens.<sup>41</sup>

Cataracts can result from a single high dose or from chronic low-dose exposure of the lens, which is why occupational exposures over time represent a major concern for fluoroscopy operators. If operators are protected by lead aprons, then radiation exposure of the eye lens represents the most significant occupational radiation safety issue related to fluoroscopy.<sup>43</sup>

Prenatal radiation exposure also can be teratogenic, meaning it can cause congenital birth defects. Animal models suggest that prenatal irradiation of developing visual system tissues can impede normal development of the eye lens, for example.<sup>44</sup> Threshold radiation doses for developing embryos, if such thresholds exist, remain unknown. No such threshold has been found for adult cataract risk among survivors who were in utero at the time of the atomic bomb attacks on Japan.<sup>40</sup>

Radiation also may cause complex cellular bystander effects in which the exposure of a given cell population

affects the radiosensitivity of other nearby cells. For example, low-dose x-ray exposure appears to reduce the radiosensitivity of adjacent cells to subsequent radiation, but increase the risk of alpha particle-induced gene mutations in bystander cells.<sup>35,45</sup> The implications of bystander effects on cumulative radiation risk has not been determined.<sup>35</sup> Similarly, we have known that synergies exist between radiation dose and other disorders and toxins, such as diabetes, cigarette smoke, cancer chemotherapy agents or viral infections.<sup>46</sup> For example, x-ray radiation increases the tumor-promoting power of chemical carcinogens by 900%,<sup>35</sup> and toxic synergies are often unanticipated. The use of St. John's wort for depression is common among cancer patients and has been tied to reduced chemotherapy efficacy. This herb also may increase the toxicity of ultraviolet (UV) solar radiation on the human lens epithelial cells.<sup>47</sup>

Since the early decades of fluoroscopy, careful radiation dose management and protection practices have helped to prevent radiation doses capable of causing the most serious deterministic effects, such as radiation sickness and damage to gastrointestinal tract lining. Contemporary research and dose-reduction efforts attempt to minimize the risks of stochastic effects. But certain tissues, such as the eye lens, are more sensitive to low-dose irradiation and more vulnerable to damage from radiation exposure.

### **Risk Models**

Because the most serious biological effects of ionizing radiation are stochastic, it is widely accepted that there is no threshold dose below which radiation exposure poses no cancer risk.<sup>48</sup> This linear, or no-threshold, model of radiation risk is probabilistic rather than deterministic; it merely predicts that the greater the cumulative exposure to radiation, the greater the probability that adverse biological effects, both deterministic and stochastic, will occur.

Based on this model, the as low as reasonably achievable (ALARA) principle has become a mainstay of radiation protection. ALARA holds that in every instance, radiation exposure should be kept to the minimum necessary to achieve a specified therapeutic or imaging goal and that the benefits of that goal should be greater than the risk of the exposure. Most epidemiologists view the linear no-threshold model of radiation risk as a responsible, precautionary position.

A small group of outspoken researchers reject the linear model, however, arguing that it grossly overstates the risks of low-dose radiation exposure. Proponents of the controversial hormesis hypothesis contend that the known and quantified radiation risks associated with high-dose exposure should not be extrapolated to low doses. They believe an as-yet unknown exposure threshold exists for stochastic effects, below which exposures are either benign or even beneficial.<sup>49</sup> Critics of radiation hormesis counter that the absence of definitive evidence showing the harmful effects of low-dose radiation is due to confounding factors connected with epidemiological studies.<sup>35</sup> Some authors have concluded that the risks from doses lower than 0.1 Gy cannot be reliably determined from epidemiological data because of unavoidable statistical issues.<sup>35</sup>

Essentially, the hormesis hypothesis claims that all harm from ionizing radiation, whether long-term or short-term, is essentially deterministic, requiring a quantifiable, threshold dose to cause harm. Although the hypothetical threshold is unknown, hormesis proponents have proposed relaxing government regulations regarding nuclear waste management and occupational exposures.<sup>49</sup> Researchers continue to explore various cellular and animal models of adaptive response to radiation to clarify radiation dose-related risks to humans.<sup>28</sup>

In reality, both the linear no-threshold model and the hormesis model may represent incomplete explanations of dose-effect relationships.<sup>35</sup> However, the current consensus is that the more conservative ALARA principle derived from the linear model better protects patients and health care personnel. Thus, the American Society of Radiologic Technologists (ASRT) has officially endorsed ALARA to minimize patient and occupational radiation exposure.<sup>50</sup>

### **Tissue Radiosensitivity**

All tissues and organs are not equally susceptible to the damaging effect of radiation. Tissue radiosensitivities involve differences in both deterministic and stochastic risks posed by a given dose of ionizing radiation. For example, tissue radiosensitivities of men and women are treated identically in the literature, but vulnerability to cataract formation appears to be quite different for the sexes.<sup>51</sup> In addition, the radiosensitivity of embryo and fetal tissues have not been established but

are likely to be different than the radiosensitivity of adult tissues.

Tissue weighting factors were devised to calculate effective radiation doses, to reflect tissue-specific vulnerabilities and, ultimately, to minimize patient radiation dose and risk. Qualitatively, the eyes, ova and testes are known to be more sensitive to radiation damage than lung tissue or bone marrow, for example, and bladder and liver tissue are less radiosensitive than bone marrow or lung tissue.

However, despite the recognition that the eyes are among the most radiosensitive organs, it has been difficult to quantify tissue weighting factors and establish radiation dose thresholds for the visual system. The minimum threshold dose for cataract formation, for example, is poorly defined and based largely on early data from Japanese atomic bomb and Chernobyl nuclear plant survivors.<sup>31,52,53</sup>

Over time, epidemiologically based estimates of the threshold dose required for cataract formation have declined. Recent analyses suggest that although atomic bomb radiation exposure correlates strongly and positively with cataract risk, there is little evidence for a lower threshold, below which radiation is unrelated to cataract risk.<sup>40,54</sup> In other words, based on the available evidence, it appears the ALARA principle may apply not only to management of stochastic risks, but also to decreasing the deterministic effects of radiation on the lens of the eye.<sup>41</sup>

### **Age at Exposure**

Age and developmental stage at the time of exposure affects the risk of radiation-induced tissue damage in complex but important ways. Although pregnancy is not a contraindication for fluoroscopy, the stage of pregnancy and the potential impact of radiation on fetal or embryologic development should be considered carefully. The benefits of fluoroscopy should be weighed in light of the risks before the examination.

