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Tuberculosis: A Review and Update

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CONTRAINDICATIONS: History of a prior allergic reaction to a gadolinium-based contrast agent.

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WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF) Gadolinium-based contrast agents increase the risk of nephrogenic systemic fibrosis (NSF) in patients with:

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ABLAVAR® Injection: As with other contrast media: the possibility of serious or life-threatening anaphylactic or anaphylactoid reactions, including cardiovascular, respiratory and/or cutaneous manifestations, should always be considered. As with other paramagnetic contrast agents, caution should be exercised in patients with renal insufficiency due to the possibility of further deterioration in renal function.

In clinical trials, a small increase (2.8 msec) in the average change from baseline in QTc was observed at 45 minutes. These QTc prolongations were not associated with arrhythmias or symptoms. Caution should be used in patients at high risk for arrhythmias due to baseline QTc prolongation.

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Please see brief summary, including boxed WARNING regarding Nephrogenic Systemic Fibrosis (NSF), on the following page.

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**WARNING. NEPHROGENIC FIBROSIS SYNDROME (NSF)**

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In these patients, avoid use of gadolinium-based contrast agents unless the diagnostic information is essential and not available with non-contrast enhanced magnetic resonance imaging (MRI). NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle, and other organs. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. When administering a gadolinium-based contrast agent, do not exceed the maximum recommended dose and allow a sufficient period of time for elimination of the agent from the body prior to any re-administration [see Warnings and Precautions].

**INDICATIONS AND USAGE**

Ablavar is indicated for use as a contrast agent in magnetic resonance angiography (MRA) and in magnetic resonance imaging (MRI) in adults with known or suspected peripheral vascular disease.

**DOSAGE AND ADMINISTRATION**

**Dosing Guidelines**

Administer Ablavar as an intravenous bolus injection, manually or by power injection, at a dose of 0.12 mL/kg body weight (0.03 mmol/kg) over a period of time up to 30 seconds followed by a 25-30 mL normal saline flush. (See Table 1 below for dosing volume).

**TABLE 1. Weight-Adjusted Volumes for the 0.33 mM/kg Dose**

<table>
<thead>
<tr>
<th>Body Weight</th>
<th>Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>40 kg</td>
<td>88 mL</td>
</tr>
<tr>
<td>50 kg</td>
<td>110 mL</td>
</tr>
<tr>
<td>60 kg</td>
<td>132 mL</td>
</tr>
<tr>
<td>70 kg</td>
<td>154 mL</td>
</tr>
<tr>
<td>80 kg</td>
<td>176 mL</td>
</tr>
<tr>
<td>90 kg</td>
<td>198 mL</td>
</tr>
<tr>
<td>100 kg</td>
<td>220 mL</td>
</tr>
<tr>
<td>110 kg</td>
<td>242 mL</td>
</tr>
<tr>
<td>120 kg</td>
<td>264 mL</td>
</tr>
<tr>
<td>130 kg</td>
<td>286 mL</td>
</tr>
<tr>
<td>140 kg</td>
<td>308 mL</td>
</tr>
<tr>
<td>150 kg</td>
<td>330 mL</td>
</tr>
<tr>
<td>160 kg</td>
<td>352 mL</td>
</tr>
</tbody>
</table>

Inspect the Ablavar vial visually for particulate matter and discoloration prior to administration. Do not use the solution if it is discolored or particulate matter is present.

Ablavar is intended for single use only and should be used immediately upon opening. Discard any unused portion of the Ablavar vial.

Do not mix intravenous medications or parenteral nutrition solutions with Ablavar. Do not store Ablavar medications in the same intravenous line simultaneously with Ablavar.

**Imaging Guidelines**

Ablavar images were completed in two stages: the dynamic imaging stage and the steady-state imaging stage. Both stages are essential for the detection of arterial lesions. During interpretation of the steady-state images, Ablavar images within the venous system may limit or confound the detection of arterial lesions.

To assess the initial distribution of Ablavar within the arterial system, begin dynamic imaging immediately upon injection. Begin steady state imaging after dynamic imaging has been completed typically 5 to 7 minutes following Ablavar administration. At this time point, Ablavar is generally distributed throughout the blood pool. Steady-state imaging was completed within approximately one hour following Ablavar injection.

**TABLE 2. Common Adverse Reactions in 802 Subjects Receiving Ablavar at 0.33 mM/kg**

<table>
<thead>
<tr>
<th>Prefixed term</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pruritis</td>
<td>45 (2)</td>
</tr>
<tr>
<td>Headache</td>
<td>33 (4)</td>
</tr>
<tr>
<td>Nausea</td>
<td>33 (4)</td>
</tr>
<tr>
<td>Vasoconstriction</td>
<td>28 (3)</td>
</tr>
<tr>
<td>Paresthesia</td>
<td>25 (3)</td>
</tr>
<tr>
<td>Injection site bruising</td>
<td>25 (3)</td>
</tr>
<tr>
<td>Dysgeusia</td>
<td>15 (2)</td>
</tr>
<tr>
<td>Rumination</td>
<td>12 (1.5)</td>
</tr>
<tr>
<td>Venipuncture site bruising</td>
<td>12 (1.5)</td>
</tr>
<tr>
<td>Tactile sensation alteration</td>
<td>10 (1.25)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>8 (1)</td>
</tr>
<tr>
<td>Feeling cold</td>
<td>7 (1)</td>
</tr>
</tbody>
</table>

**Post-marketing Experience**

Because post-marketing reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The profile of adverse reactions identified during the post-marketing experience subsequent to labeling changes was similar to that observed during the clinical studies experience.

**DRUG INTERACTIONS**

Concurrent use of medications that bind to blood albumin and have the potential to alter the binding of other drugs that also bind to albumin. No drug interaction reactions were observed in clinical trials. Consider the effects of any other concurrently administered medications that bind to albumin. An interaction may enhance or decrease the activity of the concomitant agent [see Clinical Pharmacology].

**Warfarin**

In a clinical trial of 10 patients receiving a stable dose of warfarin, a single dose of Ablavar did not change the prothrombin time under the anticoagulant activity of warfarin as measured by the International Normalized Ratio (INR).

**USE IN SPECIFIC POPULATIONS**

**Pregnancy**

Category C

There are no adequate and well-controlled studies of Ablavar in pregnant women. Because animal reproduction studies are not always predictive of human response, use Ablavar during pregnancy only if the potential benefit justifies the potential risk to the fetus.

**Nursing Mothers**

It is not known whether gabofosveset is secreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Ablavar is administered to a nursing woman.

**Pediatric Use**

The safety and effectiveness of Ablavar in patients under 18 years of age have not been established. The risks associated with Ablavar administration to pediatric patients are unknown and insuffi cient data are available. Ablavar is not recommended for use in pediatric patients.

**ADVERSE REACTIONS**

Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice.

**Clinical Studies Experience**

Anaphylaxis and anaphylactoid reactions were the most common serious reactions observed following Ablavar injection administration [see Warnings and Precautions].

In all clinical trials evaluating Ablavar with MRI, a total of 1,676 (1379 patients and 297 healthy subjects) were exposed to various doses Ablavar. The mean dose received was 40 mg/kg (range 18 to 91 mg/kg; 86% were men and 34% (476) were women. In this population, there were no reports of non-Asian, 8% (107) Black, 12%, (159) Hispanic, 1% (7) Asian, and < 1% (6) patients of other racial or ethnic groups. See Table 2 for listing of the most common adverse reactions.

**NONCLINICAL TOXICOLOGY**

**Carcinogenesis, Mutagenesis, Impairment of Fertility**

Long-term reproductive studies have not been conducted with the gabofosveset potential of gadofosveset. Gadofosveset was negative in the in vitro bacterial reverse mutation assay, the in vivo micronucleus assay, and the in vivo gene mutation assay. Administration of up to 3 times the human dose (0.3 mg/kg) to female rats for 2 weeks and to male rats for 4 weeks did not affect fertility [see Use in Specific Populations].

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EDITOR’S NOTE

A Mix of Old and New

Katie Faguy, ELS, is ASRT publications manager.

As Radiologic Technology begins its 82nd volume year, we are pleased to introduce a new cover artist, radiologist Kai-hung Fung of Hong Kong.

Dr Fung is a self-taught new media artist who creates digital artworks using computed tomography and magnetic resonance images and a 3-D computer rendering program. He pioneered a technique that uses contour lines rendered in a rainbow of colors to define 3-D forms and space.

Dr Fung’s artwork has been featured on many websites and in magazines and journals, as well as in several museum exhibitions, both in Hong Kong and the U.S. In 2007, he was the first place winner in the International Science and Engineering Visualization Challenge sponsored by Science and the National Science Foundation.

This issue’s cover artwork, based on a lung scan, is titled “Tropical Rainforest.” The patient has interstitial lung disease, and in this image the terminal branches of the lungs resemble the top of the rainforest’s canopy at twilight, Dr Fung said.

As for this issue’s content, it combines the ancient and the modern: Directed Reading author Bryant Furlow updates readers on tuberculosis, which may have plagued even our proto-human ancestors and is evolving today into dangerously drug-resistant strains. Readers also will learn the latest on molecular imaging’s role in the war on cancer or cutting-edge techniques for targeting breast biopsies, depending on their area of interest.

In the peer-reviewed section of this issue, researchers examine the best way to image an injury as old as humankind — sprained ankles — and the best way to run a modern mammography center in light of federal requirements and new technology designed to streamline patient throughput.

We hope you enjoy this issue and, as always, welcome your comments and suggestions. E-mail us at communications@asrt.org. ◆
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September/October 2010

Volume 82/Number 1

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On the Cover: “Tropical Rainforest,” based on a lung scan, is the first of 6 cover images by radiologist Kai-hung Fung. For more on Dr Fung’s artwork, see the Editor’s Note on Page 9.
Heparin Confusion

Editor:
I am concerned about an error in the July/August 2010 issue of Radiologic Technology. In the Directed Reading “Bleeding Risks in Interventional Radiology,” on page 552 there is a discussion of heparin therapy.

Fractionated and unfractionated heparin are confused in this section. Low molecular weight heparin (LMWH) is referred to as unfractionated when in fact the opposite is correct. LMWH should be properly referred to as fractionated heparin. The article also refers to the delivery methods of fractionated and unfractionated heparins. The typical method of delivery for LMWH is subcutaneous and for unfractionated heparin by IV. The entire section on heparin is very confusing and misleading due to these errors. It also should be noted that it is unfractionated heparin that is usually given in emergencies or during invasive procedures.

Marvin Mullin, BSRT, R.T.(R)(CV)
(via e-mail)

The editor responds:
Thank you for clarifying this matter. Our apologies for the confusion the error caused. •
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Self-stress vs Manual Stress In Talar Tilt Radiography

GARY LENTELL, DPT
ROBERT J DESCH, MA, R.T.(R)
SUSAN M TRACZ, PhD
LISA M NYBERG, PhD

**Background** Radiographic study following inversion ankle sprain commonly is used to determine the presence of anatomic laxity across the talocrural joint.

**Purpose** To compare the degree of talar tilt derived from a radiographic ankle stress exam under 2 conditions: self-stress vs manual stress applied by the clinician.

**Methods** Twenty-four subjects seeking medical care following ankle sprain underwent talar tilt stress exams of both ankles. The involved ankle was imaged with self-stress by use of a strap and with the clinician providing manual stress during the imaging exam. Mean talar tilt for the self-stress method was 2.2°, compared with 5.9° for the manual stress method (P < .001).

**Results** Significantly greater and clinically meaningful differences in talar tilt angle were found when manual stress was provided by the clinician. To avoid false negative findings of anatomic laxity in stress talar tilt studies at the ankle, a standardized procedure in which the clinician provides manual stress may be necessary.

Ankle sprains are one of the most common complaints managed in the musculoskeletal practice setting. It is estimated that 25,000 sprains occur daily in the United States, and these can account for up to 1 in 10 emergency department visits. Many people with past acute ankle sprains report frequent recurrence and a sense of instability.

It is accepted that standardized and reproducible radiographic procedures, along with the medical history and physical examination, are vital components of the diagnostic process involving the musculoskeletal system. In both acute and chronic conditions of ankle instability, radiographic study with applied inversion stress, promoting a talar tilt to the ankle, is used to determine the presence and magnitude of anatomic laxity. In many settings, this protocol calls for the radiologic technologist or other medical professional to manually place and hold the patient’s ankle in a position of inversion stress when obtaining the radiograph. In other settings, the patient self-positions and holds the ankle in inversion stress by use of a strap. Self-positioning protocols are less demanding of resources and result in less radiation exposure to radiographic department personnel than manual positioning protocols.

It is not known whether the results of talar tilt radiographs of the ankle performed using the patient self-stress method produce similar findings compared with the manual-stress exam method. Therefore, the purpose of this study was to determine whether there were significant differences in the outcome of the talar tilt stress radiographs using the 2 different methods in patients with suspected anatomic laxity of the ankle.

**Literature Review**

While the use of talar tilt stress radiography is commonly identified in the literature for the assessment of ankle instability following a history of sprain, very little is found comparing the outcome between manual stress and self-stress techniques. A search utilizing the CINAHL Plus, Google Scholar and Science Digest databases found no articles directly comparing outcomes between these 2 procedures. Therefore, the research question addressed by this study was whether the radiographic outcome from a stress radiograph talar tilt carried out manually by the clinician would be comparable to that obtained when self-stress was applied.
Ankle sprains occur when excessive external forces are applied to the joint, typically owing to unexpected movement initiated by body segments above the ankle, over the planted foot. Although sprained ankles occur across many activities of daily living and work, sports frequently are associated with ankle sprains. The most common of these are basketball, football and cross-country running.

Between 80% and 90% of all ankle sprains are due to an inversion injury, which sprains the lateral ligamentous complex of the ankle. The ankle joint is constrained laterally by the anterior and posterior talofibular ligaments, the large calcaneofibular ligament centrally and the joint capsule. Inaba reported that of the 3 lateral ligaments, the anterior talofibular ligament is the weakest and most subject to injury. As a result, 65% of ankle sprain injuries are confined to the anterior talofibular ligament; an additional 20% also involve tearing of the calcaneofibular ligament.

Following standard radiographs to rule out fracture, the clinical severity of ligament damage following an acute inversion sprain generally is assessed as 1 of 3 grades. Grade I sprains usually are marked clinically by minimal pain, swelling or loss of functional ability. Grade II sprains tend to be accompanied by moderate pain and swelling, with difficulty in bearing weight. In Grade III sprains, there is a complete rupture of soft tissue constraints with substantial pain, swelling, bruising and inability to bear weight. Patients with Grade I injuries, which may involve a minor anatomic tear, present with pain, but no abnormal movement in the ankle joint under stress. Grade II injuries are characterized by pain and some degree of abnormal excessive movement upon clinical examination. Integrity of both the calcaneofibular ligament and the anterior talofibular ligament are questionable if there is abnormal movement caused by talar tilt stress. Grade III injuries show gross laxity under stress, without a discernible end point.

Grading the severity of the acute ankle sprain assists in establishing a prognosis and provides a guide for management interventions. Grade II ankle injuries typically remain symptomatic more than a month following injury, with residual edema, loss of mobility, strength and function. Documenting the presence of major anatomic instability following a grade III ankle injury in a high-demand athlete traditionally leads to consideration of surgical reconstruction of the torn ligaments.

Improper evaluation and management of an acute ankle sprain may lead to chronic ankle instability, pain, swelling, giving way and repetitive injury. Up to 40% of those with a substantial episode of acute ankle sprain may develop functional instability at the ankle, defined as giving way of the ankle under normal activities of daily living. In addition to mild anatomic laxity, contributing factors to this condition can include chronic strength deficits and deficits in proprioception, as defined by loss of passive movement awareness involving the ankle joint complex.

Stress radiographs of the ankle are a vital tool for identifying the degree of anatomic instability associated with the inversion injury in both acute injury and chronic complaint. A common radiographic study is an anteroposterior radiograph of the talocrural joint with inversion stress applied across the ankle complex. This study assesses the relationship between the talocrural joint mortise proximally and the dome of the talus distally. Talar tilt under radiographic study is operationally defined as the angle created by the intersection of the reference lines parallel to the articular surface of the tibial-fibular articulation and the proximal surface of the talus.

In the healthy ankle, the lateral ligaments of the ankle complex fully constrain the dome of the talus within the mortise, leading to a minimal talar tilt angle of less than 3° to 5° (see Figure 1). Breitenseher et al found that 1 in 3 patients with a talar tilt of 6° to

Figure 1. Stress inversion radiograph of the healthy ankle, demonstrating minimal talar tilt within the ankle mortise.
Although medical facilities currently use either the manual stress or the patient self-stress method when performing ankle stress exams, there is lack of consensus concerning the relative effectiveness of these 2 methods. A literature review found no studies directly comparing the findings of the 2 procedures. Therefore, the purpose of this study was to determine whether the patient self-stress method created a similar amount of talar tilt as the manual stress method.

**Methodology**

A convenience sample of 24 subjects, 12 men and 12 women, aged 18 to 46 years (22.4 ± 6.5) participated...
in this study. The use of subjects in this study received approval through the Committee for the Protection of Human Subjects at California State University, Fresno. Subjects were recruited from a patient population of the Student Health Center at California State University, Fresno. All patients presented with a primary complaint of acute or chronic ankle pain or injury to one ankle, for which an inversion injury was medically suspected and a talar tilt stress radiograph was medically indicated.

Following collection of demographic information, including mechanism of ankle injury and presence or absence of swelling (see Table 1), each subject underwent radiographic ankle stress exams. A manual stress talar tilt exam was performed on both ankles to allow comparison of findings between the involved and uninvolved ankles. Each subject in this study also underwent a self-stress exam of the involved ankle. To determine whether the order in which the 2 exams were performed influenced the results, the manual stress exam was performed before the self-stress exam for the first 12 subjects tested, and the order of the exams was reversed for the second half of the subjects in this study.

All manual stress exams were performed by a single radiologic technologist with 16 years of full-time practice in the radiology department of the Student Health Center of California State University, Fresno. An anteroposterior projection of the ankle was taken with the technologist holding the patient’s lower one-third of the leg in the anterior position with one hand, while the other hand created and held the inversion stress position through the midfoot (see Figure 4).

The patient self-stress method to create talar tilt was carried out as follows: The patient was positioned in an upright seated position with the leg to be radiographed in the frontal plane. A Kendall bandage (Covidien, Dublin, Ireland) was wrapped once around the midfoot, with the 2 equal ends of the bandage given to the patient to hold. Keeping the leg in the frontal position, the patient was instructed to pull on the inner strap as hard as he or she could tolerate to create inversion positioning stress at the ankle. The procedure was explained to each patient once before he or she was asked to perform it independently for the exposure, which used a 40 in source-to-image distance (see Figure 5).

All radiographs were obtained using a Trans-Continental radiographic high-frequency generator TM 40 unit (Trex Medical Corporation, Danbury, Connecticut). Cassettes used were rare earth detail screens with green sensitive film. The film processing system used was a Dupont 90-second processor (Dupont Imaging Systems, Bridgeport, Connecticut).

<table>
<thead>
<tr>
<th>Variable</th>
<th>n   (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recalled injury</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
</tr>
<tr>
<td>No</td>
<td>1</td>
</tr>
<tr>
<td><strong>Twisted</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19</td>
</tr>
<tr>
<td>No</td>
<td>5</td>
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<tr>
<td><strong>Fell</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>23</td>
</tr>
<tr>
<td><strong>Kicked</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>1</td>
</tr>
<tr>
<td>No</td>
<td>23</td>
</tr>
<tr>
<td><strong>Time since recalled injury</strong></td>
<td></td>
</tr>
<tr>
<td>Less than 1 week</td>
<td>15</td>
</tr>
<tr>
<td>One week to 1 month</td>
<td>1</td>
</tr>
<tr>
<td>More than 1 month</td>
<td>8</td>
</tr>
<tr>
<td><strong>Able to bear weight</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>23</td>
</tr>
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<td>No</td>
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<tr>
<td><strong>Swelling present</strong></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19</td>
</tr>
<tr>
<td>No</td>
<td>5</td>
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</tbody>
</table>

Figure 4. Talar tilt radiographs using the manual stress method.
Finally, a 2 x 2 repeated measures ANOVA determined whether there were significant differences in talar tilt values based on the type of talar tilt and the order of stress testing. This analysis was conducted to compare differences in talar tilt between self-stress and manual stress exam procedures, to determine whether any differences occurred depending on the order of the self-stress and manual stress exams, and to test for the interaction between the type of exams and the order in which they were administered.

Results
Seventy-nine percent of subjects recalled a specific twisting injury to their ankle, and 4% recalled a kick or a fall as causing their injury. Ninety-six percent were able to bear weight or walk into the x-ray exam room, and 79% presented with observed swelling (see Table 1). The talar tilt values across the sample between the self-stress and manual stress methods are presented

One radiologist used a standard goniometer to measure the angle of talar tilt on all radiographs. This was done by placing the goniometer on the ankle radiograph with the midline fulcrum point on the outer point of the medial malleolus at the level slightly above the talus bone on the distal end of the tibia. A first line was drawn tangential to the superior talar surface, and a second line was drawn tangential to the tibia articular surface. The intersection of these 2 lines documented the talar tilt present, measured in degrees (see Figure 6).

Talar tilt values were documented across the sample as collected under manual stress of the involved ankle, manual stress of the uninvolved ankle and self-stress of the involved ankle. A paired t-test was calculated to determine whether significant differences were present in the talar tilt generated between the manual and self-stress methods of the involved ankle. Two independent t-tests were conducted to examine differences in mean talar tilt values by sex and the presence of swelling.

![Figure 5. Talar tilt radiograph using the self-stress method.](image)

![Figure 6. Documentation of talar tilt in degrees, using goniometer.](image)
greater, and presumably more accurate, talar tilt values than did the alternative method of stress supplied by the patient. In the sample of 24 subjects used in this study, the magnitude of difference in talar tilt value under manual vs self-stress in the same patient was as great as 10°.

The design of this study did not directly attempt to determine why manual vs patient-created talar tilt stress should yield measures so dissimilar. Sex differences were not a factor, as the differences in values between the 2 groups were statistically significant and clinically meaningful.

Talar tilt values generated through the self-stress method are broken down by sex and presence of swelling in Table 3. Although the mean tilt of 3.0° generated across female subjects was more than double that generated in male subjects, this was not a statistically significant (P < .05) finding. The presence of swelling in the subject’s ankle had no effect on the talar tilt values generated by self-stress for men vs women, with mean values equal between the 2 groups.

Three research questions were addressed in Table 4. First, a statistical test of the order in which the 2 stress tests were administered was calculated. In half of the patients, the manual test was administered first followed by the self-test. In the other half of the patients, the self-test was administered first followed by the manual test. However, there was no significant order difference (F1,22 = 0.07, P = .79). The ANOVA test of type (manual vs self) duplicates the t test reported in Table 2, and therefore is also significant (F1,22 = 2.49, P < .01). The interaction of the combined effect of the test type (manual vs self) and the order in which the exams were administered was not significant (F1,22 = 0.23, P = .64).

### Discussion

The purpose of this study was to determine whether there was a significant difference in talar tilt between the manual stress exam and the patient self-stress exam. Results of this study found the manual stress method of performing ankle stress radiography yielded significantly

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Comparison of Talar Tilt Values for Manual Stress vs Self-stress (N = 24)</th>
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<tbody>
<tr>
<td></td>
<td>Mean</td>
</tr>
<tr>
<td>Self-stress</td>
<td>2.2</td>
</tr>
<tr>
<td>Manual stress</td>
<td>5.9</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Talar Tilt Values Generated Through Self-stress Method by Sex and Presence of Swelling (N = 24)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>12</td>
</tr>
<tr>
<td>Female</td>
<td>12</td>
</tr>
<tr>
<td>Swelling</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>19</td>
</tr>
<tr>
<td>No</td>
<td>5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Summary for Repeated Measures ANOVA of Talar Tilt by Stress Test and Order Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source</td>
<td>SS</td>
</tr>
<tr>
<td>Order</td>
<td>1.40</td>
</tr>
<tr>
<td>Error (order)</td>
<td>413.52</td>
</tr>
<tr>
<td>Type</td>
<td>169.93</td>
</tr>
<tr>
<td>Type by order</td>
<td>1.18</td>
</tr>
<tr>
<td>Error (type)</td>
<td>115.07</td>
</tr>
</tbody>
</table>

SS = self-stress method; MS = manual stress method.
conditions were not significantly different when findings were compared between male and female subjects.

One possible reason for the patient not creating positions of full ankle instability though the self-stress positioning method may be hesitation, consciously or subconsciously, to fully move the joint in this manner when inflamed or swollen. Indirectly, this hypothesis was not supported through the study’s findings, as there were no significant differences in mean values between subjects with edema compared to those with no swelling. Future studies documenting the magnitude of pain or discomfort present immediately before and after the 2 stress methods may clarify this concern.

Future studies would be beneficial to determine whether increasing the rigor of self-stress protocols may lead to similar results in talar tilt values between self-stress and manual stress protocols. Perhaps having the medical professional provide a greater focus in manually demonstrating to the patient the direction and magnitude of needed stress for the study, on the involved or uninvolved ankle as acuity allows, would lead to the self-stress exam more fully demonstrating the laxity. Another potential modification to the self-stress method may be to incorporate use of the movement strap positioned around the rear foot rather than midfoot, more directly promoting any abnormal talocrural motion.

Limitations of this study include a small sample size, as well as an inherent variability of subject presentations by severity and acuity, associated with any study sample collected from a clinical population. The purpose and design of this study did not consider results obtained when talar tilt stress was provided by mechanical methods, which have been recently refined and presented as viable alternatives in the literature. Protocols for the use of such devices rely on a predetermined, standardized amount of force to be administered across various subjects. In our study, manual handling, which incorporated the intuitive skill of the clinician in addressing reflexive responses of the patient, led to significant differences in the outcome of the test compared with the self-stress method. Similar manual handling influences also may substantially affect outcomes compared with those created by using manual devices to produce the inversion stress for an imaging study of an injured or unstable ankle.

The findings of this study suggest that if present, anatomic laxity of the ankle mortise is less likely to be identified when a self-stress protocol is routinely used in clinical practice. This practice could be associated with an unacceptable level of false negative findings in patients complaining of ankle sprains or instability. Falsely concluding that laxity is not present could contribute to inappropriate decisions regarding the need for surgery or rehabilitation for such a patient. This, in turn, could potentially contribute to chronic recurrence and instability.

**Conclusion**

This study suggests that for consistently optimal and accurate results, manual inversion stress by a trained professional should be used in talar tilt radiographic studies of the ankle. As described in this study, relying on the patient to determine and create adequate stress to the ankle during the radiographic examination of talar tilt may not create the needed movement or end range stress to document anatomic instability. Radiographic protocols used to determine anatomic laxity at the ankle for this study will need to consider and balance the desire for optimal and accurate documentation of suspected talar tilt laxity with the costs and with risks to the health care professional who provides manual stress during the examination.

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Managing a Mammography Center: A Model To Thrive

STEPHANIE JOHNSTON, MSRS, R.T.(R)(M)(BS)
JAMES JOHNSTON, PHD, R.T.(R)(CV)

Background
With the ever-increasing burdens of adhering to the Mammography Quality Standards Act (MQSA), it is important for mammography centers to use technology to work smarter and faster and capture as much revenue as possible. At the same time, patient satisfaction and employee satisfaction have a synergistic effect on the quality of patient care and the financial status of the clinic.

Method
This comprehensive literature review examines the effects of MQSA, technology and patient and employee satisfaction on the operations of a quality breast imaging center.

Results
A best practice model is offered that combines the best of these elements based on current literature.

Commonly, facilities struggle with volume and demand mismatches that lead to long delays in the patient care process. These challenges become obvious with long lines in the waiting room and delays in the emergency department or operating room.

Technological solutions offer improved communication and improved patient flow with a set cost and time frame for installation and training. Purchasing and installing new technology is a common approach to improving patient flow. The goals in upgrading to new technology are to reduce overcrowding, improve patient flow without losing quality care and increase physician and staff satisfaction.

Reimbursement, Coding and Costs
With today's economic environment, reimbursement and coding and the costs of running a breast center are more challenging. The possibility of costs exceeding reimbursements is a constant concern. Even with these concerns, breast imaging centers continue to provide high-quality, efficient services. Striving for greatness is a journey, not a destination, and reaching excellence should be ongoing and relentless.

Patient and Employee Satisfaction
Women's experiences and satisfaction with breast services are important factors influencing their attendance and participation in a clinic. Bairati et al showed that a patient care model that offers high levels
of consistency and continuity has a positive effect on patients’ well-being. They also reported that 64% of women have at least one impeding event during their breast care. Almost 66% of these women stated that a waiting list at the clinic was the biggest hindrance. This included both waiting for an available appointment and waiting at the time of the appointment. Lorden et al reported that patient satisfaction is very important and is a fundamental part of an organization’s mission and culture. In addition, employee satisfaction, though complex, has been positively correlated to patient satisfaction, and therefore goes hand in hand with it. Some studies indicated that high turnover among health care workers is aggravated by the emotional demands of the work itself. Peluchette and Karl stated that if employees are happy, patients will be happy too.

**Methods**

An electronic database search was conducted through Midwestern State University’s Moffett Library. EBSCOHOST provided access to the following databases: Academic Search Complete, Alt HealthWatch, Business Source Complete, CINAHL Plus, Computer Source, Consumer Health Complete, ERIC, Health Source – Consumer Edition, Health Source: Nursing/Academic Edition, Information Science & Technology Abstracts (ISTA), Legal Collections, MEDLINE, Military and Government Collection, Professional Development Collection, Psychology and Behavioral Sciences Collection, PsycINFO, Public Administration Abstracts, Regional Business News and EBSCO’s Science and Technology Collection. The Health & Wellness Resource Center database also was searched.

The key search terms used were “MQSA,” “technology,” “patient flow,” “health care,” “mammography,” “reimbursement,” “coding,” “costs,” “patient satisfaction,” “employee satisfaction” and “clinic.” From the MQSA literature, 3 subtopics were identified: the benefits of MQSA, the burdens of MQSA and the evolution of breast imaging. Based on the technology literature, 4 subtopics were identified: quality care issues, increased staff satisfaction, new technologies and the consequences of new technologies. Through the reimbursement literature collected, a definition of reimbursement and description of coding were identified. A brief history of reimbursement and some common mistakes made in coding also were identified, as well as a summary of breast center costs. Literature on satisfaction yielded a definition of patient satisfaction and employee satisfaction. Contributors to both patient and employee satisfaction were determined, as were the effects of patient and employee satisfaction on the clinic setting. The literature then was synthesized and is presented here as it relates to each of the identified subtopics.

**Effects of MQSA**

**Benefits of MQSA**

Before the MQSA was passed, mammography screening exams varied greatly from facility to facility. Radiation dose and image quality were quite different from site to site. Additionally, equipment was shoddy, physicians did not have proper training, and screening pioneers used terms like “horrible” and “desperately bad” to describe the state of mammography. Many improvements occurred in 1987, when the American College of Radiology introduced the Mammography Accreditation Program, but these efforts were voluntary and only supervised at the state level. MQSA provided a general framework for ensuring national quality standards in facilities performing mammography. Each facility must be accredited, certified and follow federal minimum standards. The accrediting bodies are responsible for reviewing equipment evaluations and quality control (QC) tests performed by the facility. They also are responsible for reviewing qualifications of mammography personnel, including the interpreting physicians, medical physicists and radiologic technologists.

Breast imagers agree that MQSA has greatly improved the quality of mammography. Screening mammography has been a major contributor to the 25% reduction in the breast cancer death rate in the United States. Birdwell and Wilcox indicated that the quality of mammography in the United States is better today than ever before. Quality mammography is still one of the most important weapons in the fight to decrease breast cancer deaths.

**Burdens of MQSA**

**Cost, Compliance and Time**

Cost, compliance and time are among the many burdens of MQSA, and the cost of maintaining compliance is of major concern. According to a 2007 issue of the Mammography Regulation and Reimbursement Report, the cost of an annual MQSA inspection was $1900 for the first unit and $250 per unit thereafter. The MQSA Regulations Quality Standards include an annual physicist survey, which has unknown fees attached. One estimate of the average annual cost of...
MANAGING A MAMMOGRAPHY CENTER

complying with MQSA is approximately $18,000,\(^1\) which equates to between $14 and $15.79 per mammogram.\(^1\,^1^4\)

Those actively involved in breast imaging do not need to be reminded of the burdens of MQSA compliance with regard to paperwork, cost, time and frustration.\(^1\)\(^3\) Complying with MQSA audit regulations and preparing for the inspection can drain time and resources from a facility’s staff and budget.\(^1\)\(^4\) In one study, staff in 46\% of facilities surveyed spent 0 to 4 hours preparing for an on-site inspection, 31\% spent 4.5 to 8 hours and 23\% spent 9 or more hours.\(^1\)\(^5\)

Paperwork, Personnel and Reimbursement

MQSA requires extensive records for QC tests, outcomes and personnel qualifications.\(^1\) QC testing protocols must be used and maintained by each accredited facility. These include equipment evaluation records and an annual physicist survey. Documentation of the daily, weekly, monthly, quarterly and semiannual QC tests must be retained for the inspection.\(^2\) Personnel qualified to perform these tests include an interpreting physician, radiologic technologist and medical physicist who have met initial educational requirements and continuing education requirements. Documentation of these requirements must be available at the time of the inspection;\(^1\) and maintaining these records takes countless hours.\(^1\)

Added to the demands of MQSA is the dwindling number of personnel in the breast imaging field. According to Dakins, 16.4\% of radiologists would withdraw from reading mammography, opting for the higher revenue and lower stress of other areas of radiology.\(^1\)\(^4\) Trends for radiologic technologists seem to be the same, with approximately 30\% of breast imaging practices reporting unfilled mammography positions and citing lack of qualified personnel as the main reason.\(^5\)

Reimbursement levels for mammography were not mandated to cover some of the costs incurred by MQSA.\(^1\) The profit margin is so low that mammography is a money loser in every radiology department.\(^1^4\) Increased reimbursement will need to be a key part of the solution in mammography or more low-volume facilities will be forced to close.\(^1^3\)

Sanctions and Litigation

The MQSA represents federal statutory standards and mammography facilities must comply to operate.\(^1\)\(^3\) There are 3 levels of noncompliance, with Level 1 representing the most serious and Level 3 considered only minor deviations.\(^1\) The Food and Drug Administration (FDA) may impose one or more of the following sanctions for noncompliance:

■ Directed plan of correction, which allows the facility to correct the violation.
■ Patient and physician notification, requiring the facility to inform both the physician and patients that the patient could be at risk for a negative effect on her health.
■ Follow-up inspection.
■ Certificate revocation or suspension.\(^2\)

In addition, civil penalties up to $10,000 per exam or per violation per day may be applied to a facility performing mammography without proper certification or for other violations.\(^2\)\(^7\)

MQSA shifts the burden of proof from the plaintiff to prove that a standard of care was not met to the radiologist, mammography facility or both to prove that the standards were met.\(^1^5\) Dakins stated that only 5\% of new radiology residents would like to spend any substantial amount of time interpreting mammograms, citing fear of lawsuits as the leading reason.\(^1^4\) Delays in diagnosing breast cancer lead to more malpractice claims than any other medical condition, and are second only to neurological impairment of newborns in terms of claims paid.\(^2\)

Evolution of Breast Imaging

Digital mammography has been incorporated into the existing standards, but quality of digital mammograms varies widely because the quality assurance (QA) program is determined by the image receptor manufacturer.\(^1\) Dakins stated that the standards that exist reflect manufacturer recommendations and inspectors only check to see that a facility is following these recommendations.\(^1^4\) In July 2006, a Fuji computed radiography (CR) mammography system was approved for use by the FDA, further complicating the digital regulations.\(^1^7\) The Mammography Regulations and Reimbursement Report stated that the FDA will regulate CR mammography in the same manner as full-field digital systems.\(^5\)

There are currently no standards mandated for image-guided breast biopsies or other breast imaging modalities such as ultrasound or magnetic resonance (MR) imaging.\(^1\)\(^8\) Breast imaging has gone beyond the standard 2-view mammogram that was common when MQSA was introduced. Currently, stereotactic biopsies, MR and ultrasound are used routinely in breast imaging, but the quality and accuracy of these techniques vary greatly.\(^1^4\) It has been suggested that
the MQSA be renamed the Breast Imaging Quality Standards Act (BIQSA). Regulations for all of breast imaging should be included in MQSA and all breast imaging should be performed by individuals who have appropriate training and qualifications, who maintain high standards of care, and who participate in continuing quality review. Accomplishing this could be the start of a new direction that provides universal consistency in breast imaging. Although there is no standardized QA for other breast imaging modalities, some voluntary accreditation programs guide breast ultrasound practice, stereotactic breast biopsies and general MR imaging and could be the basis for national standards. The positive side of agreeing to more regulations is that patients will receive the highest quality breast imaging.

The Table presents a best practices model, listing several elements and recommendations a breast center can implement. The first 3 elements correspond to MQSA requirements. A center that adheres to MQSA can be assured that it is abiding by the regulations and performing quality patient exams.

**Effects of Technology**

*Quality Care Issues*

The goal of patient care is to perform procedures promptly, with good quality care provided to the patient. Over time, patient flow problems may become the norm for an organization and could lead to the loss of its key employees. The facility may suffer a reduction in referrals and ultimately develop a reputation in the community for poor patient service or quality of care. Often, a decision about patient flow may be made in response to physicians’ needs and usually has nothing to do with the quality of care. Bottlenecks in patient flow usually lead to the same results: waiting room delays, strained relationships with employees and inefficient use of resources in the organization.

Technological advances eliminate the need for paper or board systems previously used for tracking patients. Technologic systems are more sensible in terms of clinical practice and workflow and they eliminate the need for paper-based systems. Moving to a paperless environment can help improve efficiency. Although the features of such systems vary from one manufacturer to the next, there are a few common features to look for. First is a system for electronic scheduling and billing. These systems can streamline and connect these elements of a practice. Second is a mammography information system. This system can stand alone or tie to other electronic systems of the center, such as a radiology information system or health information system. This system tracks all patient exams and provides reports, follow-up letters and result letters. It is particularly desirable for the 2 broad categories of systems to “talk” to each other and be integrated. This greatly reduces duplication of data entry and opportunities for human error, streamlining overall workflow.

Another positive aspect of any technological system is the ability to generate reports. Continuous QC reports can be generated from most programs and should become part of the standard operating procedures for mammography providers striving for better patient care.

*Increased Staff Satisfaction*

Stresses and struggles with patients and personnel interactions can cause staff dissatisfaction. The primary cause of staff turnover is dissatisfaction and the second is workload or staffing issues. Staff satisfaction could increase with improved communication, improved morale and the sense of accomplishment that can occur after implementation of a good patient flow system and other technological advances. Patient flow systems give staff members a sense of accomplishment because they can easily see their workflow improve. Staff members are better equipped to handle delays and know where they can make adjustments.

Before their technological upgrade, staff members at the Hospital of the University of Pennsylvania in Philadelphia would take 20 to 30 minutes to schedule a patient using the phone or fax or walking around trying to locate a physician. After the patient flow management system was installed, adjustments to the schedule could be made in minutes and every department was alerted to the change.