Radiation-induced cancers in adults tend to have long latency periods, sometimes involving decades between radiation exposure and cancer diagnosis. Because older adults often do not live long enough to receive a cancer diagnosis, the risk of developing radiation-associated cancers is lower than is the case for children or young adults.<sup>55</sup> For example, the lifetime cancer risk from

CT scans is twice as high for people aged 20 years as for individuals 40 years old.<sup>56</sup> Whereas CT heart scans can result in an estimated 1 cancer case for each 270 women aged 40 years, that number may be as high as 1 case per 135 women aged 20 years.<sup>56</sup> Breast cancer risk is elevated among tuberculosis patients who underwent repeated diagnostic chest radiography when they were younger than 20 years old.<sup>57</sup> Relatively little is known about the effects of patient age on fluoroscopy-specific risk of visual system cancers, but it is reasonable to assume that children and young adults are at increased risk for these malignancies as well. The cancer risk for adolescents is a complex middle ground, involving “an adult-sized body but a child’s elevated (cancer) risk coefficients.”<sup>72</sup>

Ionizing radiation delivered to embryos, fetuses and children poses a greater risk of tissue and DNA damage than the risk for adults. The DNA of rapidly dividing cells in a developing organism is arranged in an uncoiled, vulnerable pattern for a longer period of time than it is for adults. Radiation teratogenesis, the disruption of normal anatomical development, can occur in fetuses as young as 2 weeks of gestation and through week 15 of gestation, resulting in brain abnormalities, retarded head and body growth and mental retardation.<sup>58</sup> Fetal development is believed to be particularly vulnerable to the teratogenic effects of radiation between 8 and 15 weeks of gestation, particularly for doses greater than 200 mSv.<sup>59</sup> Some authors who question the linear no-threshold model of radiation risk have presented empirical evidence contesting claims that repeated pediatric CT scans of the head represent a substantive risk of cancer or developmental delay, but these studies have tended to involve small sample sizes and therefore have relatively little statistical power to detect risk.<sup>60</sup>

Children are up to 10 times more sensitive to tissue and DNA damage from ionizing radiation than adults; a single CT scan is estimated to significantly increase the lifetime risk of fatal cancers.<sup>61</sup> For example, a single abdominal CT scan of a 1-year-old child carries an estimated lifetime cancer risk of 1 in 1,000.<sup>59</sup> Younger children face greater lifetime risks from exposure to ionizing radiation than do older children.<sup>62</sup> Radiation doses from pediatric CT examinations frequently outweigh their clinical benefits; thus, it stands to reason that the same might be true for fluoroscopy.<sup>63</sup>

The causes of childhood cancers, and particularly visual system cancers, are poorly understood. They are

almost certainly multifactorial, involving more than 1 acquired genetic mutation. For example, acute childhood leukemias are among the most common pediatric malignancies. The pioneering research of University of California-San Francisco epidemiologist Joseph Wiemels has shown that patients are frequently born with 1 leukemogenic mutation, acquired during prenatal development, and then suffer a second mutation, close to the time of carcinogenesis during early childhood.<sup>64,65</sup> One consistently reported risk factor for childhood cancers is prenatal exposure to medical ionizing radiation.<sup>66</sup>

As a general rule, ionizing radiation represents a greater overall cancer risk to younger individuals than older ones. Prenatal and early childhood represent windows of particular vulnerability for radiation-induced cancers, and adolescents and young adults are at greater risk of radiation-associated cancers than are older adults. But noncancer radiation risks to visual system integrity, particularly cataract formation, do not follow a similarly simple rule: Embryos and elderly adults may both be at increased risk of cataracts because of developmental issues and overlapping, synergistic risk factors.

### Radiation and Visual System Pathobiology

Fluoroscopy is used in numerous diagnostic and interventional radiologic procedures, such as angiography, barium contrast gastrointestinal imaging, image-guided cardiac catheterization and orthopedic surgery. Radiation dose is influenced largely by the type and duration of examination; however, operators should not assume that a procedure involving anatomy other than the head or visual system will not deliver radiation dose to the eyes. In particular, the eyes of fluoroscopy operators or team members are vulnerable regardless of the type of procedure.<sup>1</sup> Over the past 2 decades, a growing proportion of fluoroscopy examinations has involved therapeutic interventional procedures.<sup>1</sup> Several of these procedures are more complex and challenging than diagnostic fluoroscopy and, therefore, involve long exposure times, frequently exceeding an hour in duration.<sup>1</sup>

The increasing utilization of interventional fluoroscopy is largely due to cost control efforts; these procedures are less expensive and less invasive than surgery.<sup>1</sup> However, longer examinations are associated with higher average radiation doses. Longer interventional procedures include cardiac catheter ablation,

neuroembolization, percutaneous transluminal angioplasty, percutaneous transjugular intrahepatic portosystemic shunt replacements, vascular embolization, interventional pain management and stent replacements.<sup>1</sup> Advances in dose reduction technologies have been negated to a large degree by the increasing complexity and duration of interventional fluoroscopy procedures.<sup>2</sup>

Although the eye and orbit frequently are not the target of such examinations, fluoroscopy and real-time CT procedures nevertheless can deliver ionizing radiation to visual system tissues.<sup>67</sup> Given the increased duration and cumulative radiation doses of fluoroscopy exams, the health risks posed by irradiation of the eye must be taken very seriously.

The benefits of interventional fluoroscopy include improved accuracy and safety over more invasive and costly surgeries. Because interventional fluoroscopy is therapeutic as well as diagnostic, the relative benefits typically outweigh the potential harm of the radiation dose.<sup>2</sup> However, the high radiation doses associated with fluoroscopy and uncertainty about the exposure levels at which visual tissues are damaged raise questions about the soundness of this assumption.

Interventional fluoroscopic procedures have lower overall morbidity and mortality rates than surgical alternatives,<sup>2</sup> but there might not be a favorable benefit-to-cost ratio for every proposed procedure and for every patient. Ideally, the benefits and risks of each fluoroscopy procedure should be considered carefully, as well as the patient's other risk factors and previous medical radiation doses. In daily clinical practice, however, staff shortages, the lack of reimbursement for planning and other factors often prevent adequate evaluation.

In 2009 the U.S. Food and Drug Administration (FDA) reported cases of "significant" radiation overdoses from CT neuroimaging, resulting in skin burns and patchy hair loss in at least 82 patients. In addition, the affected patients are at an increased risk for cataract formation.<sup>68,69</sup> High doses of radiation, including exposure from radiation therapy and radiologic imaging, have been tied to several diseases and functional disorders of the visual system, including blindness, scleral necrosis, radiation retinopathy and ischemia, neovascular glaucoma and dry eye syndrome.<sup>70-72</sup>

The severity of impairment in the eye's ability to focus (accommodation) correlates significantly and posi-

tively with radiation dose. For example, among survivors of the Chernobyl nuclear accident, higher doses caused greater impairment to the range of accommodation.<sup>73</sup> Radiation therapy for melanoma of the eye can cause several visual system complications, including cataracts, retinopathy, severe neovascular glaucoma and scleral necrosis. Unfortunately, the extent to which chronic or repeated exposure to fluoroscopy may contribute to disorders of the eye has not been established.

### Visual System Diseases and Disorders

The following section describes different types of visual system diseases and disorders and their relation to ionizing radiation exposure.

#### Cancers of the Eye

Ionizing radiation is a well-established carcinogen, and irradiation of visual system tissues can trigger carcinogenesis. The risk of any radiation-induced cancer from a single fluoroscopy exam is approximately 5% per Sv.<sup>2</sup> Repeated and prolonged fluoroscopy doses can increase cancer risk for patients and health care personnel performing fluoroscopy. Primary cancers of the visual system are relatively rare, and in most cases, the health risks posed by radiation are outweighed by the clinical utility of imaging.