*New Technologies*

Some patient flow systems are role-based, which means a user may log in as a nurse, technologist, physician or entry clerk. However, these individuals can only access the part of the chart that is significant to them, and make changes or add notes regarding their interactions with the patient. Wireless local area networks (WLANs) may be another consideration. They can hold small data files such as patient demographics and electrocardiogram (ECG) data. WLANs are very attractive because there are no power cables, installation is easy and the technology is affordable.
## Table

### Best Practices Model

<table>
<thead>
<tr>
<th>Element</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>MQSA general requirements</td>
<td>Abiding by personnel requirements, equipment evaluation and quality control (QC) tests will guarantee that a clinic operates properly without sanctions or risk of closure.</td>
</tr>
<tr>
<td>Costs of compliance with MQSA</td>
<td>Minimize costs by efficiently performing all requirements in a timely manner and being prepared for inspection. Comply with MQSA standards for accreditation and certification.</td>
</tr>
<tr>
<td>Paperwork and personnel demands of MQSA</td>
<td>QC tests and paperwork must be completed at the required intervals to ensure accuracy and completeness. Ensure that personnel meet all federal requirements.</td>
</tr>
<tr>
<td>Other breast imaging modalities</td>
<td>Other breast imaging procedures should be completed by appropriately trained individuals on equipment that is in good working condition with continuous quality review. This will increase the likelihood of quality imaging and reduce costs.</td>
</tr>
<tr>
<td>Technology related to patient care</td>
<td>Use technological advances to improve efficiency and patient care while reducing errors. Implement a system that continually tracks and reports quality assurance as standard operating procedures. The use of technology may eliminate the need for paper and/or manual tracking.</td>
</tr>
<tr>
<td>Technology related to staff satisfaction</td>
<td>A patient flow system can keep employees up to date on the flow of the clinic and allows them to easily make adjustments. The use of scanners, laptops and compatible systems decreases stress, confusion and discontent of staff.</td>
</tr>
<tr>
<td>Implementing new technology</td>
<td>Ensure that all personnel, including the physician, are introduced, completely trained and understand any new technology adopted by the center.</td>
</tr>
<tr>
<td>Reimbursement</td>
<td>Proper coding and capturing all eligible reimbursement is a must in the clinic. Ensure that billing personnel have the training, knowledge and necessary tools.</td>
</tr>
<tr>
<td>Costs</td>
<td>Most clinic costs will be fixed; increasing the volume of exams will lower the costs per procedure. Ensuring that procedures are performed efficiently and with the best use of FTEs is crucial. Optimum use of personnel becomes important.</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>Work to make the patient’s experience efficient, professional and positive. Polite reception, short wait times and easy access create excellent first impressions. Up-to-date equipment and technology are a must. Well-trained staff, up-to-date equipment and timely results will contribute to return visits. Remove as many barriers as possible to increase patient satisfaction. In particular, use automated electronic information systems to reduce delays and wait times for results. Pay attention to the physical environment and make it “cozy” and comfortable. Be sure that staff is well trained on the equipment used and communicates well with patients.</td>
</tr>
<tr>
<td>Employee satisfaction</td>
<td>Pay attention to employee satisfaction. A positive and organized workplace with the proper tools empowers employees, resulting in their best performance. Support from leaders, recognition of good performance and respect are far more attractive than monetary rewards. Open communication allows all employees to participate in change and voice concerns. Provide high-quality training and a good support system. Strive to remove causes of failure and assist employees in doing their jobs well. Find ways to help employees reduce stress in the workplace such as use of humor and fun. Work to foster a bond between the employee and the organization by giving the employee some autonomy in decision making, showing respect and providing support, establishing employee recognition programs and providing a family atmosphere. Finally, monitor turnover rate of employees and if it becomes excessive, work to identify and correct the root cause(s).</td>
</tr>
<tr>
<td>Interactions of patient and employee satisfaction</td>
<td>Patient and employee satisfaction influence each other. A cohesive team is a must in a clinic where there are few employees multitasking and providing quality patient care. Keeping turnover down and constantly improving quality are crucial.</td>
</tr>
</tbody>
</table>

MQSA = Mammography Quality Standards Act; FTEs = full-time equivalents.
Another positive side to the WLAN is the ability to use cell phones for internal communication in facilities. Cell phones are less disruptive than overhead pages or speakers.

Adding new technology changes old habits and saves on operating costs. Clinical information systems can eliminate the use of all forms of paper records. Paper files can limit the clinic workflow, and breast imaging centers cannot achieve full efficiency until they completely eliminate the physical files.

**Consequence of New Technologies**

The ultimate acceptance or rejection of any new technology depends on the level of use by staff. Inadequate training for new technologies is a primary concern of staff members. Failure to sufficiently prepare staff for new systems and inadequate leadership also may be problems. Mammography staff members do not want to look unqualified or unprepared to the patient. It is important to have strong leadership in the director or manager and involve all users, including physicians, in every stage of developing and implementing new processes. Dissatisfied staff may revert to using the old manual or paper-based system that was supposed to be replaced. This could result in expensive new technology being used inconsistently, inaccurately, or not at all.

The Table has 3 elements and recommendations regarding technology, as it relates to patients and staff. In today’s more advanced environment, most staff welcome the use of technology and patients favor the efficiency of a center that takes advantage of technology.

**Reimbursement and Costs**

Reimbursement does not equal revenue. It represents the payment that is received for a procedure and is set by contract, regulation or both. Reimbursement for mammography is based on the facility location or site of service. Physician offices or nonfacility settings are considered different from hospital-owned facilities. Reimbursement for mammography exams in these settings is less than 80% of the Medicare physicians’ fee schedule (MPFS). Mammography and other breast imaging exams are highly valued by women, but less valued by payers. The current reimbursement guidelines are not in line with the public’s expectations of mammography or other breast imaging procedures.

**Coding**

Current procedural terminology (CPT) codes were first used in 1966 to create a more uniform and precise way to identify physician services. Information from medical records and procedural notes could be applied to detailed billing information for the payers using CPT codes. Coders must apply the most exact match when assigning a CPT code to an exam. The International Classification of Diseases, Clinical Modification (ICD-CM) assists providers with accurately defining a disease process and is the basis of the rationale for ordering an exam. ICD-CM codes are used to determine the appropriateness of an exam. Health care common procedure and coding system (HCPCS) codes are used to identify professional services, procedures and supplies for reimbursement. Most payers require these codes to report medical services and supplies. Evaluation and management (E/M) CPT codes are used for problem-oriented visits. Although there are many rules and guidelines for the use of E/M CPT codes, breast imaging facilities may use these to bill for E/M during certain diagnostic or biopsy procedures.

**Mistakes**

Some mistakes in coding include up-coding, incorrectly billing the technical and professional component and billing for services not provided. Up-coding is billing for an exam that is more complex than the one performed or that has a higher reimbursement value. If a mammogram is performed on one day and dictated on another or the technical component and professional component are delivered in different locations, payers will look upon those bills with suspicion. Deliberately billing for services not provided, such as patient no-shows, is a more obvious error.

**History**

In 1990, the Omnibus Budget Reconciliation Act established coverage for mammography services for Medicare-eligible women. In 1992, physicians and outpatient facilities began to receive reimbursement under the Medicare physician fee schedule. Instead of the previous fee schedule of “usual, customary, and reasonable” fees, payment for services relied on the resource-based relative value system (RBRVS). This system is based on the resources needed to provide a service and is divided into 3 components: practice expenses, physician work and professional liability insurance costs. A complex numerical value is assigned to each component and the
resulting value is called a resource value unit (RVU). The costs associated with screening or diagnostic mammograms exceed the Medicare and other insurers’ reimbursement rates.

Costs

Costs in mammography are fairly fixed. The costs for a facility and the equipment are stationary, unless a new piece of equipment is purchased, and the costs for staff do not vary much. The costs associated with volume vary, however, with increased volume lowering the cost per procedure. Unfortunately, increased numbers of screening mammograms mean increased diagnostic mammograms and follow-up breast procedures. Screening mammography could be profitable; however, the subsequent diagnostic mammograms and other breast-related exams are not cost effective. Reimbursement for these exams does not cover costs. The problem of mammography costs outweighing reimbursement began in the 1980s and became a barrier for patients who need screening mammography.

Improvements

Mammography does not attract the staff needed to meet the demand. To most outside of radiology, the belief is that mammography is a profitable and easy exam to perform. In reality it is highly specialized and time consuming. Mammography practice is complicated further by federal regulation through MQSA, litigation threats and low reimbursement.

Reimbursement and cost are fairly straightforward. The best practice model presented in the Table outlines the important factors relating to reimbursement, coding and costs. This aspect of a center relies heavily on the expertise of personnel who can accurately code and collect the maximum reimbursement and who continually work to minimize costs.

Patient and Employee Satisfaction

Patient Satisfaction

A patient’s satisfaction depends on his or her experience at the clinic. Patients describe quality service as efficient, flexible and punctual. Behavior, professionalism and the interpersonal skills of the staff are included in that perception of quality service. Being greeted at the front desk by friendly, courteous staff is very important, especially to the first-time patient, and politeness and proper communication with all staff are very important to patients. An excellent relationship between personnel and patients is a quality care indicator in patient satisfaction. Patients expect a helpful and skilled staff in a breast clinic.

Patients expect quick, efficient service in today’s fast-paced society, but many experience long wait times for their appointments. These long wait times for scheduled appointments must be addressed. Additionally, processes within the clinic should flow efficiently so patients can be taken care of quickly and at their appointed time.

Many breast clinic patients today expect results promptly, even on the same day, if possible. If results are not communicated promptly, patients may become anxious and upset, especially if results are inconclusive or positive. Rust reported that 24.6 days was the average time for receiving results and some patients found it to be a 3 to 6 week ordeal. Timely reporting is a quality indicator of patient satisfaction because the discovery of an abnormality can be extremely traumatic for the patient.

Many delays can be reduced and patient care and satisfaction improved by using automated information systems. The information system can be used for patient result letters, reminder letters and, most importantly, to encourage follow-up. Improving the consistency of information transfer eliminates gaps in service delivery. The reminder letter or invitation letter function of these systems should be used to prompt women to come to the clinic for screening.

Contributors to Patient Satisfaction

There are several contributors to patient satisfaction. The physical environment of the clinic is one. Women prefer an easily accessible clinic that is “cozy” and “personal.” This helps alleviate anxiety and embarrassment associated with the exam. Women appreciate the privacy and accessibility of a clinic compared with a hospital setting that is large and not as easily accessible. Another contributor to the physical environment is up-to-date technology. Patients expect a facility to have the latest equipment and technology. They also expect well-trained and competent personnel to perform their exam, reducing pain and uneasiness. Trained staff also reduce the need to call patients back for suboptimal exams. A detailed explanation of the exam and what will transpire decreases anxiety and allows the patient to interact with the technologist before, during and after the exam. Therefore, the physical environment and technical quality are important components of patient satisfaction.

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In one study, slightly less than half of the patients believed they were not given enough information.\textsuperscript{26} Another study reported that many women indicated information about breast self-examinations, the screening process, or what to expect if called back could be emphasized more during the admission process.\textsuperscript{8}

Some barriers that decrease patient satisfaction are excessive distance to the center, lack of signs and parking, perceived lack of privacy and lack of competent staff.\textsuperscript{7} Most patients consider the seamless process of having multidisciplinary care all in the same clinic a high-quality characteristic and very appealing.\textsuperscript{27} Most dislike having to travel to a regional hospital or another facility for these services.\textsuperscript{8} Trust in the clinic staff and the multidisciplinary approach assure patients that their needs will be met and that they will receive quality care.\textsuperscript{27}

Effects of Patient Satisfaction on the Clinic

Patient dissatisfaction can have serious effects on a clinic, affecting its standing in the community. Satisfied patients are more likely to return to the clinic and continue their relationship with that provider.\textsuperscript{8} They are also more likely to tell friends and family to use the facility if the experience was positive, vs dissuading them if the experience was substandard.\textsuperscript{8} An inefficient and disorganized clinic can cause gaps in quality of care and patient follow-up, disappointing patients and prompting them to seek care elsewhere.\textsuperscript{8} Loss of market share and revenue adversely affect the clinic, and the dissatisfied patient may negatively influence the facility’s reputation.\textsuperscript{27} Lack of access due to waiting weeks or months for a scheduled appointment or waiting at the clinic on the day of the appointment also could cause a patient to go elsewhere for care or, worse, elect not to receive care.\textsuperscript{9} A closer partnership between the patient and the provider may be fostered if patient dissatisfaction is identified and considered. Satisfied patients will return to the clinic.\textsuperscript{26}

Employee Satisfaction

Employee satisfaction is more complex and can be defined several ways. Lorden et al reported that employee satisfaction includes employee workload, perception of the work environment and empowerment.\textsuperscript{10} Employees are not fond of being overworked and underappreciated. Good job performance requires the right tools. Having the necessary materials and technology and the opportunity to do one’s best work are underlying factors for employee satisfaction.\textsuperscript{10}

Recognition for work completed, respect from others and supervisor support are other reasons to stay in a job.\textsuperscript{29} Additionally, recognition by peers, attention and sincere appreciation for doing a job well are underlying factors.\textsuperscript{29}

The work environment is critical in determining employee satisfaction.\textsuperscript{10,29} Lorden et al indicated that high-quality training and a good support system from supervisors allow employees to meet the customers’ needs.\textsuperscript{10} This level of involvement and participation between the supervisors and employees is significant to the employees. Micromanagement by supervisors, on the other hand, creates distrust and uneasiness among employees. Conversely, allowing them some freedom within their job description is seen as more supportive.\textsuperscript{10} The leaders of an organization should strive to remove causes of failure and help employees do their jobs well and as efficiently as possible. Appropriate rewards and recognition can assist in satisfying employees.\textsuperscript{30}

Emotionally demanding work can intensify situations at work.\textsuperscript{11} Stress can be one reason why employees are repeatedly absent from work or leave an organization altogether.\textsuperscript{12} However, the use of humor has been reported to be an effective coping strategy for handling work-related stress and has positive implications for employee satisfaction.\textsuperscript{12}

Contributors to Employee Satisfaction

Commitment to the organization is an important contributor to the employee’s satisfaction. The bond formed between an employee and an organization is commitment. The findings by Humphreys et al indicated that employees with high organizational commitment are most likely to satisfy patients.\textsuperscript{11} In turn, the organization’s commitment to employees can be seen directly in employee satisfaction and indirectly in employee loyalty to the organization.\textsuperscript{29}

Operational success is an important contributor to employee success.\textsuperscript{30} An organization that is continually improving and increasing profits appeals to the employee in the customer service role. Increased profits usually translate to increased salaries or bonuses for employees. However, respect, support from coworkers and supervisors and a family atmosphere satisfy employees far more than money.\textsuperscript{29}

Communication also contributes to employee satisfaction. The cycle of communication from employees to leadership and back again is critical in any organization.\textsuperscript{31} The cycle involves 2-way communication,
MANAGING A MAMMOGRAPHY CENTER

problem solving, action, measurement and reward and recognition. Shockey stated that involving the employee in this cycle allows him or her to communicate openly with leaders and take part in solving the organization’s problems.31

Fun in the workplace may play an important role in employee satisfaction. According to Peluchette and Karl, introducing fun in the health care setting has gained attention for improving employee satisfaction.12 They reported the top 3 fun activities were casual dress days, employee recognition and rewards and company-provided food. These activities allow employees to break away from daily routines and provide more interaction with other employees and supervisors. However, they need to be appropriate to the work environment so as not to be perceived negatively by patients.12

Effects of Employee Satisfaction on the Clinic

Benefits of employee satisfaction are high productivity, lower turnover, loyalty and overall competitiveness.30 The most visible sign of employee dissatisfaction is employee turnover.30 Excessive turnover is a serious challenge to the efficiency and effectiveness of an organization and low employee satisfaction can have a great impact on patient satisfaction.11 Employee turnover has more than twice the impact of the next largest variable, poor work environment, on patient satisfaction.29 This impact on patient satisfaction can erode the physician/patient relationship and the physician/clinic relationship, which can affect the business. The interactions between an employee and customer can potentially make or break the relationship.30

Employee satisfaction can positively affect an organization. Employees want to be recognized for the skills they bring to a job and for the contributions they make to the organization. Professionals want respect, appreciation and opportunities for intrinsic rewards.29 Satisfied employees ensure quality patient care, which increases profits and referrals to the organization.29

Health care organizations may consider interjecting fun in the workplace as an approach to make the work environment better. Peluchette and Karl’s claim that employees who have fun with their jobs are more energized, more motivated, get along better and provide better service means that breast center managers should consider introducing fun activities. Conducting activities that focus on food or contests can be highly successful and practical in the health care setting without being disruptive. Organizations should set some boundaries for fun activities and select only activities that will not interfere with patient care or disrupt the clinic, such as supervisor-sponsored lunches, potluck meals or casual dress on Fridays to avoid perceptions from some employees that fun activities are nonproductive.22

Management of Patient and Employee Satisfaction

Patient satisfaction and employee satisfaction are unquestionably interrelated. Patient satisfaction may be influenced by efficiency of care, communication with health care professionals, or the state of the facility.10 A cohesive team can provide exceptional patient service and quality care.27 Recruitment and training of high-quality staff with good interpersonal skills are essential to a clinic and some of the most important contributors to patient satisfaction.26 The quality of the employee determines the quality of the service given to the patient and ultimately the success of the clinic.30 Developing a program to recognize employees who go beyond expectations and show an extraordinary level of caring and compassion to patients can increase employee satisfaction.27 Recognition by peers, and especially by supervisors, is an important factor in employee satisfaction.29,31 Consistency, continuity and collaboration all can be used to increase satisfaction, both for patients and employees.28 Quality practice standards should be developed and consistently followed by employees to provide the best patient care. Collaboration with referring physicians and specialists, and within the clinic team will increase the quality of patient care.28

The last 3 elements and recommendations in the Table correspond to patient and employee satisfaction. An understanding that each contributes to the other will create a center with a positive, efficient environment that provides quality patient care.

Conclusion

The MQSA has laid a stable foundation for the regulation of quality mammography exams. Although the costs of compliance are high and reimbursements are low, the decrease in death rates from breast cancer indicates that facilities are following the regulations and are providing quality patient care. Now that digital mammography, both full field and computed radiography, is more mainstream, additional detailed modifications to MQSA must include this technology and the inspectors must have knowledge and training on how to inspect these units. Changing the legislation’s name from MQSA to Breast Imaging Quality Standards Act
The introduction of technology to improve patient flow is a positive advancement. However, it must be implemented correctly. Staff and physicians must be involved in the planning and implementation of the system for it to be successful, effective and efficient. As stated by Sharrock, an effective clinic should run just like an efficient factory, getting the right part in the right place at the right time. Managers must organize their operation so that the patient spends less time at the facility and the physician’s time is maximized. It is important to get the right people in the right place and with the right equipment. When it comes to healthcare technology, every second saved is crucial to the patient and the physician. Up-to-date technology allows a good manager to save time and cut costs without sacrificing quality patient care.

Because the costs for operating a breast center are relatively fixed, increasing patient volume is key to lowering the cost per procedure. It is imperative that a center employ personnel who can properly code and collect as much reimbursement as possible for the procedures provided. Avoiding mistakes and capturing the most from every exam help ensure the clinic’s success. 

Patient satisfaction depends greatly on the aesthetics of the clinic and the patient’s interactions with the staff. Today’s women are more educated and judge the quality of their care by 3 components: efficient processes, pleasant environment and advanced technology. With their busy lifestyles, patients want fast, friendly service in a multidisciplinary facility. Any indication that staff is incompetent or unqualified to complete duties gives rise to dissatisfaction. Patients expect all the latest technological advances. Up-to-date equipment and information systems allow the movement of patients through the clinic with an effortless flow. A standardized set of QA guidelines should be established and enforced to ensure that proper procedures and patient care standards are followed.

Similarly, employee training and support guidelines ensure that an employee is taught to do a job properly and rewarded for doing it well. An employee’s dedication and commitment to an organization can reduce turnover and maintain high-quality patient care. Recognition for a job well done by peers and supervisors does not go unnoticed by the employee. Most employees would rather have the recognition than a raise. This in turn will increase retention, and employee retention and customer satisfaction are directly related.

Communication is a key issue with employees. Their input into an organization gives them ownership. Supervisors who practice listening to employees will have greater success with them. Adding some fun into the workplace also could contribute to employee satisfaction. Most fun activities are usually not disruptive to patient care. According to Peluchette and Karl, fun in the workplace can have positive effects on the employees, but sometimes may be perceived negatively.

Both patient and employee satisfaction involve aspects of the other. Patients are dissatisfied with impolite, inefficient staff and employees are not happy with demanding, rude patients. A vicious cycle can send an organization into a tailspin. A solid group of employees who are well trained and patient oriented is a must for a clinic to remain competitive. The financial impact of employee satisfaction and turnover becomes apparent when patients choose to go elsewhere for care. The clinic may receive poor publicity or develop a negative reputation in the community. People are the No. 1 asset in health care. Employees, patients and the organization should align to support that concept.

Based on the literature reviewed, the Table was created as a best practice model that incorporates critical elements for running a quality breast center. A perfect center would employ all the best practices in the model. However, most centers may be able to follow only some of the elements suggested. Determining what works best in a particular center’s environment is a task for the center leaders. It is up to them to establish the best practices for that center.

Call for Future Research

Although many studies were reviewed that examined some of the aspects of a quality breast center, research is needed that focuses on the synergistic effects of MQSA, technology, reimbursement and costs, and patient and employee satisfaction as the 4 major areas that create a quality center.

References

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Tuberculosis: A Review and Update

BRYANT FURLOW, BA

After completing this article, readers should be able to:

■ Describe trends and patterns in TB infection rates.
■ Evaluate the risk TB represents to health care workers.
■ Distinguish between latent and active TB, and pulmonary vs disseminated disease.
■ Explain how TB is diagnosed.
■ Discuss the challenges that hamper efforts to control and eradicate TB worldwide.
■ Outline treatment regimens for TB.
■ Compare and contrast the strengths and weaknesses of different imaging modalities in detecting and evaluating different types of TB.
■ Summarize new developments in TB detection and screening.

More than 2 billion people worldwide are infected with Mycobacterium tuberculosis, the bacterium that causes tuberculosis (TB). Nine million more are infected each year. Although extensively drug-resistant TB strains are very rare in the U.S., these strains represent a major emerging global public health challenge and likely will become more common in the U.S. in coming years. Diagnostic imaging plays an integral role in TB diagnosis, screening and control efforts, but the risk of occupational infection among radiologic technologists is unclear. This article discusses TB epidemiology, diagnosis, prevention, screening and treatment, as well as the role of diagnostic imaging.

This article is a Directed Reading. Your access to Directed Reading quizzes for continuing education credit is determined by your area of interest. For access to other quizzes, go to www.asrt.org/store.

in the 1980s that coincided with the emergence of the global HIV/AIDS epidemic. Three decades later, the TB epidemic remains “embedded” in the HIV/AIDS crisis, complicating TB diagnosis and treatment.3 TB and HIV coinfection hastens the progression of both diseases, and some anti-TB drugs can interfere with HIV/AIDS drug treatments.5

Worldwide, between 20% and 70% of new active TB cases occur among HIV-positive individuals, reflecting overlapping risk factors for the diseases as well as the increased susceptibility of HIV-positive people to TB.2,4

The United Nations’ Millennium Development Plan lists as one of its goals halting or reversing the resurgence of TB by 2015.5 The number of new cases per capita globally declined between 2003 and 2007, leading public health officials to anticipate meeting that goal.2 However, in the face of global economic challenges, donor nations started to slash funding in 2009 for future years’ global anti-TB, anti-HIV/AIDS and antimalaria efforts. These cuts occurred just as the National Academy of Sciences and the U.S. Institute of Medicine (IOM) released a report urging increased U.S. government investments in global health.5,6

Active TB cases in the U.S. are demographically concentrated among young adults and ethnic minorities and are geographically concentrated in California, New York and southern states.7 Approximately 5% of U.S. HIV/AIDS patients have active TB.7 The U.S. Centers for Disease Control and Prevention (CDC) reported 13 779 new cases of tuberculosis in the U.S. for 2006 and 13 299 new cases in 2007, the most recent year for which infection rate data are available.7 The U.S. had 644 TB deaths in 2006, the most recent year for which complete mortality data are available.8

Overall U.S. infection rates have declined steadily since 1992, when the resurgence peaked. However, the rate of decline has slowed markedly during that time, and recent reductions in funding for global TB efforts have raised concerns that recent gains may be lost.9 Because most new TB cases in the U.S. occur among foreign-born individuals, global infection rate trends are likely to influence U.S. rates as well.

Diagnostic chest radiography is a central component of TB diagnosis and screening.9 Chest radiographs, skin and blood tests and microscopic exams of sputum (coughed-up mucus) cultures are the mainstays of TB diagnosis, but imaging advances are expanding the roles of computed tomography (CT) and magnetic resonance (MR) imaging in TB medicine.

Box 1 presents a glossary of common abbreviations used in TB medicine.

**History**

TB is an ancient disease that has afflicted humans since at least the Neolithic period, some 9000 years ago.10 Based on fossil bone evidence, some archeologists controversially contend that TB plagued even our prehuman ancestors, Homo erectus.11

Until recently, it was believed that human strains of M. tuberculosis originally were acquired from cattle, which can transmit the disease to humans. But recent genetic research shows that human TB strains did not evolve directly from bovine TB, and instead suggests that the reverse may have been the case: Cattle probably acquired TB from people.12-15 DNA sequences from the M. tuberculosis in the remains of a woman and child who died 9000 years ago, prior to animal domestication, reveal that the strains infecting many humans today are genetically more similar to ancient human strains than M. bovis.10 Genetic analyses indicate that TB emerged at least 40 000 years ago in Africa, and that the strains of TB infecting cattle today evolved from human strains.13

The Arab physician Ibn Sina first described pulmonary tuberculosis as a contagious respiratory disease and devised patient quarantine for TB control.14 Before the widespread dissemination of the germ theory of disease, TB sometimes was attributed in England and its North American colonies to witches or vampires, possibly because TB victims frequently exhibit light sensitivity, red eyes, pale skin and cool body temperatures, and cough up blood.15

The various types of TB were recognized as variants of a single disease during the early 1800s, when the disease was commonly known as “consumption” or “the White Plague.” Sanitariums were first established to treat patients in the 1850s.9

Physician Robert Koch first described M. tuberculosis as the cause of TB in 1882, for which he received the 1905 Nobel Prize in Medicine. However, evidence-based treatment was lacking well into the 20th century, leading playwright George Bernard Shaw to write in The Doctor’s Dilemma that the practice of medicine in 1903 was “a huge commercial system of quackery and poison.”16

Radiography played a growing role in the diagnosis of TB throughout the 1920s and 1930s, and was used in screening programs to identify individuals for isolation.
Leading risks for TB infection include silicosis, hemodialysis for chronic renal failure, diabetes, organ transplantation, cancer radiation therapy or chemotherapy and the interlinked socio-demographic factors of male sex, poverty, HIV-positive status, homelessness and prior imprisonment.\textsuperscript{21,22} Poverty drives the spread of TB through poor hygiene, overcrowded living conditions, poor home ventilation, significant delays in diagnosis and subsequent diagnosis at later disease stages, malnutrition and HIV/AIDS coinfection. Most of the global TB morbidity (95%) and mortality (98%) occur in developing countries where diagnostic and treatment tools considered standard in wealthy countries are largely unavailable.\textsuperscript{23}

The pace of development of new drugs for TB treatment has been surprisingly slow, considering the disease’s deadly global toll. However, because TB disproportionately affects the poor, there has been little economic incentive for private-sector development of new anti-TB drugs.\textsuperscript{24}

\begin{center}
\textbf{Infection Rates and Trends}
\end{center}

Global epicenters of TB, including multidrug-resistant TB (MDRTB) and extensively drug-resistant TB (XDRTB), are in Africa and eastern Europe, where annual infection incidence rates exceed 300 new cases per 100 000 population.\textsuperscript{9} Within the U.S. and Canada, infection incidence rates range from < 1 case per 100 000 to 24 cases per 100 000 population; the nationwide prevalence of TB in the U.S. is 10 per 100 000.\textsuperscript{8,9} (Incidence rates represent the number of new cases per year. Prevalence rates represent the total number of cases in a population at any given time.)

In the U.S., TB case loads today are concentrated in California, New York, Washington, D.C. and the south.\textsuperscript{8} Just 4 states — California, Texas, New York and Florida — accounted for nearly half (48\%) of new U.S. TB cases in 2007.\textsuperscript{8} TB incidence in the U.S. is concentrated among young adults, peaking among those aged 25 to 44 years.\textsuperscript{7,8} American men have a significantly higher TB infection rate than women (5.5 vs 3.4 per 100 000 population).\textsuperscript{8}

There are dramatic differences in TB infection rates between U.S. racial and ethnic groups. Asian Americans have the highest annual TB new-case rate: 26.3 cases per 100 000 population, a slight increase from 25.9 in 2006.\textsuperscript{8} Native Hawaiians and other Pacific Islanders had the second-highest TB case rate for 2007, at 25 cases per 100 000 — an as-yet-unexplained jump from 13.4 cases per 100 000 in 2006.\textsuperscript{7} The instability in

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\begin{table}[h]
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\begin{tabular}{|l|l|l|l|l|l|}
\hline
\textbf{Glossary of Tuberculosis Abbreviations} & BCG & CDC & DOT & DOTS & IGRA & XDRTB \\
\hline
The Bacille Calmette Guerin vaccine against TB. & U.S. Centers for Disease Control and Prevention, located in Atlanta, Georgia. The CDC spearheads U.S. anti-TB efforts and has authority to impose interstate and international isolation and quarantine orders to prevent the spread of TB. & Directly observed therapy. The U.S. standard for supervised antibiotic therapy. & Directly observed therapy, short course. A strategy for HIV/TB coinfected patient therapy. & Interferon gamma release assay; an in-vitro assay of host T-cell function used as an alternative to tuberculin skin testing to determine TB infection. & Extensively drug-resistant TB. \\
\hline
WHO & World Health Organization. & & & & \\
\hline
\end{tabular}
\caption{Box 1}
\end{table}
rates for Pacific Islanders may not be surprising in light of their small populations; only 73 U.S. cases in 2007 were among Pacific Islanders.\(^8\) White non-Hispanic U.S. residents are far less affected, with just 1 new case per 100,000 population.\(^8\)

Even more dramatic is the order-of-magnitude difference in infection rates between immigrants and U.S.-born individuals. In 2007, the TB case rate was 2.1 per 100,000 for U.S.-born people and 20.7 for people born in other countries.\(^8\) Foreign-born patients have represented an increasing proportion of U.S. TB cases since 1993 and have made up the majority of TB cases since 2001.\(^8\) In 2007, 58% of U.S. patients with TB were individuals born overseas.\(^8\)

Sustained, precipitous declines in U.S. TB infection rates occurred between 1953 and 1984. In 1953, the earliest year for which nationwide TB surveillance data are available, more than 84,000 Americans were newly infected (a rate of 52.6 cases per 100,000). By 1984, rates had improved to 9.4 per 100,000 (22,255 new cases).\(^8\) These declines ceased along with an increase in HIV/AIDS cases in the 1980s. After 1988 (when the rate was 9.2 per 100,000 or 22,436 cases), the U.S. saw increasing infection rates until 1992, when rates reached 10.4 cases per 100,000 (26,673 cases).\(^8\)

Although these increases constituted a resurgence in infection rates, the net result was essentially to pause the long-term decline of TB; even at the peak of the resurgence in 1992, the rate was far lower than in 1953 (52.6 per 100,000).

The decline in U.S. infection rates resumed after 1992, dropping by 50% overall between 1992 and 2007.\(^8\) Declines among foreign-born individuals during this period were substantial (39%), but less than those among U.S.-born individuals (72%).

Annual infection rates for Hispanics dropped by more than half, from 19.9 cases per 100,000 population to 8.5 per 100,000.\(^8\) Among African Americans, rates during the same period dropped from 28.5 to 9.4 cases per 100,000.\(^8\) For non-Hispanic whites, infection rates dropped from 3.6 to 1.1 per 100,000.\(^8\)

However, these declines have slowed from an average annual decline of 7.3% per year from 1993 through 2000 to 3.8% for 2000 through 2007.\(^8\) Despite the overall decline in U.S. infection rates between 2006 and 2007, 14 states and Washington, D.C., reported increased infection rates for 2007 compared with 2006 (see Table 1).\(^8\)

For the 46 U.S. states reporting data on TB patients’ HIV status, an average of 11% of TB patients were HIV positive.\(^8\) This data must be interpreted with caution, however. Even the most recent available data, for 2007, is incomplete because HIV testing among TB patients is voluntary and because some states do not report HIV status information to federal TB registries, citing patient privacy concerns.\(^8\)

**Table 1**

<table>
<thead>
<tr>
<th>State</th>
<th>2006 Infection Rate</th>
<th>2007 Infection Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. (total)</td>
<td>4.4</td>
<td>4.6</td>
</tr>
<tr>
<td>Alabama</td>
<td>3.8</td>
<td>4.3</td>
</tr>
<tr>
<td>California</td>
<td>7.5</td>
<td>7.7</td>
</tr>
<tr>
<td>Georgia</td>
<td>5.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Idaho</td>
<td>0.6</td>
<td>1.4</td>
</tr>
<tr>
<td>Kansas</td>
<td>2.1</td>
<td>3.0</td>
</tr>
<tr>
<td>Montana</td>
<td>1.1</td>
<td>1.4</td>
</tr>
<tr>
<td>Nevada</td>
<td>4.0</td>
<td>4.1</td>
</tr>
<tr>
<td>New Jersey</td>
<td>5.4</td>
<td>5.9</td>
</tr>
<tr>
<td>North Dakota</td>
<td>1.1</td>
<td>1.6</td>
</tr>
<tr>
<td>Pennsylvania</td>
<td>2.2</td>
<td>2.8</td>
</tr>
<tr>
<td>South Carolina</td>
<td>4.9</td>
<td>5.1</td>
</tr>
<tr>
<td>Tennessee</td>
<td>3.8</td>
<td>4.6</td>
</tr>
<tr>
<td>Virginia</td>
<td>4.0</td>
<td>4.3</td>
</tr>
<tr>
<td>Wyoming</td>
<td>0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>District of Columbia</td>
<td>10.2</td>
<td>12.3</td>
</tr>
<tr>
<td>Puerto Rico</td>
<td>2.5</td>
<td>2.9</td>
</tr>
</tbody>
</table>

**Imprisonment: Jails and Prisons as TB Incubators**

Since the emergence of HIV/AIDS-associated TB, jails and prisons around the world have become epicenters of TB infection and transmission, and rates of imprisonment help explain international variation in TB infection rates.\(^21,22,25\) Because prisoners are disproportionately male, the male-skewed sex ratio in TB infections may be due in part to incarceration rates.

A recent study comparing TB rates for 26 eastern European and central Asian nations revealed that countries in which a larger proportion of citizens are imprisoned exhibit significantly higher levels of TB infection.\(^25\)
For each additional percentage point in incarceration rate, TB incidence increases 0.34%, even after statistically controlling for differences in HIV/AIDS incidence rates, surveillance programs and economic factors. Overall, more than half of the increases in TB rates in these countries between 1991 and 2002 were attributable to increased incarceration rates. \(^\text{25}\)

TB is also a longstanding problem in U.S. jails and prisons, which release more than 10 million individuals back into the general U.S. population each year. \(^\text{26}\) Crowded living conditions and lack of medical resources have facilitated higher incidence rates for TB among inmates and prisoners than the general public, although reliable numbers are unavailable. \(^\text{26}\) Many jails in the U.S.— in both urban TB epicenters like New York City and even in remote, rural jails like the Rio Arriba County Detention Center in northern New Mexico — have installed negative-air pressure TB isolation facilities in an effort to stem the spread of active TB infections among inmates \(^\text{27}\) (Bidal Candelaria, Rio Arriba County, New Mexico, jail administrator, oral communication, March 5, 2009).

**Drug-resistant TB**

Drug resistance is a human-made crisis, the result of inappropriate use and overuse of antibiotics. \(^\text{27,28}\) For example, the routine repeated prescription of fluoroquinolone drugs for pneumonia in Canada has been tied to the evolution of fluoroquinolone-resistant TB strains. \(^\text{27}\) Patient noncompliance and abandonment of antibiotic therapy also contribute importantly to drug resistance. \(^\text{18}\)

Antibiotic resistance in a patient’s TB may involve either acquired or primary drug resistance. \(^\text{26}\) Acquired resistance evolves within a patient during treatment, whereas primary resistance is defined as a previously untreated patient’s TBisolates exhibiting drug resistance — a strong indicator that he or she was infected with an already-resistant strain. \(^\text{26}\)

TB resistance to more than one antibiotic is defined as MDRTB. When the TB is resistant to isoniazid and rifampin, plus any fluoroquinolone drug and at least one second-line drug, it is defined as XDRTB. Confirmation of XDRTB status is cumbersome and slow, requiring 4 to 8 weeks of culture-based lab work. \(^\text{27,29}\)

An estimated 900 000 people worldwide are infected with drug-resistant strains of TB, 500 000 of them XDRTB. \(^\text{27}\) Eastern European and central Asian countries have the highest rates of XDRTB infections — 15% of TB cases in Ukraine and 24% of Estonian TB cases involve XDRTB strains. \(^\text{27}\) Portugal has the highest XDRTB rate in western Europe, at more than 50%. \(^\text{27}\) The absence of drug-susceptibility testing lab equipment has precluded reliable estimates for most of Africa and much of the Middle East, including Iraq and Afghanistan, despite the presence of U.S. military medical personnel and equipment. \(^\text{27}\) Overall, only 30% to 50% of XDRTB patients survive the disease, although survival rates of up to 65% have been reported in some patient groups. \(^\text{25}\)

XDRTB is very rare in the U.S.; only 6 cases were identified in 2006 and 2007 combined. \(^\text{27}\) However, worldwide rates are increasing dramatically, and U.S. health care workers must be aware of this threat, particularly among patients born overseas and patients who have recently traveled outside of North America.

**The Role of Substandard and Counterfeit Drugs**

The global effort to control TB is severely undermined by the distribution of substandard and counterfeit drugs, which facilitate the spread of morbidity and mortality due to all strains of TB, as well as other diseases, such as HIV/AIDS, pneumonia and typhoid disease. \(^\text{28,30-33}\) Substandard-quality medications contain low concentrations of active ingredients, facilitating the evolution of drug resistance; \(^\text{32}\) counterfeit drugs contain no active ingredients and thus contribute to morbidity and mortality among individuals who believe they are receiving treatment, as well as the spread of the disease. \(^\text{32,34}\) For example, substandard rifampin and pyrazinamide are believed to have contributed to the evolution and spread of MDRTB. \(^\text{32,35}\) The counterfeit drug trade has become so bad in much of the world that some authors have argued it will “fatally undermine” efforts to identify optimal treatment policies for the third world until the trade is stopped. \(^\text{32}\)

**Nosocomial TB and Health Care Workers**

During the HIV-associated TB resurgence in the U.S., several hospitals experienced nosocomial outbreaks of MDRTB. \(^\text{26}\) Nosocomial infections (those acquired in a health care facility) remain commonplace in eastern Europe and sub-Saharan Africa, particularly among health care workers who have regular direct patient contact. \(^\text{21,27}\) In Romania, for example, MDRTB and XDRTB rates among all health care workers approach a magnitude higher than rates in the general public at 942 cases per 100 000 annually vs 98.6 per 100 000. \(^\text{27}\)

The TB risk faced by radiologic technologists is not known and radiology departments are often neglected...
in hospitals’ infection control programs. But when radiology personnel perform procedures involving exposure to infected patients, they obviously must observe precautions to minimize their risk of infection and the risk of cross-infesting other patients.

Published studies that compared TB infection rates for specific categories of health care workers have consistently identified nurses and physicians as facing the highest risks of infection. Very few cases were identified among radiology department personnel in the handful of studies that included radiology personnel. In a study of Romanian hospital workers, for example, only 1 of the 50 hospital employees identified with TB worked in a radiology department, compared with 21 nurses, 12 maintenance and cleaning staff, 6 physicians, 5 lab technologists and 5 clerks. A 2007 study of latent TB infections in Russian medical school personnel found that incidence was more than 4 times higher in physicians and nurses than in medical students (39% vs 9%).

In the early 1990s, when the U.S. TB resurgence peaked, a study of workers at a large hospital with a nosocomial outbreak of MDRTB found that staff in departments where TB patients were seen were nearly 14 times as likely to test positive on a tuberculin skin test (TST) as other employees, regardless of whether the workers had direct contact with patients. Risk was highest for nurses and clerks. Furthermore, the year-to-year fluctuation in hospital workers’ TB risk was related to the number of TB patients admitted to the hospital.