Visual system tumors may be either benign or malignant, and malignant tumors may be primary, secondary or metastatic. (For a list of the different types of eye cancers, see the Eye Cancer Network website at [www.eyecancer.com](http://www.eyecancer.com).) Primary tumors originate in the affected tissue as a result of genetic damage within that tissue. Secondary tumors are caused by therapeutic medication or irradiation of a tissue, delivered as a treatment for an earlier cancer or other disorder. Metastatic tumors represent the spread of malignant cancer cells to the eye from primary tumors in other tissues, usually the lung or breast; metastatic eye cancers are rare.<sup>74,75</sup>

Ionizing radiation can produce both primary and secondary eye malignancies, though primary intraocular malignancies are rare. Adult orbital lymphoma and pediatric retinoblastomas are the most common intra-orbital malignancies diagnosed in the United States, neither of which has been strongly tied to ionizing radiation exposure.<sup>76,77</sup> The skin of the eyelids may form squamous cell or sebaceous carcinomas, malignant melanomas or, more commonly, basal cell carcinomas,

all of which have been linked to ionizing radiation and UV sunlight.<sup>76</sup>

Most human cancers arise in epithelial cells, so it is not surprising that the retinal epithelium is susceptible to radiation-induced carcinogenesis. Studies of human retinal epithelial cells have revealed several specific genetic mutations underlying retinal tumor formation: 2 tumor-suppressing *10p* genes and the *PARD3* gene, which promotes epithelial cell proliferation and has been implicated in liver carcinogenesis.<sup>78,79</sup>

Visual system cancers have not been tied to x-ray or fluoroscopy examinations per se in the medical literature. However, standard treatment for some visual system cancers, such as melanoma of the eye, include brachytherapy or external beam radiation therapy, which can cause radiobiological pathologies.<sup>21</sup>

Although studies have found elevated incidence rates of leukemia, myeloma, breast cancer and thyroid cancer among different radiologic technologist populations, there is no established evidence of an increase in visual system cancer rates in radiologic technologists.<sup>80</sup> Thus, a greater area of concern regarding the effects of fluoroscopic radiation on the eyes may be tissue damage, particularly the formation of cataracts.

#### Radiation Retinopathy and Ischemia

Radiation retinopathy, a progressive disorder caused by the loss of vascular endothelial cells in the retina, can cause blindness. It frequently involves microaneurysms, neovascularization of the retina, hemorrhage of the aqueous humor and macular edema.<sup>21</sup> Given the differential loss of endothelial cells in the interior lumen of the retinal blood vessels, one suspected mechanism for the disorder is the creation of free radicals from blood.<sup>21</sup> Retinal ischemia (loss of local blood supply) caused by retinopathy can trigger neovascularization, hemorrhage and retinal detachment.<sup>21</sup>

Radiation retinopathy appears to be a classic example of deterministic radiation injury, with a dose threshold and dose-severity relationship. Risk appears to be related both to total or cumulative dose and the timing of exposure. The condition occurs in up to 63% of brachytherapy patients, reflecting the higher risk associated with higher radiation doses (approximately 90 Gy).<sup>21</sup> Among patients exposed to lower doses, retinopathy is markedly less common. For example, it is a relatively rare side

effect of intensity modulated radiation therapy of the head. In 1 recent study, retinopathy affected only 1 of 84 patients (a patient who also developed neovascular glaucoma).<sup>72</sup> Fractionated treatment of 1.2 Gy or less per fraction when total doses exceed 40 to 50 Gy reduces the risk of radiation retinopathy, suggesting that at lower doses, repair or healing mechanisms can reverse some of the damage between exposures.<sup>81</sup> However, fractionated doses exceeding 1.8 Gy significantly increased the risk of radiation retinopathy in 1 study of 26 patients.<sup>82</sup>

Other risk factors can confuse diagnosis and increase a patient's overall risk of retinopathy. Diabetes and certain cancer chemotherapies are risk factors for retinopathy, for example, and may increase the risk of radiation retinopathy in a synergistic fashion.<sup>82,83</sup> Retinopathy caused by radiation therapy has been misdiagnosed as hypertensive retinopathy, an error detected in at least 1 case only after diagnostic imaging of the eye and a careful review of clinical history.<sup>83</sup>

### **Neovascular Glaucoma and Rubeosis Iridis**

Glaucoma is caused by pressure on or damage to the optic nerve. The disorder results in partial visual field blindness (ie, blind spots) or complete blindness and is a leading cause of vision loss among the elderly (see Figure 7). One frequent cause of glaucoma is neovascularization, or the growth of new blood vessels within the tunica vasculosa. The new blood vessels exert pressure on the visual system's nerves. Neovascularization is a common post-trauma repair process that can be triggered by radiation damage to visual system tissues.<sup>21</sup>

Neovascular glaucoma frequently involves the anterior iris tissues, in which case the disorder is also called rubeosis iridis; neovascular glaucoma and rubeosis iridis are therefore sometimes treated as synonyms in the medical literature. Neovascular glaucoma has published latency periods of 2 to 58 months after eye irradiation. It also can be caused by diabetes. There is little consensus on the best treatment for neovascular glaucoma or rubeosis iridis. In addition to surgery, beta blockers, x-adrenergics, anti-VEGF (vascular growth factor) therapy and glucocorticoid therapy are commonly used for treatment.<sup>21</sup>

### **Dry Eye Syndrome and Keratitis**

Radiation can cause a loss of conjunctival goblet cells and, hence, a loss in some of the secretions that make up



**Fig. 7.** Example of the effects of glaucoma on a patient's visual field. (Used with permission from the National Eye Institute, National Institutes of Health. [www.nei.nih.gov](http://www.nei.nih.gov). Accessed September 28, 2010.)

the tear film.<sup>21</sup> This impairment of tear film organization and function, called dry eye syndrome, is a common problem affecting up to 20% of adults older than 45 years; an unknown minority of cases are caused by radiation exposure.<sup>84</sup> Severe cases of dry eye syndrome can cause corneal ulcers, a condition known as keratitis. Frequently caused by brachytherapy and external beam radiation therapy of the eye, dry eye syndrome and keratitis also were among the most common radiation effects observed in children living near the 1986 Chernobyl nuclear accident.<sup>21,35</sup> Radiologic technologists are more likely than patients to develop dry eye syndrome and conjunctival cellular abnormalities.<sup>70</sup>

### **Radiation Cataracts**

Cataracts have been diagnosed in up to 13 million Americans, a number that will likely increase sharply as baby boomers age.<sup>38</sup> Cataracts are disruptions of lens transparency, commonly described as lens opacities, that can be classified anatomically as nuclear, cortical, posterior subcapsular or mixed.<sup>38</sup>

Ionizing radiation damages the lens fiber cells that produce crystallin proteins and disrupts the arrangements of crystallin. However, the relative importance of this damage to cataract formation is not currently clear.<sup>85</sup> Immature lens fiber cells have a high rate of mitotic division, leaving their DNA uncoiled for a longer period of the time and vulnerable to radiation damage.<sup>21</sup> Damaged fiber cell DNA slows mitosis and crystallin production and delays the

repair or stabilization of damaged crystallin proteins. In the mean time, compensatory (hastened) mitosis can lead to the creation of swollen Wedl cells, which further compromise lens transparency. Increasing molecular disorganization and decreasing lens transparency results in what is clinically known as cataract formation.