A 2007 study in England found that foreign-born health care workers were significantly more likely to have latent TB, but found no evidence that these workers represented a transmission risk to patients or fellow health care workers.

**Biology**

TB is one of the leading causes of death in the world, but only 5% of cases are active. The vast majority of cases are instead latent (quiescent), diagnosed only when patients undergo tuberculin antibody response tests or in vitro T-cell function assays called interferon gamma release assay (IGRA). An unknown proportion of latent cases represent a persistent immune response to TB bacterial proteins without surviving bacteria in the host.

Active TB cases immediately following infection are called primary TB. Each year, between 1% and 2% of latent TB cases become postprimary (or active) infections. The transition from latent to postprimary TB represents a neglected opportunity for medical intervention; however, little is known about what causes reactivation to postprimary disease, other than a suspected link to immune suppression (eg, cancer, malnutrition, intravenous drug abuse, diabetes mellitus, renal disease, other infections or advanced age). Reactivated TB is not clinically or radiographically distinct from primary TB.

Although TB is blood-borne, most infections begin with inhalation of infectious aerosols. The bacteria then travel from the lungs, through the lymph system to the bloodstream. From there, TB can infect any organ system in the body. TB spreads more rapidly to organ systems outside the lungs in HIV-positive individuals than in others.

This section introduces the functional anatomy and pathobiology of the respiratory system and describes the broad anatomic subtypes of TB.

**Functional Respiratory Anatomy and Pathobiology**

The respiratory system contains several antibacterial adaptations. The nose and nasal passages connect to the anterior nasal mucus trap that stops inhaled particulate matter and pathogens. Nevertheless, some bacteria and viruses survive this gauntlet to pass through the pharynx—a muscular sac that routes air and food to the trachea and esophagus—to the larynx, trachea and ultimately the lungs. From the mainstem bronchi, the airways within the lungs repeatedly subdivide and bifurcate into the smaller-diameter bronchioles of the “tracheobronchial tree.” The tracheobronchial tree is coated with a mucus-covered epithelial lining. Ciliary movement on this lining pushes mucus and trapped bacteria up a “ciliary escalator” toward the pharynx and away from the lungs. Beyond the smallest, terminal bronchioles are respiratory alveoli, where gas exchange occurs with capillaries’ circulating blood (see Figure 2).

Collectively, the bronchioles, alveoli and associated capillaries at the myriad termini of the bronchial tree are referred to as the lungs’ parenchyma. The total alveolar surface area in an adult is roughly that of a tennis court, providing ample habitat for bacteria that have circumvented the anterior nasal mucus trap and ciliary escalator. The destruction of lung parenchyma leads to the collapse, or failure to fully inflate during inhalation, of segments of the lung. This situation prevents normal oxygen delivery to the capillaries, a condition called atelectasis. Parenchymal infection also can cause consolidation, in which chronically inflamed and fluid-filled alveoli become swollen and firm.
The lungs’ surfaces are divided into lobes by deep fissures, with the right human lung possessing 3 lobes and the left, 2. Lobes are further subdivided into functional segments, each supplied by a major branch of the tracheobronchial tree.

Pleurae are the thin membranes lining the thoracic cavity and covering each lung. The outer or parietal pleura attaches to the thoracic wall, while the inner or visceral pleura adheres to each lung. Liquid between these pleural layers allows low-friction lung movement during breathing. Pleural thickening is another anatomical sign of infection and impedes normal lung function.

Bacteria drain from infected alveoli into the tracheobronchial tree’s lymph nodes, causing them to swell. The resulting enlargement of lymph nodes at the top of the large bronchi entering each lung is called hilar lymphadenopathy.

**Pulmonary TB**

Pulmonary TB is either primary or reactivated (postprimary) disease. Primary pulmonary TB accounts for a third of adult TB. Primary and postprimary pulmonary TB are infectious and represent the pathway through which most new victims are infected each year.

After inhaling cough or mucus droplets from a pulmonary TB patient, the new host develops small infectious lung granulomas. Pulmonary TB can cause fever, weight loss, night sweats and coughing up of blood-tinged sputum (hemoptysis). As with some other chronic lung diseases, people with advanced cases may develop clubbed fingers and toes. Patients also may experience chest pain, wheezing and difficulty breathing. Initial diagnosis often is made with chest radiography, tuberculin skin tests and sputum microscopy and culture. Sputum culture for *M. tuberculosis* is considered the gold standard in the U.S. for definitive TB diagnosis.

**Disseminated TB**

Disseminated (extrapulmonary) TB may occur in less than a month after primary infection, or may remain quiescent in different organs for years before progressing to symptomatic disease (see Figure 3). Pulmonary TB spreads to other organ systems via the lymph and, less commonly, circulatory systems, particularly when the patient’s immune system is compromised, aged or immature. Lymph system infection in either pulmonary or disseminated TB is called miliary TB. Miliary TB mortality rates are as high as 50%, but only a third of those with miliary TB have detectable *M. tuberculosis* in their sputum. Approximately 50% of patients who have full-blown AIDS (ie, HIV-infected individuals with CD4 white blood cell counts < 200 per mm$^3$ who also develop TB will have disseminated disease.

Disseminated TB can affect any organ system, including the eyes, central nervous system (CNS), the bones and joints, the lymph system, bronchus, larynx, the abdominal cavity’s peritoneal lining, the gastrointestinal tract, skin, heart and reproductive organs. Symptoms can include chills, joint pain, pale skin...
Clinical Testing

TB diagnosis is based on clinical histories and symptoms, diagnostic imaging examinations and laboratory tests. Chest radiography has long been a mainstay of TB diagnosis and is discussed in detail below; CT is now considered the gold standard for TB imaging. However, when possible, definitive diagnosis is based on sputum culture. Only in rare cases are biopsies of affected tissues undertaken to make a definitive diagnosis.

TST is a screening tool that involves injecting *M. tuberculosis*-derived protein tuberculin under the skin on the forearm. A positive test result is defined as a red welt developing at the injection site within 72 hours. However, the test is not perfectly sensitive; false positives may occur if the individual has been exposed to pathogens similar to *M. tuberculosis* or if the individual was vaccinated against TB outside the U.S.

A positive TST result is not the basis of a definitive TB diagnosis, but rather indicates the need for further testing, such as laboratory sputum culture. Culturing TB isolates in the lab is a very slow process, typically requiring up to 8 weeks. This includes 4 weeks for the actual culture, because *M. tuberculosis* is a slow-growing bacterium, and then another 3 to 4 weeks to test isolates' susceptibilities to different antibiotics and produce antibiograms.

TST remains a common screening test in the U.S. In 2001, however, the U.S. Food and Drug Administration approved a more accurate alternative to TST testing. IGRA is a blood test that detects the release of interferon from blood incubated with proteins that are very similar to *M. tuberculosis* proteins.

Two IGRA tests have been approved by the Food and Drug Administration for use in the United States, although only one is widely used. The original QuantiFERON-TB (QFT) test was approved in 2001; the subsequently developed QFT-gamma (interferon gamma) test (Cellestis Limited, Carnegie, Australia) was approved in 2005 and quickly replaced its predecessor. The original test helped diagnose only cases of latent TB, whereas QFT-gamma IGRA is useful in diagnosing both latent and active TB.

QFT-gamma is a more specific test than TST because it uses proteins simulating *M. tuberculosis*-specific proteins and, molecules that are absent from both the Bacille Calmette Guerin (BCG) vaccine and other, non-*M. tuberculosis* mycobacterial species.

Sputum microscopy (visual inspection of sputum isolates under a microscope) remains the traditional basis for diagnosing pulmonary TB in poor countries where

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or swollen lymph nodes. Physical exams may reveal enlarged lymph nodes, spleen or liver — or none of these, depending on the progression and anatomic location of the disease.

**TB Diagnosis**

When TB is detected early and treated, the patient is soon noninfectious and likely will be cured. Active pulmonary TB, particularly early in disease progression, can be completely asymptomatic or may be associated with mild or progressive dry cough. It also may involve a complex of symptoms, including fever, weight loss, fatigue, night sweats and cough with bloody sputum.
more definitive diagnostic techniques are frequently unavailable. Microscopy is inexpensive and widely considered to be accurate, despite studies showing a range of specificity from 20% to 80% for pulmonary TB.23 (Diagnostic specificity refers to a test’s percentage of true-negative test results; sensitivity refers to the percentage of true-positive results.)

Some of the variation in sputum microscopy’s specificity appears to be due to tested individuals’ HIV status; false-negative test result rates are at least 11% higher in HIV-positive individuals than among HIV-negative individuals.23 This complicates the diagnosis, treatment and even determination of basic epidemiology for HIV/TB coinfection.25

**TB Control**

The impact of TB on economic development is difficult to calculate, but 85% of TB cases occur among young and middle-aged adults, in the prime of their working years.5 A 2008 World Bank study concluded the economic returns to the global economy for fully implementing the Global Plan to Stop TB would exceed 1500%.5

Nevertheless, budgetary challenges in affluent countries facing a global economic recession could hasten the global resurgence of TB. Despite the IOM’s recommendation that the U.S. increase its investment in global public health and infectious disease control efforts, the 2008-2009 global financial crisis led to a $5 billion shortfall in the $10 billion pledged for the Global Fund to Fight AIDS, Tuberculosis and Malaria.5,6

During the January 2009 World Economic Forum in Switzerland, UN special advisor Jeffrey Sachs argued that the failure of affluent nations like the U.S. to make good on pledged levels of funding for these efforts was “absolutely in violation of the life and death pledge that the rich world has made.”7 The prior U.S. commitment of $2 billion to $2.7 billion in support of the Global Fund for 2010 was cut to $1 billion during January 2009 congressional budget negotiations. Committee members cited the financial sector bailout as the reason for the cuts.5,6

**The Global Plan To Stop TB**

The Global Plan to Stop TB emphasizes coordinated international confrontation of TB, MDRTB and HIV as interconnected crises; expanded patient access to existing diagnosis and treatment resources in underserved areas like sub-Saharan Africa; and the dissemination of new TB diagnostic tools, treatments and vaccines.25

Using only existing diagnostic techniques and treatments (not investing in the development of new diagnostic or treatment tools), full implementation of the plan would cost $56 billion and would treat 50 million patients, saving an estimated 14 million lives by 2015, including an estimated 800,000 patients with MDRTB.24

The plan also established international working groups on strengthening health systems and screening and the role of poverty and TB in children and women. In addition, it called for providing antiretroviral therapy for 3 million HIV-positive TB patients.24

**Prevention and Infection Control**

Infection control policies are devised to slow, contain and reverse environmental contamination and person-to-person transmission. Infection control strategies include contact precautions, surveillance, treatment and adherence to standard infection precautions. Fundamentally, controlling the spread of all drug-resistant organisms, including MDRTB and XDRTB, requires regular and thorough cleaning of the health care environment and vigilant hand hygiene by health care workers.53 In addition, reusable equipment that comes into contact with patients must be regularly disinfected.55 By carefully adhering to standard infection-control practices, health care personnel will reduce the incidence of TB strains and other nosocomial infections.52 A study of nosocomial TB in South Africa found that simply implementing existing infection-control strategies could prevent half of nosocomial XDRTB cases and 75% of cases among hospital workers.4 Preventing TB infection among radiology department workers requires observance of standard infection-control precautions (particularly respiratory protection), disinfection practices, routine monitoring of these practices and periodic surveillance (testing) of workers, particularly when TB patients are known to have been seen at a facility.58

**Standard Precautions**

CDC guidelines recommend that health care workers wear gloves and gowns when caring for patients with drug-resistant infections. The CDC’s universal precautions for blood and infectious materials became “Standard Precautions” in 1996, and address efforts to avoid transmission of blood-borne and non-blood-borne infections.56 Hand hygiene and respiratory hygiene (cough etiquette), safe injection practices and the use of masks are standard precautions against nosocomial infection.55
After each procedure, all equipment or devices that came into contact with an active TB patient must be handled as though they are contaminated. The following standard precautions should be observed vigilantly:

- Wash hands thoroughly and promptly after contact with a patient, body fluids or secretions.\(^5^6\)
- Immediately after use, discard disposable sharps (eg, needles and scalpels) in puncture-resistant containers close to the point of use.\(^5^6\)
- All personnel present at procedures involving potential exposure to patient blood, body fluids, secretions, excretions, mucus membranes or wounds should use barrier precautions (eg, gloves, gowns, masks, goggles or face shields).\(^5^6\)
- Facility staff, patients and visitors should be educated regarding respiratory hygiene, including observance of droplet precautions (wearing masks to contain infectious aerosols), tissue use and physical separation (more than 3 feet) from patients with respiratory infections. Tissues should be disposed of promptly and hands immediately washed. Facilities should post signs illustrating respiratory hygiene.\(^5^5,5^6\)

Cleaning and Disinfection

One recent study of hospital workers during a nosocomial outbreak of MDRTB found that workers employed in rooms where TB patients had been present, regardless of whether those workers had direct contact with the patients, were nearly 14 times as likely to test positive \(^5^5\) in rooms where TB patients had been present, regardless of whether those workers had direct contact with the patients, were nearly 14 times as likely to test positive of MDRTB, regarding the patients, were nearly 14 times as likely to test positive of MDRTB, regarding the patients, were nearly 14 times as likely to test positive of MDRTB, for TB as other hospital workers.

In addition to standard precautions and hand hygiene, therefore, radiology department infection control depends on effective cleaning of environmental surfaces and sterilization of medical devices after TB patients are seen. Cleaning and disinfection are health care workers’ basic responsibility to patients and fellow workers.

Rinsing is not cleaning and visual inspection does not indicate whether a room or surface is free of bacteria. Regular environmental sampling for bacterial contamination should be scheduled with hospital infection control personnel. Electronic controls and wires can be very difficult to clean effectively and must be covered with disposable or readily disinfected covers (eg, clear plastic).

Janitorial staff often cannot be relied on to perform proper disinfection and cleaning of storage areas or rooms. Cleaning staff does not typically receive special training or education regarding disinfection techniques. The terms quarantine and isolation are frequently treated as synonyms in the medical literature, but they are not. A quarantine occurs when individuals who are not yet ill but who have been exposed to an infection are kept away from unexposed individuals (eg, told to stay in their home).\(^5^5\) Isolation, in contrast, refers to separating infected individuals from uninfected people.

State health departments have the authority to issue quarantine or isolation orders to prevent the introduction or spread of infectious diseases. The CDC’s Division of Global Migration and Quarantine is the federal government agency with the authority to impose interstate quarantine orders.\(^5^7\)

However, enforcing patient isolation or quarantine orders can be challenging. Following orders from the division to curtail travel generally is voluntary and recent history provides examples of individuals who refused to change their travel plans, violating do-not-travel orders and endangering others.

For example, a 31-year-old Atlanta, Georgia, lawyer underwent chest radiography after a fall in 2007, a few months before he was to fly with his fiancée to Europe for their honeymoon.\(^5^7\) The radiograph suggested pulmonary TB, a finding supported by a subsequent chest CT but not by the initial analysis of sputum samples.\(^9\)

Follow-up bronchoscopy definitively diagnosed pulmonary TB.\(^9\) More than a month later, lab work indicated the man’s TB strain was MDRTB, resistant to at least 2 standard TB-treatment antibiotics.\(^9\)

When the man was informed, he revealed that he was about to travel to Europe for his honeymoon. Health authorities claim they told him not to travel, but the man rescheduled his honeymoon flight to Europe.\(^9\) Four days after he left, the CDC determined (possibly erroneously) that he had XDRTB, not merely MDRTB, and that his disease was caused by a strain from rural South Africa.\(^9\)

The CDC located the man in Italy and told him not to travel but to check into an Italian hospital for immediate medical care.\(^9\) However, the man subsequently flew to the Czech Republic, and from there flew to Montreal, Canada, where he rented a car and drove back to the U.S.\(^9\)

Upon his return, a federal isolation order was issued against the man — the first since a 1963 order to control the movement of an individual believed to be infected with smallpox.\(^9\) Subsequent testing indicated that he had MDRTB rather than XDRTB. The CDC alerted 245 U.S. citizens that they had been seated on flights with the man.
BCG vaccination prevents latent infections from developing into active disease, but even repeated vaccinations do not reliably prevent latent infections with *M. tuberculosis*. Vaccination efficacy varies between 0% and 80% protection in different study cohorts. Vaccination is most protective against the development of TB meningitis (infection of the membranous lining of the brain).

**Treatment**

Disseminated TB, such as spinal TB, may require surgical excision of affected tissues, but antibiotic therapies are the mainstay of TB management.

**Drug Therapies**

TB drugs are categorized as first-line and second-line antibiotic agents (see Box 2). First-line drugs are increasingly losing their efficacy in the face of MDRTB and XDRTB, while second-line drugs cause sufficient toxicity that 40% of patients suffer serious side effects and more than half of patients discontinue second-line therapies prior to cure.

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**Box 2**

**Antibiotic Agents Used To Treat TB**

<table>
<thead>
<tr>
<th>First-line Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampin</td>
</tr>
<tr>
<td>Isoniazid</td>
</tr>
<tr>
<td>Pyrazinamide</td>
</tr>
<tr>
<td>Ethambutol</td>
</tr>
<tr>
<td>Streptomycin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Second-line Agents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
</tr>
<tr>
<td>Aminosalicylic acid</td>
</tr>
<tr>
<td>Capreomycin</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
</tr>
<tr>
<td>Clofazimine</td>
</tr>
<tr>
<td>Cycloserine</td>
</tr>
<tr>
<td>Ethionamide</td>
</tr>
<tr>
<td>Levofloxacin</td>
</tr>
<tr>
<td>Moxifloxacin</td>
</tr>
<tr>
<td>Rifabutin</td>
</tr>
<tr>
<td>Rifampentine</td>
</tr>
</tbody>
</table>

---

TB screening refers to the testing of populations or cohorts, whether or not they exhibit TB symptoms. Screening typically involves antibody tests such as TST or IGRA, and in some cases, chest radiography. Epidemiological surveillance refers to tracking the incidence rates or new cases identified in a given population or cohort.

Because the majority of new TB cases in the U.S. occurs among foreign-born individuals, the U.S. government’s screening and surveillance efforts focus on immigrant populations. The CDC is working with other U.S. and international public health agencies such as the World Health Organization (WHO) to reduce the immigration of individuals with TB to the U.S. by establishing systematic screening programs abroad, particularly for monitoring TB in refugee communities, and by strengthening notification systems that inform state and local health departments about immigrants who may be infected. The CDC has emphasized the importance of coordinating U.S. and Mexican TB control efforts to ensure that TB treatment regimens are not disrupted for individuals who cross the border — a daunting task for a “shadow population” that often appears on public health radars only when patients with advanced, infectious TB come to hospital emergency departments.

Immigrants arriving in the U.S. from countries with high TB infection rates are tested for latent infection. Immigrants with latent TB undergo supervised treatment. The CDC is surveying foreign-born TB patients in the U.S. to devise additional screening, surveillance and control strategies.

**Vaccination**

The BCG vaccine, the only available anti-TB vaccine, was developed by French researchers and first used in 1921 to inoculate infants. It contains a live but weakened strain of *M. bovis*, a relative of *M. tuberculosis*, which causes most human cases of TB. More than 1 billion people worldwide have received BCG vaccination and it is generally considered to be very safe. However, vaccination may cause TB infection in immunocompromised people. Immunocompromised individuals also may develop the disease as a result of exposure to recently vaccinated individuals.

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close enough to the man during his airline travel that they may have been exposed to MDRTB. None contracted TB, although 8 filed a lawsuit in Canada against the man.
The first-line “essential” drugs are gold-standard agents included in any short-course treatment regimen. First-line essentials include 4 medications: rifampin, ethambutol, isoniazid and pyrazinamide.

Of these, rifampin is the most powerful weapon against TB and a range of other bacteria. Rifampin blocks bacterial RNA synthesis, preventing cellular division by TB bacteria. Rifampin’s adverse effects are relatively rare (occurring in fewer than 1% of cases) and include rash, flu-like symptoms, fever with chills and gastrointestinal upset. Fever and chills are strong indicators for discontinuing rifampin therapy. Because rifampin increases liver enzyme production, its use can affect the efficacy of other drugs, including methadone, oral contraceptives and, importantly, anti-HIV drugs.