A recent review concluded that dose thresholds for cataract formation are far lower than previously believed — not higher than 0.5 Gy, and quite possibly lower.<sup>85</sup> As noted above, several groups of researchers have questioned the assumption that cataracts represent a deterministic effect of radiation exposure with a dose threshold below which radiation poses little risk of cataract formation.<sup>31,38,41,42,85</sup> Typical among such critiques is one French author's conclusion, published in late 2009, that the very existence of a dose threshold is "no longer an absolute certitude insofar as radiation-induced cataract pathogeny might consist of not really a deterministic effect ... as believed until now, but rather a stochastic effect."<sup>41</sup>

Although the lower threshold dose for cataract formation has not been established definitively and its very existence is an increasingly controversial assumption,<sup>41</sup> it has been clear since the 1990s that 5 Gy is sufficient to cause radiation cataracts.<sup>31</sup> A 2009 review of epidemiological studies concluded that an exposure of less than 2 Gy is enough for cataract formation.<sup>85</sup>

Age at exposure may be an important risk factor for radiation cataracts. Embryos, children and elderly adults all may experience increased risk of cataracts from radiation, but for different reasons. Children, and presumably embryos, are more vulnerable to lower-dose radiation cataract formation than adults. Pediatric total body irradiation doses of 10 Gy invariably result in the formation of cataracts; adult total body irradiation with median fractionated doses of 14.4 Gy produce cataracts in 33% of adult patients after a median latency period of 4 years.<sup>31,86</sup> Among adults, doses of 16.5 Gy or higher consistently cause cataracts that impair visual acuity.<sup>87</sup> No relationship between radiation dose and adult cataract risk was identified among Japanese atomic bomb survivors who were in utero in 1945, but for children younger than 11 years of age at the time of the bombings, cataract risk was significantly tied to dose (without evidence of a minimum dose threshold), an effect that became weaker with increasing age at the time of exposure.<sup>40</sup>

A retrospective study of more than 16,000 Finnish children exposed to radiation therapy for congenital hemangiomas during the early- to mid-20th century found that radiation therapy increased the risk of both cortical and posterior subcapsular cataracts.<sup>59</sup> A dose of 1 Gy to the lens increased children's odds of developing posterior subcapsular cataracts by 50% and represented a 35% greater risk of developing cortical cataracts.<sup>59</sup>

Older adults may be more likely to develop radiation cataracts because of synergistic risk factors that are more common among the elderly. Diabetes and hypertension, for example, may increase the risk of radiation pathologies of the eye.<sup>46</sup> Although age is frequently described as a risk factor for cataract formation, this may be an oversimplification for an underlying relationship between cumulative UV radiation exposure over a lifetime and cataract risk.<sup>88</sup> In other words, cataracts among the elderly may really be a subset of radiation cataracts.

Chronic radiation exposure to the lens of the eye is of obvious interest to radiologic personnel. One source of information concerning chronic exposure involves the construction of residential housing in Taiwan using gamma radiation-contaminated steel in the 1980s. Studies of 114 residents found that doses were 8 mSv or lower for all residents. The research established a strong dose-effect relationship between radiation and minor opacities that were unlikely to degrade visual acuity among 3- to 20-year-olds; a similar, but statistically insignificant, dose-effect correlation was found among older adults (aged 20-65 years).<sup>85</sup> The study results suggested that children and young adults are more vulnerable to radiation-induced opacities than older adults.<sup>85</sup>

Some authors have argued that the duration between exposure and the formation of radiation cataracts is roughly inversely proportional to radiation dose.<sup>85</sup> Epidemiological studies of atomic bomb survivors suggest latency periods as short as 2 years.<sup>38</sup> Lower radiation doses seem to involve longer latency periods (3 to 4 decades) for cataracts, similar to the latency periods for cancer.<sup>39</sup>

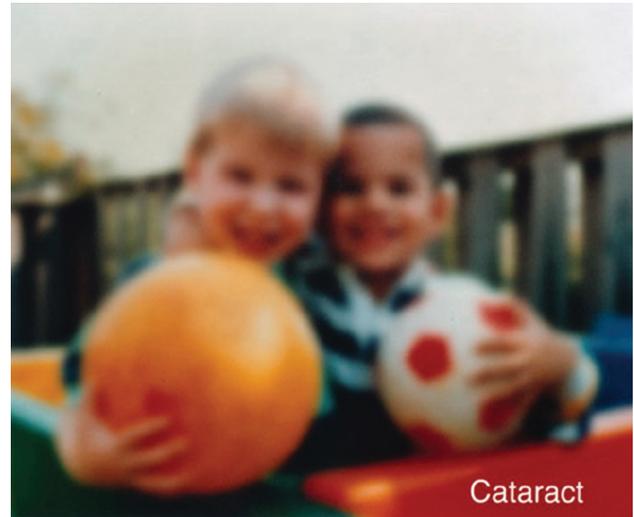
Radiation therapy for eye cancer can deliver 24 Gy or more, yielding a 5-year cataract incidence rate as high as 92%.<sup>21</sup> The location of the target tumor can predict the latency period of postradiation cataract formation, probably reflecting the fraction of ionizing radiation directed to the lens tissues.<sup>21</sup> Radiation therapy of melanomas in the anterior eye deliver significantly more ionizing radiation to

the lens and is associated with more rapid cataract formation, for example, than is the case for melanomas of the posterior eye (a median latency of 11 months vs 26 months for radiation therapy of tumors in the posterior eye).<sup>21,89</sup>

The clinical signs of radiation cataracts typically evolve from a small initial dot in the posterior lens to an essentially solid-appearing opacity as large as 2 mm in diameter.<sup>21</sup> The spreading cataract may eventually reach 4 mm in diameter, with a clarifying center that creates a doughnut appearance.<sup>21</sup> Posterior subcapsular cataracts are the most common form of cataracts, and refer to opacities found anterior to the posterior lens capsule. Clinical symptoms may include night glare and poor visual acuity and accommodation (see Figure 8). Radiation exposure typically produces posterior subcapsular or cortical cataracts, both of which appear to be dose dependent but neither of which clearly involves a lower dose threshold.<sup>21,54</sup>

Radiation cataracts are treated by surgically removing the affected tissue, but surgical success can be complicated by radiation retinopathy and detachment, and radiation optic neuropathy.<sup>21</sup> Although the lens is very radiosensitive, ionizing radiation is not the only risk factor for cataract formation, and risk estimates for radiation cataract formation are confounded to some degree by other risk factors, such as advancing age, tobacco use, diabetes, hypertension and obesity. Some research suggests that men are more vulnerable to radiation cataracts, but study results are inconsistent. Much about the interaction of different risk factors remains unknown.

Researchers have studied sex differences in radiation cataract risk. Case-control studies strongly suggest that postmenopausal women have higher rates of cataracts, although some studies report that women receiving hormone replacement therapy have lower rates of cataracts.<sup>42</sup> Estrogen may lessen chemically and age-induced cataract formation, but animal studies suggest the opposite might be true for radiation cataracts. In rats, estrogen treatment reduces latency periods and increases severity of posterior subcapsular cataracts.<sup>90,91</sup> Radiation cataracts also were found to be more common among rats with intact ovaries than among rats whose ovaries had been removed when the animals received doses of 15 Gy to the eyes.<sup>90</sup> Limited animal experiments suggest that gender differences in radiation cataract formation noted in lab animals might not be associated with sex differences in estrogen production.<sup>42,91</sup>



Cataract

**Fig. 8.** Example of the effects of a cataract on a patient's visual field. (Used with permission from the National Eye Institute, National Institutes of Health. [www.nei.nih.gov](http://www.nei.nih.gov). Accessed September 28, 2010.)