In some cases, rifampin is used in combination with ethambutol, isoniazid and pyrazinamide. These combination therapies develop hepatitis.

Isoniazid also is included in most TB patients’ treatment, unless the strain is drug-resistant. Isoniazid is inexpensive and involves a low incidence of adverse effects (fewer than 5%), which include liver toxicity and peripheral neuropathy (numbness of the hands and feet), rash, fever, seizures, acer, arthritis and an autoimmune syndrome similar to systemic lupus erythematosus. The risk of chemical hepatitis increases with regular alcohol consumption, active hepatitis B infection and current or recent pregnancy.

Chemical hepatitis has been reported in rare cases after coadministration of either rifampin or pyrazinamide with isoniazid—a common combination therapy for TB patients. Between 3% and 5% of patients receiving these combination therapies develop hepatitis.

Isoniazid is inexpensive and involves a low incidence of adverse effects (fewer than 5%), which include liver toxicity and peripheral neuropathy (numbness of the hands and feet), rash, fever, seizures, acer, arthritis and an autoimmune syndrome similar to systemic lupus erythematosus. The risk of chemical hepatitis increases with regular alcohol consumption, active hepatitis B infection and current or recent pregnancy (up to 3 months after delivery).

Second-line antibiotics are less effective, older drugs that entail higher risks of adverse reactions and are therefore used only rarely. Amikacin, for example, can cause kidney damage and is ototoxic, meaning it can damage the auditory nerves and hearing. Other examples of second-line TB agents are ethionamide, cycloserine and capreomycin and for the treatment of MDR TB, 2 fluoroquinolone antibiotics: levofloxacin and moxifloxacin.

Patient noncompliance and premature abandonment of antibiotic therapy are major barriers to successful TB treatment and control efforts. Two very different antibiotic therapy strategies, known as DOT and DOTS, were developed to address these issues.

Supervised or directly observed therapy (DOT) has become a centerpiece of modern TB treatment in affluent countries, leading to the development of intermittent rather than daily antibiotic treatment regimens. Commonly, DOT regimens consist of 6 months of antibiotics given 3 times a week or 2 weeks of initial daily antibiotic administration followed by twice-weekly doses. Both of these are as effective as daily antibiotic therapy.

In the U.S., DOT regimens were adopted at the height of the resurgence in TB infection rates and have been credited with helping reverse the resurgence throughout the late 1990s. Only 4% of patients were treated with DOT regimens in 1990, but that proportion reached 70% by 2000 and 86% by 2005.

Although DOT has been successful in wealthy, developed nations like the U.S., medical personnel shortages mean that patient supervision throughout an entire course of antibiotics is often unrealistic in many poor countries. This led the WHO to develop a modified regimen, called DOTS (directly observed therapy, short course).

DOTS has 5 components:
2. Assured supplies of antibiotics.
4. Outcome analysis of patient cohorts.
5. Directly observed treatment during the first 2 months.

DOTS forgoes meaningful surveillance of drug-resistance patterns because microscopy cannot detect drug-resistance patterns. Furthermore, in clinical practice, most DOTS programs around the world have been implemented as daily, unsupervised patient-administered treatments with periodic supervised doses. As a result, DOTS has not had the impact originally anticipated.

DOTS guidelines for TB treatment allow local variation from standardized international TB treatment guidelines and regimens. First-line drug regimens vary around the world and in many poor countries, second-line drugs are used instead of first-line ones because of availability. An August 2009 study by the Global Alliance for TB Drug Development concluded that this flexibility is a strength rather than a weakness in the global TB control effort because it allows local public health authorities to adapt to changing local and national conditions, including the emergence of drug-resistant TB strains.

**Treating MDR TB and XDR TB**

XDR TB represents one of the most significant challenges to the clinical management of TB, but it can be successfully treated in 30% to 65% of patients who...
are not coinfected with HIV by rapidly identifying the antibiotics to which the strain is susceptible and using prolonged antibiotic therapy regimens. The susceptibility of cultures or isolates from a given patient’s TB strain to these drugs should be determined before treatment to identify cases of MDRTB or XDRTB and to help formulate optimal antibiotic therapy regimens. Antibiograms are summary reports of lab results from such testing, detailing the proportion of isolates susceptible to each of a panel of antibiotic drugs.

Medical Imaging’s Role in the Fight Against TB

Modalities

Medical imaging is a routine, central component of TB diagnosis. Chest radiography can reveal evidence of pulmonary TB before any clinical symptoms appear, and incidental discoveries of TB cases are not uncommon.

Chest radiography and CT commonly are used to determine the extent of pulmonary, pleural and parenchymal involvement in pulmonary TB. MR and CT also demonstrate mediastinal and hilar lymph node enlargement with excellent sensitivity.

Positron emission tomography (PET) is not in widespread clinical use as a diagnostic imaging modality for TB, in part because of its poor infection specificity and the superior anatomic imaging of CT and MR. For example, pulmonary TB sensitivity for gallium-based infection scintigraphy is between 80% and 97%, but because positive results reflect uptake of gallium by inflamed tissue, any pulmonary infection and many other lung diseases yield positive results. In cases of laboratory-confirmed pulmonary TB, however, gallium scintigraphy has shown promise in confirming the efficacy of antibiotic therapy. High-resolution CT also shows promise for this application, but no comparative studies of PET and high-resolution CT for treatment monitoring have been published.

Two specific PET examinations, fluorodeoxyglucose F 18 and choline C 11, sometimes are used to differentiate TB granuloma of the lung from cancerous lung tumors.

Laboratory identification of MDRTB can require several weeks to complete, delaying effective treatment. The discovery by Korean researchers of radiographic and CT differences between pulmonary MDRTB and drug-susceptible TB strains might lead to the use of diagnostic imaging as a more rapid, probabilistic screening tool for differentiating patients likely to have MDRTB from those likely to have drug-susceptible TB. This would allow labs to prioritize drug susceptibility testing of isolates likely to exhibit some form of resistance. These findings are described in the next section.

In this section, the imaging modalities used in TB diagnosis are introduced and the specific applications of each modality are described.

Radiography

Posteroanterior chest radiography remains the imaging mainstay of pulmonary TB screening and diagnosis. Radiographs of active pulmonary TB often reveal parenchymal consolidation, atelectasis, pleural effusion and, sometimes, lymphadenopathy (enlarged lymph nodes) along the trachea. Pleural effusion is particularly common in children. These signs in the upper lobes often indicate reactivated or postprimary TB. However, CT and MR imaging can offer significant advantages over radiography when assessing suspected cases of pulmonary and disseminated TB.

Bronchoscopy sometimes is used to follow up chest radiographs, particularly when biopsies are required for lab analysis.

Computed Tomography

CT is a rapid and more detailed modality for TB assessment than radiography, and is considered the gold standard for diagnostic imaging of active TB, both as a confirmatory follow-up modality in the imaging of pulmonary TB, and the detection and characterization of disseminated TB in other organ systems. CT more clearly visualizes classic pulmonary TB signs than radiography, including parenchymal consolidation, atelectasis and hilar lymphadenopathy.

CT scanners use x-ray tubes and detectors, arrayed opposite one another in a semicircular yoke. The fan-shaped x-ray beam passes in preselected slice thicknesses through the target anatomy. Patients are positioned on their back on the CT table, which advances through the scanner field as sequential slices are acquired. X-ray attenuation is calculated and digitized for computer image reconstruction and computer postprocessing. CT values represent tissue densities and are calculated from attenuation coefficients.

Because CT involves higher ionizing radiation doses than chest radiography, this imaging modality should be used only when necessary, in observance of the ALARA (as low as reasonably achievable) principle. The diagnostic superiority of CT often outweighs radiation risks, however.
Magnetic Resonance

MR is not yet a standard modality for the diagnostic imaging of TB, but it can be very useful in detecting and characterizing disseminated TB infection foci, particularly of the CNS and spine. It does so more sensitively than PET or CT, and does not involve exposure to ionizing radiation.

MR imaging exploits subatomic-level tissue interactions with powerful magnetic fields to construct images that reflect variations in tissue density. Gadolinium contrast agents may be used to enhance resolution of CNS tuberculosis lesions.

Contraindications include cardiac pacemakers or other ferromagnetic foreign bodies such as shrapnel or aneurysm clips.

Imaging Pulmonary TB

The main radiographic features of pulmonary TB are parenchymal disease with cavitation and pleural enlargement (see Figure 4). Lobar consolidation with hilar adenopathy is a classic radiographic sign of tuberculosis, but alone is not sufficient for definitive diagnosis. Lymphadenopathy usually progresses through the first 10 weeks of infection.

Primary pulmonary tuberculosis often appears in posteroanterior chest radiographs as parenchymal disease, pleural effusion (excess fluid between the membranes around the lungs) and thickening, cavitation and lymphadenopathy, within specific lobes or segments. Heterogenous consolidation (with or without atelectasis in early disease stages), especially in the apical segments of the upper lobes frequently is seen. TB bronchopneumonia appears on chest radiographs as patchy densities, particularly in terminal bronchial segments.

CT more sensitively detects consolidation, atelectasis, calcification and particularly lymphadenopathy than does chest radiography (see Figure 5). Marked lymphadenopathy is common in CT scans of pulmonary TB and consolidation is well-defined and homogeneous. Lymph nodes in close association with parenchymal disease are more enlarged than distant nodes. Cavitation and lobar consolidation are frequently seen in close association in CT, and tumor-like masses called tuberculomas, which can be misdiagnosed as cancer, frequently are visualized. Bronchopneumonia may be accompanied by multiple, heterogeneously sized, thin-walled cavities.

High-resolution CT demonstrates early parenchymal disease well. Progressive cavitation can be detected using sequential high-resolution CT scans over time, and can be visualized well before it becomes evident in chest radiographs. High-resolution CT shows very early miliary disease as patchy irregular opacities (sometimes described as having a “snowstorm” appearance). MR imaging is rarely used with pulmonary TB. CT is more sensitive for demonstrating focal calcification, shows other TB signs just as sensitively as MR imaging and is more widely available. CT therefore remains the gold standard for diagnostic TB imaging.

Bronchoscopy may be used rarely after imaging to help diagnose pulmonary TB, particularly when imaging strongly indicates TB in the absence of TST, IGRA or microscopic support for a TB diagnosis. The procedure sometimes is guided by ultrasonography.

Flexible bronchoscopes with diameters less than one-half inch typically are used after the patient receives a local anesthetic. The bronchoscope is inserted through the patient’s mouth or nose, down the trachea and into the lungs. In some cases, lavage is used to collect biological samples. Alternatively, fine needles or forceps are introduced through the bronchoscope for lung tissue biopsies.
CT of pulmonary XDRTB also was found to be more likely to reveal the presence of pleural thickening than CT of either MDRTB or drug-susceptible pulmonary TB. Contrary to the study’s findings with chest radiography, however, MDRTB CT was more likely than drug-susceptible TB CT to reveal the presence of large pulmonary nodules.

The study’s authors concluded that their most significantly different finding was the visualization of multiple cavities in pulmonary MDRTB.

No signs were unique or exclusive to MDRTB, XDRTB or drug-susceptible TB, however, so the correlations between radiographic appearance and drug-susceptibility status are probabilistic. The study included relatively small numbers of patients: 53 MDRTB patients, 15 XDRTB non-AIDS patients and 141 drug-susceptible TB patients, all of whom had received less than a month of anti-TB antibiotic therapy when imaged.

The results described here are preliminary and in need of confirmation in larger studies.

Pulmonary MDRTB Imaging

Recent research suggests that the radiographic and CT appearances in active pulmonary MDRTB are frequently and significantly different from that of drug-susceptible TB, although differences were not reliably detected between XDRTB and MDRTB using radiography.

In the most recent study, comparing drug-susceptible TB with XDRTB and MDRTB, posteroanterior chest radiographs revealed that both XDRTB and MDRTB were less frequently associated with lung nodule lesions such as ground-glass opacity than drug-susceptible TB. Large pulmonary nodules and pleural effusion also were significantly less frequent in MDRTB than drug-susceptible cases of pulmonary TB.

Transverse CT scans acquired in 2.5-mm sections also revealed differences between drug-susceptible and MDRTB pulmonary infections. CT was significantly more likely to show multiple cavities, bronchial dilatation and tree-in-bud signs in MDRTB than drug-susceptible TB. (The “tree-in-bud” sign is a finding that involves small, well-defined peripheral nodules of soft-tissue CT attenuation connected to branch-like opacities resembling a tree in spring bud, typically within 3 to 5 mm of the pleural surface. This sign correlates with mucus or fluid impaction of the bronchus lumen of the peripheral airways in the lungs.)

Imaging Disseminated TB

Diagnosis of disseminated TB outside the lungs can be notoriously difficult, as negative TST test or chest radiography results do not preclude the presence of this disease. CT and MR imaging are each more sensitive imaging modalities, particularly when used to identify TB in the CNS, spinal canal or abdomen.

Miliary disease presents as millet-sized micronodules, while disseminated TB often involves larger, tuberculosis lesions. In disseminated TB, larger and more readily detected lesions are seen in immunocompromised patients than others. Lymphadenopathy associated with disseminated TB occurs much more frequently in children than adults (95% vs 12% of cases).

Abdominal TB

Abdominal TB commonly involves lymphadenopathy and in 90% of patients involves gastrointestinal infection, particularly of the ileum and cecum, where the small intestine connects to the large intestine. Bowel wall thickening, ileum/cecum valve thickening and terminal ileum narrowing are radiographic signs of TB.

Hepatic and spleen TB occur in 2 types, miliary or, much more rarely, tuberculosis. After 12 hours of patient fasting, CT reveals miliary TB as numerous...
low-attenuation foci smaller than 1 cm in diameter.\textsuperscript{75} Larger (1 to 3 cm diameter) foci in the liver or spleen are tuberculoma.\textsuperscript{75}

Genitourinary TB

Genitourinary tract TB usually includes the kidneys and represents the most common form of disseminated TB.\textsuperscript{75} Kidney parenchymal cavitation is common. In men, the prostate and seminal vesicles are often infected initially (via the bloodstream), with TB subsequently spreading to the bladder and causing reduced bladder capacity that is readily discernable with x-ray cystography.\textsuperscript{75} Transrectal ultrasonography sometimes is used to detect prostate TB as hypoechoic prostate peripheries; contrast-enhanced CT reveals calcification and dead or inflamed prostate tissue as hypoattenuating foci.\textsuperscript{75} T2-weighted MR imaging of prostate TB abscesses reveals irregular low-attenuation foci.

When indicated by diagnostic imaging, suspected genitourinary TB is confirmed by biopsy and histopathology.\textsuperscript{75}

Central Nervous System TB

CNS TB presents as meningitis, abscess or tuberculoma of the brain or spinal cord, and is confirmed with cerebrospinal fluid culture.\textsuperscript{75,78} Vertebral involvement does not necessarily imply spinal cord involvement because TB usually spreads to the brain and spinal cord through the bloodstream. TB meningitis indicates involvement of cerebrospinal fluid.\textsuperscript{75,78}

TB meningitis is imaged using CT or T1-weighted MR imaging, which reveals high signal-intensity thickening of the meninges or accumulations of cerebrospinal fluid and resulting spinal cord compression.\textsuperscript{75}

Musculoskeletal TB

Skeletal TB occurs in up to 3\% of patients,\textsuperscript{51} and half of these cases are spinal TB. TB infection in the spine results in spondylitis or infection-caused vertebral inflammation, also known as Pott disease. The infection often presents with low back pain.\textsuperscript{51,75} Vertebral and intervertebral disk narrowing (loss of vertebral height)\textsuperscript{75} usually is evident and new bone does not replace bone destroyed at TB lesions; vertebrae collapse as the disease progresses and TB may spread to the adjacent muscle, causing calcified abscess.\textsuperscript{51} Epidural abscesses (pus between the spinal cord and interior vertebral surface) also may occur.

Clinical neurologic symptoms are a late manifestation of spinal TB, occurring only after more than half of the spinal canal has been infected.\textsuperscript{51}

CT and particularly MR imaging offer sensitive visualization of the extent of spinal infection and spinal canal involvement.\textsuperscript{51} MR imaging reveals low to intermediate T1-weighted signal intensity and high T2-weighted signal intensity in vertebral marrow.\textsuperscript{51} Epidural abscesses generate intermediate and high-signal intensities in both T1- and T2-weighted MR images.\textsuperscript{51}

Nonspinal skeletal and joint TB is detected using CT or MR imaging. Reduced joint space is evident, as are the loss of outer bone cortex and foci of bone fragmentation with poorly defined margins.\textsuperscript{51} Foci of low MR signal intensity reveal cortical bone loss, whereas abscess (pus) generates increased T2 image signal intensity.\textsuperscript{51} Hip and knee joints and hand bones are most often involved, particularly in children, and usually involve only one joint (the right or left knee or hip, for example, rather than both).\textsuperscript{51,75} Joint TB often presents as arthritis, and may be mistaken for autoimmune rheumatoid arthritis, but rheumatoid arthritis involves early and profound loss of articular spaces.\textsuperscript{79}

On the Horizon: Emerging TB Imaging Technologies

Traditional lab culture approaches to confirming TB cases are slow and cumbersome, requiring up to 8 weeks to complete.\textsuperscript{27} Rapid DNA-based analyses and advances in portable imaging modalities promise to simplify the process and would hasten diagnosis. If sufficiently inexpensive, these tools could allow more effective screening in the poor countries that most need it.\textsuperscript{80}

In July 2009, officials at Harvard Medical School’s Center for Molecular Imaging Research and University of California, Berkeley proposed 2 devices that may speed diagnosis and screening.\textsuperscript{80,81} Both devices are largely untested, speculative and mostly conceptual. But either device, if validated and mass-produced, could revolutionize and hasten TB diagnosis and screening around the world.\textsuperscript{80,81}

According to media reports, the Harvard team developed a prototype hand-held molecular magnetic imaging device for rapid TB bacterial cell detection in sputum samples.\textsuperscript{80} Reportedly weighing 1 pound, the experimental, low-image-quality MR imaging unit mixes sputum with iron nanoparticles coated with bacterial antibodies; when the antibodies contact specific bacterial cells, they adhere to the cells, “painting” them with the iron nanoparticles. The mixture is loaded into a screen that separates iron-painted bacteria and free-floating nanoparticles; the chamber
is surrounded by electromagnetic coils that operate on the same principles as traditional MR, causing the nanoparticles to emit magnetic signals. The device is still unproven and has not yet been tested on TB cells; a test run with another bacterial species and antibodies reportedly worked well, with the magnitude of magnetic signals from the nanoparticle-painted cells correlating with the number of cells imaged. The team’s peer-reviewed technical report and data on the device’s sensitivity and specificity were not available as this Directed Reading went to press.

The Berkeley team’s blood and sputum TB-imaging device, according to a July 2009 media report, is a “cell-scope,” an optical imaging device attached to a cell phone camera. Essentially a microscope, lenses magnify the image of microscope slide-mounted sputum or blood samples that have been treated with auramine dye, which coats M. tuberculosis cells. A blue wavelength light-emitting diode causes the dye to emit green wavelengths (to fluoresce green light), allowing software in the cell phone to calculate the number of bacterial cells and to send the image as a cell phone picture file to a clinician or laboratory for diagnosis.

Conclusion

TB infection rate declines are slowing in the U.S. and the success of international TB-control plans and funding for those plans now are in doubt.

Radiography remains a mainstay of pulmonary TB screening and diagnosis, and can reveal active pulmonary TB before the emergence of clinical symptoms. CT is a more sensitive follow-up modality for diagnostic imaging of pulmonary and disseminated TB, and both CT and MR imaging offer superior visualization of abdominal organ involvement. MR is a particularly sensitive modality for CNS and spinal TB imaging.

In the U.S., radiography, CT and MR will represent the majority of medical imaging examinations for TB for the foreseeable future. PET scintigraphy may prove useful for confirming the efficacy of antibiotic therapies for laboratory-confirmed pulmonary TB, but it is not yet clear that PET is any more effective than high-resolution CT for treatment outcomes monitoring.

In coming years, hand-held magnetic TB imagers and cell-scopes may bring diagnostic imaging for TB to poor countries that today must rely on inexpensive diagnostic tools like sputum microscopy to identify new cases of the leading bacterial killer of humankind.

References


Bryant Furlow, BA, is a medical journalist and a regular contributor to Radiologic Technology and The Lancet Oncology. His reporting for the Rio Grande Sun newspaper on the impact of hospital budget cuts on rural ambulance response times and the off-label use of psychiatric drugs to sedate jail inmates has been nominated for awards in public service and investigative journalism. Mr Furlow is a member of the Association of Health Care Journalists and Investigative Reporters and Editors. He graduated with honors in biology from the University of New Mexico and studied international relations, including international pharmaceutical patent regimes, at California State University, Sacramento.

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**Errata**

The answer sheet for the Directed Reading article “Adrenal Gland Disorders” contains a typographical error. The article was published in the main version of the September/October 2009 issue of Radiologic Technology (volume 81, number 1). The correct credit amount for this Directed Reading is 1.5 Category A+ CE credits.

The Directed Reading article “Bleeding Risks in Interventional Radiology,” which appeared in the July/August 2010 issue, contained an error on Page 549. Vitamin K promotes blood clotting. Therefore, high intake of supplements containing vitamin K decreases the effectiveness of warfarin therapy.
Tuberculosis: A Review and Update

To receive Category A+ continuing education credit for this Directed Reading, read the preceding article and circle the correct response to each statement. Choose the answer that is most correct based on the text. Transfer your responses to the answer sheet on Page 58 and then follow the directions for submitting the answer sheet to the American Society of Radiologic Technologists. You also may take Directed Reading quizzes online at www.asrt.org. Effective October 1, 2002, new and reinstated members are ineligible to take DRs from journals published prior to their most recent join date unless they have purchased a back issue from ASRT. Your access to Directed Reading quizzes for Continuing Education credit is determined by your Area of Interest. For access to other quizzes, go to www.asrt.org/store.

#10805-01
Expiration Date: October 31, 2012
Approved for 2.0 Cat. A+ CE credits

1. Up to _______ % of TB-infected individuals develop active forms of the disease.
   a. 5
   b. 10
   c. 15
   d. 20

2. Each year, _______ million people die of TB and _______ million new victims are infected.
   a. 1.3; 5.2
   b. 1.3; 9.2
   c. 1.7; 5.2
   d. 1.7; 9.2

3. Active TB in the U.S. is concentrated in:
   1. ethnic minorities.
   2. California.
   3. southern states.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2 and 3

4. The Centers for Disease Control and Prevention (CDC) reported _______ new cases of TB in the U.S. in 2006 and _______ in 2007.
   a. 12 779; 12 299
   b. 13 779; 13 299
   c. 14 779; 14 299
   d. 15 779; 15 299

5. Most strains of TB affecting humans today are more similar genetically to _______ than _______ .
   a. ancient human strains; M. bovis
   b. ancient human strains; M. simiae
   c. M. bovis; ancient human TB
   d. M. simiae; ancient human TB

6. Risks for TB infection include:
   1. diabetes.
   2. HIV.
   3. imprisonment.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2 and 3

*Your answer sheet for this Directed Reading must be received in the ASRT office on or before this date.

Continued on next page
7. Within the U.S. and Canada, TB infection incidence rates range up to ______ cases per 100,000 population per year; in the U.S., the nationwide prevalence of TB is ______ per 100,000.
   a. 44; 20
   b. 34; 15
   c. 24; 10
   d. 14; 5

8. Which group has the highest TB incidence rate, at 26.3 cases per 100,000 population?
   a. Native Hawaiians
   b. Hispanics
   c. Asian Americans
   d. African Americans

9. In 2007, ______% of U.S. TB patients were individuals born overseas.
   a. 58
   b. 48
   c. 38
   d. 28

10. Declines in U.S. TB infection rates have decreased from an average annual decline of ______% per year between 1993 and 2000 to ______% per year between 2000 and 2007.
   a. 6.3; 4.8
   b. 7.3; 3.8
   c. 8.3; 2.8
   d. 9.3; 1.8

11. An average of ______% of TB patients in the U.S. are HIV positive.
   a. 11
   b. 12
   c. 13
   d. 14

12. Routine prescription of ______ antibiotics for pneumonia in Canada has been tied to the evolution of drug-resistant TB strains.
   a. pyrazinamide
   b. rifampin
   c. fluoroquinolone
   d. amikacin

13. Studies that compared TB infection rates for specific categories of healthcare workers consistently identified ______ as facing the highest risk of infection.
   a. medical technologists
   b. radiologic technologists
   c. clerks
   d. nurses

14. Each year, between ______% and ______% of latent TB cases become postprimary (or active) infections.
   a. 1; 2
   b. 3; 5
   c. 10; 12
   d. 15; 20

15. ______ is the condition caused by chronic inflammation when fluid-filled alveoli become swollen and firm.
   a. Lymphadenopathy
   b. Consolidation
   c. Atelectasis
   d. Cavitation

16. According to the Directed Reading, clinical symptoms of disseminated TB include:
   1. petechiae.
   2. joint pain.
   3. enlarged liver.
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2 and 3

Continued on next page
Directed Reading Continuing Education Quiz

17. When possible, definitive diagnosis of TB is based on _______.
   a. chest radiography
   b. a sputum culture
   c. computed tomography (CT)
   d. a tuberculin skin test (TST)

18. _______ uses proteins similar to M. tuberculosis proteins to screen for TB.
   a. Interferon gamma release assay (IGRA)
   b. Bacille Calmette Guerin (BCG)
   c. Sputum microscopy
   d. none of the above

19. A 2008 World Bank study concluded that the economic returns to the global economy for fully implementing the Global Plan To Stop TB would exceed _______.
   a. 15
   b. 150
   c. 1500
   d. 15 000

20. A South African study found that simply implementing standard infection-control strategies could prevent half of nosocomial extensively drug-resistant TB cases and _______ % of cases among hospital workers.
   a. 45
   b. 55
   c. 65
   d. 75

21. Before 2007, the last U.S. federal isolation order was issued by the CDC in what year?
   a. 1953
   b. 1963
   c. 1973
   d. 1983

22. How many U.S. airline passengers were told by the CDC that they may have been exposed to drug-resistant TB during flights between the U.S., Europe and Canada by an American traveler who had been informed that he had drug-resistant pulmonary TB?
   a. 45
   b. 145
   c. 245
   d. 345

23. First-line essentials in TB treatment include:
   a. rifabutin.
   b. rifapentine.
   c. levofloxacin.
   d. rifampin.

24. Only 4% of U.S. patients were treated with _______ regimens in 1990, but that proportion had reached 70% by 2000 and 86% by 2005.
   a. QuantiFERON
   b. BCG
   c. directly observed therapy (DOT)
   d. IGRA

25. _______ sometimes is used to differentiate pulmonary TB granulomas from cancerous lung tumors.
   a. Positron emission tomography (PET)
   b. Magnetic resonance (MR) imaging
   c. CT
   d. Radiography

26. Lobar consolidation with hilar adenopathy is a classic _______ sign of tuberculosis, but alone is not a sufficient basis for definitive diagnosis.
   a. PET
   b. MR
   c. CT
   d. radiographic

Continued on next page
27. ______ demonstrates early parenchymal
disease well.
   a. PET
   b. MR
   c. CT
   d. Radiography

28. CT was significantly more likely to show multiple
cavities, bronchial dilatation and tree-in-bud signs
in ______ TB.
   a. multidrug resistant (MDR)
   b. primary
   c. disseminated
   d. drug-susceptible

29. ______ associated with disseminated TB occurs
much more frequently in children than adults
(95% vs 12% of cases).
   a. Lymphadenopathy
   b. Tuberculoma
   c. Pleural thickening
   d. Multiple cavitation

30. Abdominal TB commonly involves
lymphadenopathy and, in 90% of patients,
involves ______ infection.
   a. renal
   b. gastrointestinal
   c. genitourinary
   d. hepatic
Directed Reading Evaluation
Tuberculosis: A Review and Update

1. What is your primary area of practice?
   - Administration/Management
   - Education
   - Quality Management
   - RIS/HIS/Information Systems
   - Bone Densitometry
   - Magnetic Resonance
   - Radiation Therapy
   - RN
   - Cardiovascular-Interventional
   - Mammography
   - Radiography
   - Sonography
   - Computed Tomography
   - Nuclear Medicine
   - Research
   - Other

2. Which of the following best describes the highest educational level you have attained?
   - Student who has not yet taken Registry exam
   - Associate degree
   - Master's degree
   - Certificate
   - Bachelor's degree
   - Doctoral degree (e.g., Ph.D. or Ed.D.)

3. Why did you choose to complete this DR?
   - Interested in the topic
   - Topic pertained to my area of practice
   - Other
   - DR had the right number of CE credits
   - Needed CE credits immediately

4. How relevant is this DR to your practice?
   - Extremely relevant
   - Very relevant
   - Relevant
   - Somewhat relevant
   - Not relevant

5. How beneficial is this DR to your professional or personal development?
   - Extremely beneficial
   - Very beneficial
   - Beneficial
   - Somewhat beneficial
   - Not beneficial

6. How would you rate the level of difficulty of this DR?
   - Too difficult
   - Somewhat difficult
   - Just the right level
   - Somewhat easy
   - Too easy

7. How would you rate the length of this DR?
   - Too long
   - Somewhat long
   - Just the right length
   - Somewhat short
   - Too short

8. Did this DR meet your expectations?
   - Yes
   - No
   - Partially

9. Would you recommend this DR to a colleague?
   - Yes
   - No

10. Overall, how valuable are the Directed Readings to you?
    - Very valuable
    - Considerably valuable
    - Valuable
    - Slightly valuable
    - Not very valuable

If you have comments about this Directed Reading, please write them below or send them separately to Ellen Lipman, Director of Professional Development, ASRT, 15000 Central Ave SE, Albuquerque, NM 87123-3909 or elipman@asrt.org.
Tuberculosis: A Review and Update

Expires: October 31, 2012
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CE Answers Section

USE A BLUE OR BLACK INK PEN. Completely fill in the circles.

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Note: For true/false questions, A=true, B=false.

1 2 3 4 5 6 7 8 9 10
0 1 2 3 4 5 6 7 8 9

3 1 5 7 9 7

No Photocopies Accepted
Cancer-focused Molecular Imaging

JANET YAGODA SHAGAM, PhD

Molecular imaging, based largely on recent advances in genetics, genomics and high-throughput computational analysis, uses isotope-labeled probes to target specific cell surface molecules, tumor proteins and enzymes. This cross-disciplinary imaging modality undoubtedly will make profound changes in medical, surgical and radiologic practice. Physiology-based imaging modalities naturally are relevant for molecular studies. As a relatively new discipline, molecular imaging is accompanied by much hope for improved cancer diagnosis and treatment.

This article is a Directed Reading. Your access to Directed Reading quizzes for continuing education credit is determined by your area of interest. For access to other quizzes, go to www.asrt.org /store.

After completing this article, readers should be able to:
- Define molecular imaging.
- Discuss the history and basis of molecular medicine.
- Understand how molecular disciplines affect medical care.
- Describe molecular imaging modalities in use now and the future potential of molecular imaging.
- Describe the role molecular imaging plays in the diagnosis, treatment and monitoring of specific cancers.
- Explain how molecular imaging technologies may influence medical and surgical practice.

The recent upsurge in genetics-based technologies is rapidly changing medical and surgical practice. Because of new sophisticated deoxyribonucleic acid (DNA) mapping and sequencing techniques, scientists are developing new ways to identify the molecular markers of many diseases and conditions. Having access to DNA-based physiological clues already is improving the ability to predict, prevent, treat and monitor diseases such as diabetes and cancer. When taken in the context of Watson and Crick’s explanation of the DNA molecule in 1953, our current capabilities, all based on understanding the structure and function of DNA, are extraordinary.

Genetic engineering, genomics and the Human Genome Project already have influenced patient care. Genetics-based medicine has raised both clinician and patient expectations by providing the means to predict, control and modify many health problems and medical conditions. Health care providers once understood cancer in the context of anatomical change and deterioration, but research shows that DNA-directed changes in gene-encoded proteins are the underlying cause of cancer.

It takes the combined efforts of a multidisciplinary team of research scientists, clinicians, computational biologists and engineers to unravel the complex relationships between genes, environment, lifestyle and disease. Researchers, estimating that genetic code errors are responsible for 3000 to 4000 hereditary diseases, are just beginning to understand that alterations in key proteins are the precursors to irreversible cell and tissue changes.

Some cancers, such as familial adenomatous polyposis and some types of breast cancer, are understood both in terms of Mendelian dominant and recessive inheritance patterns and the altered proteins that increase cancer risk. Other cancers, such as skin and lung cancer, have a genetic component and involve a mixture of environmental and lifestyle factors, such as sun exposure, smoking, obesity and exposure to industrial chemicals that alter DNA-encoded information.
The complexity of these factors makes the ability to understand cancer at the molecular level all the more important. The influence of molecular imaging on medical and surgical practice will reshape radiology, education, practice and patient care.

Genetics and Genomics

Genetic engineering and genomics are the culmination of more than 100 years of basic research in genetics, biochemistry, microbiology and physiology. In addition to advances in the supporting basic sciences, genetic engineering and genomics require concurrent and parallel developments in applied science and engineering disciplines such as bioinformatics, material science and robotics.

Scientists estimate that human genome research will reveal up to 10,000 new treatment targets. According to Dr. Elias Zerhouni, chairman of radiology at Johns Hopkins University in Baltimore, Maryland, molecular imaging will become particularly important in monitoring drug delivery and efficacy.

Genetic Engineering

Recombinant DNA (rDNA) technology, or genetic engineering, involves taking DNA from one organism and expressing segments or portions of its DNA-encoded information in an unrelated organism. The expression of human insulin genes in the bacterium *E. coli* is an example of rDNA technology. Human insulin has been available since the early 1980s and marketed under the trade name Humulin. More than 4 million people with diabetes around the world use genetically engineered insulin. Other genetically engineered products include human growth hormone, calcitonin salmon nasal spray to treat osteoporosis and erythropoietin to combat anemia caused by chemotherapy or ongoing kidney dialysis.

Genomics

The genome is an organism’s DNA-encoded library; genomics is the study of DNA sequences. Using a palette of DNA-cutting enzymes, sophisticated fragment separation methods and rigorous computational technologies, scientists have dissected, sequenced and cataloged genomic information from many different organisms. The ability to read the DNA “alphabet” enables scientists to:

- Study evolutionary relationships between organisms.
- Identify difficult-to-culture microbes.
- Identify forensic and anthropological remains.
- Diagnose and treat infectious and noninfectious diseases.

Proteomics

Proteomics, an offshoot of genomics, is the translation of the genomic alphabet into a nuance-rich protein language. Proteomics is the systematic cataloging of all of the proteins produced by genes and the complex interactions between proteins.

High-throughput technologies such as protein-chip arrays and multitime-of-flight molecular scanners help scientists identify and isolate medically useful human proteins. Proteomics, in concert with genomics, provides another wave of invention and innovation.

Molecular Imaging

Medical imaging research is changing our understanding of the genetic, molecular and cellular causes of various diseases, such as depression, schizophrenia, Parkinson disease and cancer. Many researchers foresee knowing the genetic factors causing most common diseases within the next 10 to 15 years. This new way of assessing patients, called molecular medicine, already is improving medical care. In addition to preventing and treating disease, molecular medicine may allow clinicians to:

- Identify individuals who are likely to respond to medications or experience adverse drug effects.
- Develop patient-specific risk factor profiles.
- Identify people who will benefit most from disease screening procedures.

Imaging modalities such as computed tomography (CT) or magnetic resonance (MR) provide the structural reference points used to locate areas demonstrating the physiological changes that often precede anatomical pathology. Therefore, developing positron emission tomography (PET) and single-photon emission computed tomography (SPECT) along with imaging probes is an area of active research.

Molecular imaging often is a two-tiered process that involves using sophisticated algorithms to fuse CT and MR images to the physiological data resulting from PET and SPECT studies. One of the challenges of this emerging technology is making the molecular imaging package both user-friendly and applicable to clinical working environments.

Positron Emission Tomography

PET is a physiology-based medical imaging modality. By imaging the distribution and accumulation of
biologically active molecules containing radioisotope tags, researchers can observe cell metabolism, perfusion and cell-surface integrity. When used in combination with structural imaging modalities such as MR and CT, PET links physiology to anatomical changes.

PET takes advantage of cells' fundamental needs for glucose, water, carbon and nitrogen-containing molecules to assess cell viability, abnormalities in metabolism and use of nutrients. Inappropriately high rates of cell metabolism or altered cell transport characteristics cause tissues and organs to accumulate above-normal amounts of radioactive imaging agents. Conversely, lower-than-normal uptake may indicate loss of cell activity or cell death. The ability to link physiological cell processes to health status makes PET a dynamic rather than static imaging modality.

**Single-photon Emission Computed Tomography**

SPECT relies on the high-energy gamma rays emitted by certain isotopes, such as iodine I 123, indium In 111 and technetium Te 99m, to create images. Because gamma rays can penetrate tissues and other dense substances, gamma emitters have many medical applications, including sterilization of medical equipment, design of innovative molecular imaging media and cancer treatment.

SPECT is a tomographic imaging modality in which a camera rotating around the patient takes multiple 2-D images from various angles. A computerized tomographic reconstruction algorithm converts a multitude of 2-D images into a 3-D data set. Using dual or triple-headed cameras reduces the time needed to complete a SPECT scanning procedure. Fusing SPECT with MR or CT scans links radioactive hot spots to their anatomical locations, and makes it easier to find and treat areas of concern such as the sentinel lymph nodes indicative of a spreading cancer.

**Molecular Imaging**

With nearly 18 million hits in less than one-tenth of a second, a Google search using the phrase “molecular imaging” provides a nearly instantaneous measure of the effect this burgeoning discipline will have on the radiologic professions. In a sense, molecular imaging is the marriage of “something old with something new.” The old is nearly 300 years of clinical observations that eventually revealed the importance of iodine as an essential nutrient. Insufficient dietary iodine causes enlargement of the thyroid gland, hypothyroidism and compromised brain development.

Based on the observation that the thyroid gland preferentially absorbs and uses iodine to make 2 essential thyroid hormones, scientists began to use iodine 123I and gamma camera imaging to diagnose, treat and monitor thyroid disease. Therefore, iodine 123I scanning was one of the first molecular imaging procedures.

Genetic engineering, in concert with its supporting disciplines, is the new contribution to molecular imaging. These disciplines provide the rapid-throughput technologies needed to link molecular probes to targets such as specific cell surface molecules, tumor proteins and enzymes. This makes molecular imaging an effective way to visualize, characterize and measure biological processes at the molecular and cellular levels in humans and other living systems.7

**Cancer Overview**

Even after many decades of intensive research, determining the exact cellular and biochemical changes that promote unregulated cell proliferation and cancerous growth still remains an area of intensive investigation. However, the data point to complicated interrelationships between various inherited, environmental and lifestyle risk factors that create a cascade of DNA-altering cellular and biochemical events. These events contribute to abnormal cell proliferation.8 Although it may seem difficult to reduce predispositions for inherited malignancies such as some types of colorectal and breast cancers, people who have a family history of cancer may improve their prognosis by undergoing regular screening procedures such as mammograms.9

The protective effect of modifying lifestyle risk factors such as obesity and diet on hereditary cancers is not clear. However, one observational study indicated that taking certain vitamins and folic acid may reduce relative colorectal cancer risk in women who have family history of this disease.10 Unlike some risk factors, individuals can modify lifestyle risks such as diet, smoking and physical activity.

Environmental risks, such as exposure to air and water contaminants and ultraviolet light, often are difficult for individuals to control or modify. Public health programs and the implementation of occupational and environmental health standards reduce cancer risk for people living and working in the community.

According to the American Cancer Society (ACS), more than 11 million, or one out of every 27, people living in the United States in 2005 had cancer as part of their medical history.11 Although this certainly is a sobering statistic, nearly 27 million people living in...
the United States, or 1 of every 12 people, had heart disease. In 2008, with an average life expectancy of nearly 80 years, heart disease and cancer were our top causes of death. These findings are in sharp contrast to the year 1900, when the average life expectancy was 47 years and infectious disease was the leading cause of death (see Table 1).