### Occupational Radiation and the Eye

Fluoroscopy delivers the highest occupational radiation doses experienced by radiologic imaging personnel.<sup>92-94</sup> Patient dose is predictive of the dose to imaging staff, and the causes of avoidable dose for patients also tend to apply to medical staff.

Interventional cardiac fluoroscopy, cine cardiac imaging and digital subtraction angiography (DSA) procedures involve scattered radiation to the eye lenses of medical personnel.<sup>92</sup> The average radiation dose to the lens during low-mode cardiac fluoroscopy is 6  $\mu$ Sv per minute and 34.5  $\mu$ Sv per minute for high-mode fluoroscopy — much higher than the 0.77 to 3.33  $\mu$ Sv per image seen with DSA exams.<sup>92</sup> There are few epidemiological studies of the effects of fluoroscopy on the eyes of operators.

Radiation exposure of the eyes is frequently the most significant occupational radiation safety issue in fluoroscopy because operators wear lead aprons and follow other protective practices but might not use eye protection.<sup>43</sup> The International Commission on Radiological Protection (ICRP) has established the annual limit for occupational exposure to the eye lens at 150 mSv.<sup>94</sup> Staff doses can vary by more than an order of magnitude (11-fold) depending on protective equipment used and 4 orders of magnitude (40-fold) based on proximity to fluoroscopy equipment during procedures.<sup>95</sup>

The failure to use radiation protection equipment during high-dose fluoroscopy can result in doses of 10 to 50 mSv per hour — doses that are sufficiently high to cause lens opacities and cataracts over a period of several years.<sup>92</sup>

Based on studies of atomic bomb survivors published in the 1960s, experts believe that radiation cataract formation requires a single dose of 1.3 to 2 Gy or a fractionated exposure of 5 Gy to the eyes.<sup>37,38,52</sup> Both the National Council on Radiation Protection and Measurements (NCRP) and the ICRP support these occupational threshold values.<sup>96,97</sup> The United Kingdom's National Radiological Protection Board published a risk assessment in 1996, based on studies from the 1950s, concluding that 1.3 Gy may be sufficient to produce lens opacities.<sup>98</sup> However, recent epidemiological analyses suggest little if any evidence for a minimum dose risk threshold for cataract formation.<sup>38</sup>

Other than an accidental overdose to a patient's eyes, radiation doses are expected to be higher for fluoroscopy personnel than for patients, particularly cumulative doses over time.<sup>92</sup> The same relationship holds true for other eye conditions. Radiologic technologists suffer markedly higher rates of dry eye syndrome than do patients (73% vs 13% in 1 recent, small cross-sectional study) and conjunctival cell abnormalities.<sup>70</sup>

A recent study of cataract formation among radiologic technologists found that workers with high average lifetime occupational radiation doses to the eye (60 mGy) were significantly more likely to develop cataracts after 20 years than those with a much lower average occupational dose (5 mGy).<sup>38</sup> The study tracked the eye health of more than 35,000 initially cataract-free technologists and investigated overall radiation doses, rather than specifically analyzing radiation doses from fluoroscopy.<sup>38</sup> Tobacco smoking, high body mass index ( $> 25 \text{ kg/m}^2$ ), diabetes, hypertension and arthritis also independently predicted cataract risk.<sup>38</sup> Differences in UV light exposure, another known risk factor for cataracts, were not considered by the authors. Echoing other recent epidemiological analyses, the study's authors questioned whether a safe lower radiation dose threshold for cataract formation exists: "Our findings and the results of recent studies suggest that likelihood of cataract formation increases with increasing exposure to ionizing radiation with no apparent threshold level, a finding that challenges the National Council on Radiation Protection and

International Commission on Radiological Protection assumptions that a radiation dose of at least 2 Gy is associated with increased cataract risk."<sup>38</sup>

Interventional procedures may require medical specialists who have relatively little experience with fluoroscopy exams or radiological imaging. Therefore, radiation risk, including risk to the eyes, and protection practices and equipment should be explained to nonradiology department staff before the procedure.

## Radiation Safety

Interventional fluoroscopy can involve very high radiation doses compared with other radiologic imaging modalities. Fluoroscopically guided transcatheter embolization, for example, can deliver doses as high as 100 mSv — 1,000 times the dose needed for a typical chest radiograph.<sup>2</sup> Higher doses are intrinsic to certain fluoroscopic procedures even when dose minimization practices are in effect, illustrating the importance of protection practices.

Dose management practices are designed to avoid deterministic side effects, but also should take into account long-term, stochastic risks, particularly when the patient is a child or young adult and might be subject to the long latency periods for radiation-induced cancers.<sup>2</sup> The risk of radiation-induced cancer from a given fluoroscopy exam (roughly 5% per Sv) is dwarfed by specific incidence rates of cancer, particularly for older adults; a single interventional fluoroscopy procedure increases the risk of a fatal case of cancer by approximately 0.5% compared with an expected lifetime risk for fatal cancers of approximately 20%.<sup>2</sup>

In general radiation dose is managed through dosimetric monitoring and minimizing the dose to target volumes. For example, higher doses delivered over brief time periods are more likely to cause deterministic harm to tissues; dose planning such as fractionation delivers lower radiation doses over a longer period of time, permitting cellular repair mechanisms to reduce the cumulative damage to those tissues.

Interventional fluoroscopy procedures represent a growing proportion of fluoroscopic examinations.<sup>1</sup> Because interventional procedures are more complex and time consuming than conventional diagnostic fluoroscopy, radiation doses and reports of significant tissue injury have climbed over the past 2 decades.<sup>1</sup> The precise incidence

rate of radiation injury from fluoroscopy to patients, radiologic technologists and physicians is unknown.<sup>1</sup>

The FDA Center for Devices and Radiological Health alerted fluoroscopy operators and hospital administrators in 1994 that the increasing use of long-duration or high-radiation fluoroscopy procedures was causing an increased incidence of radiation burns among patients, some severe enough to require skin grafts.<sup>99</sup> In 1994 the FDA learned of 50 fluoroscopic radiation burn injuries to patients.<sup>1,100</sup> Interventional procedures listed in the FDA advisory included cardiac catheter ablation, transluminal angioplasty, vascular embolization and neuroembolization.<sup>99</sup>

After the FDA alerts regarding the potential harm posed by interventional fluoroscopic procedures, the American College of Radiology and the Society of Interventional Radiology developed guidelines for the management of fluoroscopic radiation dose.<sup>2</sup> These guidelines emphasize the importance of patient selection, informed consent, safe performance of procedures, and monitoring and documentation of actual administered doses for quality assurance and quality control purposes.<sup>2</sup> Patient selection criteria to consider when weighing the risks and benefits of a fluoroscopy procedure include relative body mass, the patient's medical radiation history and other risk factors such as hypertension or diabetes. Informed consent is typically perfunctory, as patients rarely opt to forego fluoroscopy after learning of the radiation risks involved.<sup>2</sup>

### Dose Management

Beam collimation, use of pulsed-mode fluoroscopy and the last-image hold feature, and reduced tube voltage and milliamperage limit the dose to both patients and staff.<sup>95</sup> A crucial paradigm for dose minimization in all radiological imaging is establishing the goal of *clinically adequate*, rather than *best possible*, visualization of target anatomy. In fluoroscopy this model might mean tolerating higher image contrast. Image intensifier low-level mode should be used whenever possible. Elevated fluoroscopy currents increase the risk of deterministic and stochastic events, particularly with longer exam durations.

In general, radiation exposure and injury to patients and health care personnel can be best managed and minimized by following 3 principles:

- **Duration.** Reduce radiation dose by minimizing the total time of exposure. Long procedures tend

to lead to higher doses, increasing the risk of deterministic and stochastic effects.

- **Distance.** The inverse square law ( $1/d^2$ ) applies to the distance between the radiation source and the individual. The intensity of the x-ray beam decreases in proportion to the inverse of the distance squared. Practically speaking, the distance between the tube and the patient should be as great as possible, with the image intensifier close to the patient. The intensifier also can shield the operator. Distance is particularly relevant for reducing dose to personnel during fluoroscopy. The ability to control distance is restricted for set-isocenter C-arm units with identifiable centers of rotation and set or fixed tube-to-receptor distances.<sup>2</sup>
- **Protection.** Patients and medical personnel should be shielded from the radiation source with all available barriers. Routine shielding protects the thyroid, breast and reproductive organs. Protection includes lead aprons and lead-lined barriers around the fluoroscopy equipment to minimize ambient radiation. ASRT has endorsed the position that imaging facilities should use shielding for all fluoroscopy and CT procedures.<sup>50</sup> Personnel in many hospitals are not aware of eye safety during fluoroscopy procedures; therefore, radiologist assistants and radiologic technologists should promote eye shielding whenever possible.

### Dosimetry and Dose Monitoring

Radiation exposure and absorbed dose can be measured using dosimetric tools such as a film badge or reusable thermoluminescent dosimeter (TLD) badge containing lithium chloride crystals. TLDs absorb x-ray energy and release light energy in wavelengths indicating radiation levels. Indirect biomolecular indicators of radiation exposure include genetic or chromosomal integrity tests that quantify actual biological damage. These tests generally are used in epidemiological studies rather than in clinical settings, but are likely to become more widespread as clinical dosimetric tools in the future.

Dosimetric monitoring of fluoroscopy is important because actual dose is difficult to predict and varies dramatically between different imaging units, even when the units are seemingly identical.<sup>92</sup> Reliable monitoring of the radiation dose to the eyes requires eye-specific

dosimetry, such as the use of forehead- or shoulder-mounted TLD dosimeters or, at a minimum, a second dosimeter placed outside the lead apron.<sup>92</sup> The latter method is not ideal because radiation field gradients may cause misleading dosimetric readings for the eyes. Whole-body dosimeters typically are worn under lead aprons, and they do not account for radiation field gradients. Thus, they cannot be relied upon to accurately indicate dose to the eye.

CT dose planning calculations are different from fluoroscopic dose calculation methods. The kerma-area product (KAP or  $P_{KA}$ ) is used in radiography and fluoroscopy, and the CT dose index (CTDI) is used for CT scanning.

The CTDI is calculated using a single axial scan dose, divided by the total nominal beam width, or the width of each active channel multiplied by the number of active channels, so that the calculation takes beam gaps and overlaps into consideration. The CTDI reflects dose profiles along the z-axis perpendicular to the x-ray tube's plane of rotation.<sup>102</sup> Although it may be based partly on empirical measurement or scanner settings, CTDI is essentially a calculated estimate, not a direct measurement of actual patient dose. For example, the CTDI does not take into account tissue-specific radiosensitivities or anatomical variations of individual patients. CT radiation dose for children or small adults can be as much as 600% higher than the dose indicated by the CTDI.<sup>103</sup> Furthermore, the reliability of CTDI dose measurement for newer multislice CT scanners has been questioned, leading some authors to argue that the KAP dose calculation should be used for CT.<sup>102</sup> For these reasons and because dose distributions can vary among imaging equipment, phantom measurements and direct dosimetry are used to calculate radiation doses to patient and staff.<sup>101</sup> It should be kept in mind, however, that all dosimetry involves significant uncertainty and tends to ignore the effects of radiation scatter.<sup>2</sup> Backscatter can cause up to 40% of actual patient dose to be underestimated.<sup>2</sup>

Fluoroscopic dosimetry involves peak skin dose and kermas. Measured in Gy units, kermas represent the x-ray energy released in matter within a known irradiated volume.<sup>2</sup> Air kermas represent the x-ray energy per unit volume of air, while reference point air kerma, also called reference dose and cumulative dose in the fluoroscopy dosimetry literature, represents air kerma for a point in space during a fluoroscopic procedure. The KAP is calculated as

the air kerma across the x-ray beam and is expressed as Gy multiplied by  $\text{cm}^2$ . KAP is used as a proxy for patient dose, but does not account for scatter radiation.<sup>2</sup>

Peak skin dose is a measure of the highest amount of radiation received by any part of the patient's skin during fluoroscopy. It can be measured using film badge or TLD dosimeters. Modern fluoroscopes record total exam time, but fluoroscopy duration is not a strong or reliable indicator of peak skin dose.<sup>2</sup> Few fluoroscopic units provide real-time peak skin dose data, but all units manufactured after June 2006 provide air kerma rates.<sup>2</sup> KAP is believed to be more useful for predicting stochastic radiation effects, while peak skin dose is more useful for predicting deterministic sequelae.<sup>2</sup>

Dosimetric measurements of actual patient dose for each exam or procedure should be documented and archived.<sup>2</sup> Digitally archived imaging exams should include radiation dose information. ASRT officially supports the position that all imaging facilities should document patient radiation doses.<sup>50</sup> Several mechanisms for tracking patient radiation doses have been proposed, including automated archiving of estimated doses in electronic patient records.

### Exam Duration

The idea of examination duration involves not simply the total time between the initiation and completion of the procedure, but also the amount of time that the patient actually is exposed to the radiation and the intensity or rate at which irradiation occurs. Switching from continuous fluoroscopy mode to 15 pulses per second, for example, can reduce the radiation dose by as much as 22%.<sup>1</sup> In interventional fluoroscopy procedures, the last-image hold function used in conjunction with collimation can provide sufficient anatomic information in place of active scanning that produces no new data but continues to irradiate the patient. Staff fatigue increases error rate and reduces attention span, which together can cause longer procedures and higher doses.

### Collimation

Collimation reduces the radiation dose to nontarget anatomy without affecting image quality within the target area. Collimators decrease radiation exposure by reducing the width or height of a beam's dose distribution curve.<sup>101</sup> Thus, collimated fluoroscopy delivers a much lower total KAP than open-field fluoroscopy.<sup>2</sup>

Partly closed collimator leaves reduce unnecessary radiation to tissue and therefore are crucial in protecting the visual system during head and neck fluoroscopy. Collimation should be used whenever possible to minimize or eliminate scatter radiation to the eyes, and careful collimation is particularly important for small children, who are more vulnerable to radiation effects.<sup>2</sup>

### **Radiation Protection**

There is no single method to reduce fluoroscopic dose to the eyes; therefore, imaging staff must use every possible dose minimization and protective technique when conducting a procedure, starting with equipment checks. For example, mobile C-arm fluoroscopy units often have removable spacer assemblies for the tube; if the spacer is not in place during a procedure, patient doses will be higher than necessary. Last-image hold, beam filtration and pulsed-mode fluoroscopy should be used as much as possible to minimize irradiation of the eyes, especially when the chest, head or neck must be imaged.

The lowest required fluoroscopy pulse rate should be used. Collimation should be maximized and image intensifier magnification should be minimized if possible without compromising image quality. Placing image intensifiers as close as feasible to the patient reduces beam intensity. The intensifier also can serve as a scatter radiation shield for staff. For a C-arm unit with an overtable x-ray tube, backscattered radiation from the point of beam entrance can increase head and eye doses for operators and staff.

Beam-on time is a key factor in patient and staff dose. For example, the beam should not be active when a dynamic image is not required and the last-image hold can be used. Because the kilovolt peak (kVp) and milliamperage (mA) usually are under automatic control, the fluoroscopy operator's single best way to limit dose is to restrict the beam-on time.

The position of the medical staff in the exam room during fluoroscopy procedures is a frequently overlooked factor in occupational exposure. According to the inverse square law, seemingly small differences in distance can have a large effect on dose; therefore, certain positioning habits during fluoroscopy can, over time, dramatically affect cumulative dose to personnel. Staff dose varies 40-fold depending on proximity to the fluoroscopy unit and x-ray beam.<sup>95</sup>

Shielding is a crucial component of radiation protection for both patients and staff. The use of multiple protective barriers, both personal (eg, wraparound aprons, gloves and thyroid shields) and mobile shielding, is an important strategy for minimizing dose to staff. For example, disposable bismuth-antimony surgical drapes can reduce scatter radiation. Fluoroscopy personnel should use wraparound aprons with at least 0.35 mm lead equivalent to protect the chest and abdomen, a neck shield to protect the thyroid and esophagus, and eye shields. As a general rule, staff not wearing lead shielding will receive 10 times the measured dose of those wearing protective equipment.<sup>95</sup>

Scatter radiation during interventional fluoroscopy of the upper body is higher for the eye closer to the x-ray beam, but both eyes are exposed to radiation. Given there is no established safe minimum dose for the eye lens, fluoroscopy staff should protect their eyes through every means possible. Eyeglasses with side shields and lead-glass lenses should be used by fluoroscopy personnel. Individuals whose faces will be close to the x-ray beam or target tissues for prolonged periods should use face masks with lead-acrylic windows.

A staff member's eye on the x-ray tube side receives higher doses during the procedure, with the amount increasing as the individual's position is closer to the tube. Fluoroscopy staff should avoid unnecessarily close proximity to the x-ray tube during fluoroscopy and should remain at least 20 cm from the beam unless absolutely necessary. Personnel should approach the side of the table at the patient's groin during C-arm unit procedures to minimize exposure to scatter radiation.<sup>95</sup> When moving away from a patient during fluoroscopy, personnel should step back in a line diagonal to the tube and path of the beam.

Unfortunately, for reasons that are not well understood, eye shielding for patients is not as effective as shielding for other areas such as the thyroid.<sup>104</sup> Although eye shields do not harm patients and should be used whenever possible to help reduce dose, the best way to protect a patient's eyes is through dose management techniques, such as collimation and limiting the duration of the procedure, dose rate and beam intensity. Bismuth eye and thyroid shielding for patients may not provide as much dose attenuation as lead shields. In a 2008 phantom study of neuroangiography patients, eye shields failed to significantly reduce patient

eye dose as measured by a TLD, leading the authors to question the utility of eye shields for this particular procedure.<sup>104</sup> Eye shielding also can interfere with neurofluoroscopy visualization.

### Postprocedure Monitoring

Patients should be monitored for radiation injury if any one of the following sentinel events occurs:

- Peak skin dose exceeds 3,000 mGy.
- Reference point air kerma exceeds 5,000 mGy.
- Kerma area product exceeds 500 Gy × cm<sup>2</sup>.
- Fluoroscopic procedure duration exceeds 1 hour.

Exam durations of more than 1 hour tend to involve significant radiation doses, but exam time is only weakly correlated with peak skin dose. Nevertheless, fluoroscopy exceeding 1 hour is considered to be a sentinel event.<sup>2</sup> In addition, any irradiation of the lens should be treated as a sentinel event, triggering follow-up monitoring for focal opacities and cataracts, which may have to be treated surgically.

If a sentinel event occurs, patients should be given written instructions before they leave the facility, explaining the need for follow-up.<sup>2,107</sup> These instructions should include information on how to perform a self-examination of affected tissues, and instructions to contact the facility if specific signs occur, such as sudden decline in visual acuity or the appearance of small dots that may become opacities.<sup>2</sup> Any patient report of possible radiation injuries should be reviewed by a medical physicist.<sup>2</sup> Documentation of sentinel events always should be included in the patient's medical record.

The sentinel event thresholds assume that a patient has not recently received other medical radiation doses. The absence of sentinel events for a given procedure is not sufficient to forego follow-up monitoring for sequelae, and even patients with no sentinel dose events should be monitored if the same target volume has been exposed during other radiological procedures.<sup>2</sup>

### Quality Control and Quality Assurance

Every facility should have quality assurance (QA) and quality control (QC) programs, and employ medical physicists to periodically check equipment function and verify calibration, resolution and entrance dose exposure rates.<sup>107,108</sup> QA programs assess the effects of human performance on image quality and patient dose. The assessment

can include periodic review of dose-minimization strategies and fluoroscopy protocols, continuing education (CE) for personnel, maintenance of staff credentials and certifications and training updates for all personnel involved in fluoroscopy examinations.<sup>107</sup>

QA programs consist of several different educational components. For example, signage in or near the fluoroscopy room can remind staff to use eye shielding whenever possible. All radiologist assistants, radiologic technologists, nurses and other fluoroscopy team members should be trained in radiation management before participating in fluoroscopy procedures. Continuing education on radiation dosimetry, radiation protection and equipment performance should be encouraged or required.<sup>107</sup>

QA programs also should include an annual facility review of the types of fluoroscopy studies conducted, numbers and doses of examinations, image quality relative to dose, and should track and compare trends in these factors over time.<sup>2,107</sup> Periodic staff lectures on ALARA improve the use of leaded eyeglasses and hanging shields during fluoroscopy procedures and have been shown to reduce pediatric fluoroscopy procedure times and dose to pediatric patients.<sup>109</sup> A QA program should review the adverse effects of staff fatigue on patient radiation dose to help determine optimal scheduling. Operator fatigue can prolong interventional fluoroscopy examinations, particularly during longer-duration procedures such as percutaneous coronary interventions.

Proper equipment maintenance and periodic calibration is a crucial component of dose management. In contrast to QA programs, QC programs determine if imaging equipment is functioning properly. A QC program should ensure the facility has the latest software updates from manufacturers, that dose-reduction equipment is used in day-to-day practice and that groups meet regularly to discuss dose-reduction procedures and adherence to the ALARA principle.<sup>107</sup>

QC programs should ensure that the size of examination rooms is adequate and that shields, including eye shielding equipment, are readily available. Because regular maintenance, cleaning and calibration of fluoroscopy equipment are important for effective dose management, facilities should establish daily QC practices and written procedures. An on-site radiologic technologist should be designated as the day-to-day QC coordinator.

Equipment performance also should be routinely monitored as part of the QC program.<sup>107</sup>

Imaging professionals are recognizing that fluoroscopy techniques, procedures and utilization guidelines must be optimized to balance image quality with ALARA, particularly for younger patients. The need for a given level of image quality always should be balanced against dose considerations.<sup>107</sup>

A dose reduction committee should periodically review patient protocols, the radiation doses of performed exams and procedures. Radiation dose error review committees, consisting of radiologic technologists and a qualified medical physicist, should meet to identify the causes of errors and take corrective action. Full-time medical physicists are rare even at larger hospitals, and contract medical physicists may be available only for annual meetings on a consulting basis. However, review committee meetings can be scheduled to coincide with annual equipment reviews, providing opportunities for the physicist to identify and discuss any equipment problems.

### **Documenting Radiation Doses**

Peak skin dose and KAP dose for every fluoroscopy procedure should be archived in the patient's medical record. When peak skin dose is unavailable, the reference point air kerma can be used instead.<sup>2</sup>

In addition to providing data for trends analysis, documentation also helps detect sentinel events that can trigger follow-up and monitoring of adverse radiation effects. Sentinel events should be noted immediately in the patient's medical record, with an explicit statement that a clinically significant dose was delivered to the patient.

Statistical reports of dose trends and documentation should be prepared at least annually to guide QA and QC programs and to help determine the need for staff-wide training.<sup>2</sup> Failing to document doses is an indicator that personnel might not appreciate the dangers of unnecessary radiation exposure. If fluoroscopy personnel fail to report patient doses for less than 95% of procedures, the facility should consider implementing new radiation safety training and continuing education.<sup>2</sup> All identified cases of deterministic radiation effects should be reported immediately to the facility's radiation protection officer and to state radiation protection or safety agencies. Within the facility, the appropriate committee should review these cases and identify ways to avoid future errors.

Currently, some physician groups use electronic patient records to track CT dose and calculate cumulative patient dose.<sup>105</sup> Federal health care legislation passed by the U.S. Congress in March 2010 contained provisions that encourage the adoption of technological cost containment strategies such as electronic patient medical records.<sup>106</sup> Thus, the new law might hasten the widespread use of radiation dose-tracking technologies. Health care reform advocates hope that tracking cumulative patient doses will reduce patient risk and limit overutilization of medical imaging exams by referring clinicians. This may eventually help reduce the incidence rates of radiation-associated visual system pathologies, particularly if the tracking systems include information about target anatomies and anatomy-specific dose estimates.

### **Informed Consent: Communicating Risk**

There is ample empirical evidence of the importance of the ALARA principle and the potential harm from unnecessary medical irradiation. However, these lessons have not been widely adopted in day-to-day clinical practice. This apparent gap is partly due to economic realities and reimbursement issues, but referring physicians and patients alike often do not appreciate the potential risks of unjustified or repeated radiologic imaging. Clinicians frequently succumb to the demands of patients who seek reassurance through clinically unjustified diagnostic imaging.<sup>110</sup>

Clearly communicating radiation risk to patients and referring clinicians is an ethical and legal obligation of radiologist assistants and radiologic technologists. Informed consent should not be treated as a perfunctory matter but rather as an active dialogue between the provider and the patient. The health care provider should explain terminology and risks, discuss the patient's medical radiation history and encourage patients to ask questions. The provider should reassure the patient that appropriate steps will be taken to minimize fluoroscopic irradiation to the extent possible.

Risks must be described objectively, but providers also must give patients a context in which to judge the risks, such as the overall lifetime cancer risk from sources other than medical imaging. In addition, practitioners should explain alternatives to the planned procedure and the risks associated with those options.

Patients scheduled to undergo certain interventional procedures should be informed about the radiation dose

delivered by the procedure and the specific risks, including the potential for scatter radiation to visual system tissues. According to the FDA, fluoroscopy procedures that are associated with potential radiation injury risk after less than an hour include cardiac catheter ablation, percutaneous procedures such as transluminal angioplasty, vascular embolization and neuroembolization.<sup>99</sup> Interventional pain management procedures, including cervical vertebroplasty, also involve significant radiation doses to the patient.<sup>2</sup>

Just as specific types of procedures may involve higher radiation doses, certain patient characteristics can affect the risk of radiation injury. Patients who are likely to receive a radiation dose to the lens, thyroid, breast or reproductive organs and who are pregnant, who have small or very large body masses (body weight < 10 kg or > 135 kg) or who are children, adolescents or young adults are at greater risk, particularly from high-dose procedures.<sup>2</sup> If the planned fluoroscopic target tissues have been treated with radiation or other medical radiation has been delivered to the same tissues within the previous 2 months, clinicians should review the anatomy in question and discuss the risk of cumulative radiation doses to those tissues. Elderly patients, patients with diabetes and those who are overweight or hypertensive should be cautioned that they could be at greater risk than other patients for radiation cataract formation.

With every fluoroscopy exam, patients should be told of the potential radiation risk to their eye health, including the relatively high radiosensitivity of the lens and uncertainty concerning safe dose levels for cataract formation. Because some patients might not know what cataracts are and are reluctant or embarrassed to admit ignorance, clinicians should briefly explain that cataracts are areas of degraded lens transparency that could significantly affect eyesight.

In addition to communicating risk to patients and improving awareness of radiation dose issues among referring clinicians, imaging personnel are responsible for implementing the ALARA principle in every situation, starting with the elimination of unnecessary radiologic imaging. This includes encouraging patients to remind referring physicians of past medical radiation exposure and to ask questions about the relative risks and benefits of fluoroscopy. Surveys have shown that referring clinicians often do not receive adequate training in radiation

protection, are frequently unaware of the relative radiosensitivities of different tissues and organs and do not appreciate the long-term health risks of radiation exposure.<sup>111,112</sup> Many times equally useful diagnostic information may be available from other imaging modalities, and in coming years, emerging health information technologies and data management tools will help alert referring clinicians to the radiation risks for individual patients.

## Conclusion

Visual system tissues, particularly the lens of the eye, are extremely vulnerable to the harmful effects of ionizing radiation. There is no well-established, “safe” level of ionizing radiation for the eyes; furthermore, recent studies suggest that there may not be any lower dose threshold, below which irradiation of the lens is without risk. Radiation doses to the lens of less than 1 Gy may be sufficient to cause cataracts. Therefore, it is absolutely critical that fluoroscopy operators strictly follow the ALARA principle.

Patient radiation doses from fluoroscopy and fluoroscopy-guided interventional procedures have increased dramatically over recent decades. Therefore, radiation dose management in fluoroscopy is important to protect the visual system of both patients and health care personnel involved in fluoroscopy exams. Dosimetric monitoring, dose minimization through planning and the appropriate use of protective equipment and shielding, implementation of effective QA and QC programs, and the comprehensive education of fluoroscopy operators play important roles in the protection of the eyes during fluoroscopy.

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