These statistics illustrate the benefits of public health regulations that protect our food and water supplies and reduce incidence of communicable disease. Vaccines and antibiotics are among the improvements that allow people to live long enough to experience the long-term effects of genetics, lifestyle and environmental exposures on their health.

In the United States, common cancers are considered those with 35,000 or more new cases diagnosed each year. Nonmelanoma skin cancer, with more than 1 million new cases diagnosed each year, places skin cancer at the top of the most frequently diagnosed cancers. Other common malignancies include cancer of the lung, breast, prostate, colon and rectum (see Table 2).

### Skin Cancer

Each year in the United States, more people are diagnosed with new skin cancers than the combined number of lung, breast, prostate and colon cancers. Demographic studies show that 1 in 5 people living in the United States and 1 in 3 whites develop skin cancer sometime during their life. The majority (95%) receive a diagnosis of either basal cell carcinoma or squamous cell carcinoma. Melanoma, a deadly form of skin cancer, accounts for approximately 3% of skin cancers and 75% of all skin cancer-related deaths. There is hope that using molecular imaging probes to stage, treat and monitor melanoma will reduce the number of deaths.

Basal cell carcinoma, with an estimated 700,000 cases diagnosed each year in the United States, is the most common of all cancers. Basal cell carcinoma develops in the deepest epidermal layers (see Figure 1). Nearly all basal cell carcinomas are located on areas of the body that receive sun exposure, such as the ears, nose and scalp. Other causes of basal cell carcinoma include ongoing skin irritation, chronic sun exposure, immune compromise, or prior radiation treatment.

| Table 1 |
| The 10 Leading Causes of Death (1900 vs 2005) |

<table>
<thead>
<tr>
<th>1900</th>
<th>2005</th>
</tr>
</thead>
<tbody>
<tr>
<td>Influenza/pneumonia</td>
<td>Heart disease</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Cancer</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Stroke</td>
</tr>
<tr>
<td>Heart Disease</td>
<td>Chronic lower respiratory disease</td>
</tr>
<tr>
<td>Stroke</td>
<td>Accidents</td>
</tr>
<tr>
<td>Kidney disease</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Accidents</td>
<td>Alzheimer disease</td>
</tr>
<tr>
<td>Cancer</td>
<td>Influenza/pneumonia</td>
</tr>
<tr>
<td>Senility</td>
<td>Kidney disease</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Septicemia</td>
</tr>
</tbody>
</table>

| Table 2 |
| Estimated New U.S. Cases and Deaths From Common Cancer Types, 2009 |

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>Estimated New Cases</th>
<th>Estimated Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin</td>
<td>&gt; 1 000 000</td>
<td>&lt; 1000</td>
</tr>
<tr>
<td>Lung</td>
<td>219 440</td>
<td>159 390</td>
</tr>
<tr>
<td>Breast (female/male)</td>
<td>192 370/1910</td>
<td>40 170/440</td>
</tr>
<tr>
<td>Colon and rectum</td>
<td>146 970</td>
<td>49 920</td>
</tr>
<tr>
<td>Prostate</td>
<td>189 000</td>
<td>31 728</td>
</tr>
<tr>
<td>Bladder</td>
<td>70 980</td>
<td>14 330</td>
</tr>
<tr>
<td>Melanoma</td>
<td>68 720</td>
<td>8650</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>65 980</td>
<td>19 500</td>
</tr>
<tr>
<td>Renal cell (kidney)</td>
<td>49 096</td>
<td>11 033</td>
</tr>
<tr>
<td>Leukemia (all)</td>
<td>44 790</td>
<td>21 870</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>42 470</td>
<td>35 240</td>
</tr>
<tr>
<td>Endometrial</td>
<td>42 160</td>
<td>7780</td>
</tr>
<tr>
<td>Thyroid</td>
<td>37 200</td>
<td>1630</td>
</tr>
</tbody>
</table>
inflammatory skin conditions and complications of tattoos, burns and scars. Although anyone can have basal cell carcinoma, those who have a fair complexion as demonstrated by light skin, red or blond hair and blue, green or gray eyes have the highest risk. Basal cell carcinoma tends to affect people older than 40 years, but in recent years, physicians have diagnosed more skin cancer among younger people. They attribute this demographic shift to sunbathing and the use of tanning booths (see Box 1).19

Basal cell carcinoma usually does not metastasize, but spreads locally and can cause disfigurement. Early treatment cures nearly 100% of these cancers.19 Squamous cell carcinoma is the second most common cancer in the United States, with more than 250,000 new cases each year (see Figure 2). The origin of this type of skin cancer is the oblong-shaped squamous cells that compose the upper epidermal layers. As with basal cell carcinoma, the parts of the body exposed to the sun are the most common sites of squamous cell carcinoma. However, this cancer also can occur in the mucous membranes and genitals. People who have fair complexions, or who already have had basal cell carcinoma are at added risk for squamous cell carcinoma. Squamous cell carcinoma rarely appears before age 50 years and is most common in people aged 70 years or older.20

In addition to sun exposure, other causes of squamous cell carcinoma include21:

- Burns and scars.
- Skin ulcers.
- Chronically injured skin.
- Chronic infections.
- Sites exposed to radiation.
- Sites exposed to chemicals such as tars and arsenic.

Direct observation of the skin, either by the patient, family member or a health care provider, is the first step in diagnosing skin cancers. A skin biopsy can differentiate between skin cancer types and provide the definitive skin cancer diagnosis.18 A shave biopsy and histological evaluation usually are the next steps following a clinical diagnosis of basal or squamous cell carcinoma. Treatment for both types depends on the size, location and depth of tumor penetration, and may include21:

- Mohs micrographic surgery for recurrent tumors or tumors located around the eyes, lips or nose.

**Box 1**

**The 5 Warning Signs of Basal Cell Carcinoma**20

- Persistent sore that does not heal
- Persistent reddish patch, often located on the face, chest or shoulders
- Shiny pearl-like bump
- Pink growth with a slightly elevated border and tiny superficial blood vessels
- Scar-like area with poorly defined borders
Excisional surgery.
■ Curettage and electrodessication.
■ Radiation for tumors too difficult to remove surgically.
■ Cryosurgery for patients who have bleeding disorders.
■ Photodynamic therapy for patients who have multiple basal cell carcinomas.
■ Topical medications that stimulate the immune system.

Melanoma, the most dangerous type of skin malignancy, is the leading cause of skin cancer deaths. The Centers for Disease Control (CDC) estimated that in 2006, nearly 54,000 people received a melanoma diagnosis. That same year, more than 8,400 deaths were attributed to melanoma.

Abnormal proliferation of the cells that produce the skin pigment melanin causes melanoma (see Figure 3). Similar to basal cell and squamous cell carcinoma, exposure to ultraviolet rays from the sun or artificial sources such as tanning booths causes the DNA changes that lead to unregulated cell division. A common first melanoma sign is a change in the size, color or shape of a mole. The ACS encourages people to self-inspect their skin to identify suspicious looking moles (see Box 2). The Skin Cancer Foundation recommends the “ugly duckling” method to differentiate the different-looking melanoma spots from other moles on the skin (see Box 3).

Direct observation of a suspicious-looking mole usually leads to a diagnostic biopsy. A suspicion of melanoma requires an excisional biopsy to sample or remove the entire lesion. A sentinel lymph node biopsy (SLN) determines whether and how far the melanoma has spread. If the SLN shows melanoma in nearby lymph nodes, the surgeon will remove the affected nodes and then request chest radiography, ultrasound, MR imaging, PET studies and assorted blood tests to determine whether the cancer has metastasized.
Melanoma staging is based on tumor characteristics, sentinel lymph node results and the presence and extent of metastases. Tumor characteristics, the T criteria, include:

■ Tumor depth — how far it has grown into the skin.
■ Mitotic rate — the number of cells in active cell division.
■ Ulceration — when present, indicates a worse prognosis.

Lymph node involvement, or N staging, involves both clinical and pathologic criteria. Injecting a radiotracer, with or without a blue tracking dye, allows the clinician to locate any “hot” sentinel and nearby lymph nodes and manually inspect them for tumors. The sentinel lymph node is the first lymph node or group of nodes reached by metastasizing cancer cells from a primary tumor.

The sentinel lymph node mapping procedure makes it possible to track melanoma with the unaided eye. The biopsy and histological inspection confirms whether the melanoma has spread to surrounding tissues or to lymphatic channels.

The presence or absence of metastasis, the M category, is the final melanoma staging factor. The M criteria range from the inability to assess distant metastasis to the presence of metastases in distant organs.

Surgery to remove the lesion and nearby tissue may be sufficient to treat early-stage melanoma. Melanoma that has spread to the lymph nodes or to distant organs requires various combinations of chemotherapy, radiation therapy and immunotherapy to slow disease progression.

Sentinel Nodes and Melanoma

Sentinel node mapping and sentinel node biopsy are a set of related procedures that play an important role in melanoma staging, treatment and prognosis. As the melanoma expands, cancer cells emerge from the primary lesion and migrate to the lymphatic system where they gain access to the rest of the body. If lymph nodes are free of cancer cells, this indicates an early stage, or in situ, cancer. The presence of cancer cells in the sentinel nodes, or in nodes further downstream from the primary site, indicates metastatic disease.

For many years, the method used to map sentinel nodes and identify those that may contain cancer involved injecting the radiotracer 99mTc sulfur colloid into the skin surrounding the melanoma. Many surgeons also inject a blue dye to provide a supplementary visual path to follow. The surgeon uses a hand-held gamma detector to identify hot nodes and to guide lymph node dissection (Frederick O Cope, PhD, FACN, CNS, vice president, Pharmaceutical Research and Clinical Development, Neoprobe Corporation, Dublin, Ohio, oral communication, June 2010). According to Dr Cope, 99mTc sulfur colloid, the current sentinel lymph node mapping standard, lacks many needed molecular imaging probes. An optimal molecular imaging sentinel node probe should have (oral communication, June 2010):

■ High affinity for a lymphoid-specific receptor.
■ Rapid injection site clearance.
■ Effective sentinel node accumulation.
■ Rapid breakdown and excretion.
■ Low incidence of side effects such as anaphylaxis.
■ Efficiency that supports patient flow through medical imaging facilities.

Because of the importance that sentinel node mapping and biopsy play in improving the outcome for melanoma patients, developing more effective molecular imaging probes to detect and develop individualized treatment plans is an active research topic.
Molecular Probes and Melanoma

Lymphoseek (Neoprobe Corporation, Dublin, Ohio), a synthetic \(^{99m}\text{Tc}\)-labeled macromolecule targeting the macrophages and dendritic cells that accumulate in lymph nodes, holds promise as an improvement over the \(^{99m}\text{Tc}\) sulfur colloid method. In phase 1 clinical trials, a comparison of Lymphoseek to filtered \(^{99m}\text{Tc}\) sulfur colloid demonstrated that Lymphoseek had improved injection site clearance, similar lymph node uptake and higher specificity. The authors reported that phase 1 study patients did not experience any adverse side effects.\(^{30}\) According to Dr. Cope, lymph node pathology studies confirm that Lymphoseek, compared with the sulfur colloid probe, is better at finding lymph node melanoma in patients who do not yet exhibit palpable nodes (oral communication, June 2010).

Positron emission tomography, using fluorodeoxyglucose (FDG) F 18 to detect areas of high metabolic activity and rapid cell division would seem an obvious method for detecting regional lymph node metastases. Although FDG-PET identifies stage III metastases in distant organs, research from several laboratories shows that PET does not have the sensitivity to reveal early-stage melanoma metastases when patients do not exhibit palpable lymph nodes.\(^{31}\)

Recent studies show that replacing \(^{18}\text{F}\)-FDG with a melanoma-specific probe may overcome PET sensitivity limitations. Melanocortin type 1 receptor (MC1R), a protein associated with many types of human melanoma, is a potential target for cell-surface based imaging and therapy.\(^{32}\) Researchers at the Stanford University Molecular Imaging Program and the Shanghai Institute of Applied Physics have developed a series of 18F-labeled metallopeptides that have a high MC1R specificity. One of them, \(^{18}\text{F}\)-FB-RMSH-1, has demonstrated good uptake and retention in mice bearing transplanted melanoma cells. However, PET showed a tendency for metallopeptide accumulation in the lungs and kidney in addition to the implanted melanomas. This is not an insurmountable problem, and these findings illustrate some of the unexpected challenges associated with developing new molecular imaging probes.

Lung Cancer

In 2009, approximately 219,000 people living in the United States received a lung cancer diagnosis. Accounting for more than 15% of all cancer diagnoses, lung cancer is the second leading cause of cancer-related deaths.\(^{11}\) The average 5-year survival rate for all lung cancer types and stages is approximately 16%.\(^{33,34}\) Following are some of the factors that may contribute to overall low lung cancer survivability:

- The average age at lung cancer diagnosis is 71 years.\(^{33,34}\)
- Early lung cancer is a silent disease with few or no signs and symptoms.\(^{33,34}\)
- Signs and symptoms, when present, often are first attributed to benign conditions.\(^{33,34}\)
- At the time of diagnosis, 75% of patients have advanced local or metastatic disease.\(^{35}\)
- There is no reliable screening method for high-risk and asymptomatic individuals.\(^{33,34}\)

Smoking is by far the most significant risk factor for lung cancer. The National Cancer Institute (NCI) has stated that 90% of lung cancer deaths among men and approximately 80% of lung cancer deaths among women can be attributed to smoking.\(^ {36} \) Secondhand smoke, both a lifestyle and an environmental risk factor, causes approximately 38,000 deaths per year and raises risk of lung cancer in an exposed nonsmoker from two-fold to three-fold compared with nonexposed individuals.\(^ {37} \)

Other environmental risk factors associated with lung cancer include radon gas, asbestos, air pollution, industrial chemicals, wood smoke and exposure to moderate-to-high doses of ionizing radiation.

A long-term cohort study by Rajaraman et al showed a slight risk of lung cancer for radiologic technologists who perform radiography examinations.\(^{38} \) However, the trend was not statistically significant when evaluated in the context of other risk factors, such as smoking habits. The authors concluded that for radiologic technologists, low-to-moderate occupational x-ray exposure is only weakly associated with increased lung cancer risk.\(^ {38} \)

Studies show that radon, a radioactive gas produced by the natural decay of uranium in the soil, is the leading cause of lung cancer in nonsmokers.\(^ {39} \) An odorless and colorless gas found throughout the United States, radon tends to seep through building foundations and accumulate in confined spaces, such as basements and crawl spaces, and in well-insulated buildings.

The 2 main types of lung cancer are nonsmall cell lung cancer (NSCLC) and small cell lung cancer (SCLC), or oat cell cancer. NSCLC accounts for nearly 80% of cases and has several subtypes.\(^ {39} \) The following list describes NSCLCs by the affected cell type and location within the lung\(^ {39} \):
Squamous cell carcinoma that forms in the bronchial tube lining.

Adenocarcinoma located in the mucus-secreting glands.

Bronchioalveolar carcinoma that forms near the air sacs.

Large-cell undifferentiated carcinoma that grows near the lung surface or outer edges.

The ability to surgically remove the tumor is a commonly used NSCLC staging criterion. Stage 0, or in situ disease, describes tumors that have not invaded nearby tissues. Stage I tumors are those that have not yet spread to any lymph nodes. Stage IA tumors are smaller than Stage IB tumors. Stage IIA tumors are < 3 cm and have spread to the lymph nodes. Stage IIB tumors are > 5 cm and have spread to lymph nodes and surrounding tissues. Because surgery may not entirely remove stage II tumors, patients also may have chemotherapy and radiation treatments. Stage III tumors may have spread to lymph nodes outside the lungs, or may have invaded nearby structures within the lung. Surgery may reduce the tumor, but not completely remove it. When the tumor has spread throughout the lung, the fluid surrounding the heart and lungs, or to distant sites, the patient has stage IV NSCLC. Even with aggressive treatment, the 5-year survival rate for advanced metastatic lung cancer, stages III and IV, is < 10%.54

Small cell carcinoma — nearly always caused by smoking — accounts for the remainder of lung cancer cases. This cancer spreads quickly and forms large tumors throughout the body. Typically, patients who have SCLC first have unexplained and quickly worsening signs and symptoms that may include shortness of breath, chronic cough, fatigue, anorexia and weight loss. These patients have widely disseminated disease.

Relative spread of disease is the most important SCLC staging criteria. During the limited stage, the tumor is small and confined to the chest and supravacular lymph nodes. Patients may have a cough and frequent lower respiratory tract infections. Because of the difficulty in making the diagnosis, only 30% of patients are identified as having limited SCLC. Even with a combination of aggressive chemotherapy and radiation treatment, the 2-year survival rate for limited SCLC is less than 20%.41

Extensive SCLC is cancer that already has spread throughout the body. Most patients receive their diagnosis when their SCLC is in this stage. Combination chemotherapy and radiation therapy may help to relieve symptoms. However, even with aggressive treatment, the 2-year survival rate for people who have extensive SCLC ranges from 2% to 4%.40

Screening and Lung Cancer

Effective lung cancer screening for asymptomatic high-risk individuals, such as those who are heavy smokers, remains an elusive goal. Early detection methods such as mammography for breast cancer, prostate specific antigen (PSA) blood levels for prostate cancer, and colonoscopy for colorectal cancer make it possible to find the precancerous conditions and early-stage cancers most amenable to treatment. Because of their success in reducing mortality, these exams are now routine health care assessments.

Large-scale studies in the United States and in several European countries show that annual chest radiography and sputum cytology screens of asymptomatic high-risk individuals can detect increased numbers of early-stage lung cancer. However, after 20 years of follow-up, screening did not reduce the number of people who eventually died of lung cancer.42

CT studies, alone or in combination with PET scanning, also help detect early-stage lung cancer. However, it is not yet clear whether using these medical imaging tools to screen asymptomatic high-risk patients will reduce overall lung cancer mortality rates.42

Overdiagnosis, the situation in which patients receive a diagnosis of a disease not likely to progress and cause symptoms or death, skew statistical analysis and makes it difficult to tell whether lung cancer screenings reduce or increase the overall number of lung cancer deaths. However, chest radiography is an effective way to screen patients who present with weight loss and other signs and symptoms associated with late-stage lung cancer (W Dan Tanberg, MD, University of New Mexico School of Medicine, oral communication, June 21, 2010).

The difference between overdiagnosis and a false-positive result is subtle but important. A false-positive result suggests the presence of a disease from exam findings when in fact there is no disease. In the case of overdiagnosis, disease is present, but the patient does not benefit from treatment for reasons that may include:

- The patient is more likely to die from a comorbid disease first.
- The cancer may never progress or cause symptoms.
- The patient experiences harm or death caused by the next diagnostic procedure, such as a lung biopsy.
The patient experiences harm or death caused by ensuing treatments, such as chemotherapy.

The patient endures harm caused by the psychological trauma of the cancer diagnosis.

The patient, the patient’s family, and the community experience economic harms resulting from the cost of treatment and the effects of having a pre-existing condition, along with the lost wages and productivity (Dr Dan Tanberg, oral communication, June 21, 2010).

The development of lung cancer-specific molecular imaging probes may someday help differentiate between the small lung lesions likely to progress from those that have inhibited growth caused by oxygen deprivation and immunological mechanisms. Until that time, PET, in combination with CT or MR, may help reduce some of the problems associated with the screening of asymptomatic patients and overdiagnosis.

PET imaging provides information about the biochemical processes that precede the anatomical changes caused by pathology. Therefore, taking an analytical approach to metabolic change and tumor physiology may help clinicians locate and assess a solitary pulmonary nodule without patients having to undergo a fine-needle or open chest biopsy to determine malignancy. This approach reduces:

- Patient risk.
- The likelihood of a false-negative result from inaccurate needle placement.
- Costs.

**Colorectal Cancer**

In 2008, approximately 150,000 people living in the United States received a diagnosis of colorectal cancer. Of these, nearly 1 of every 29 eventually will die of this disease. In the United States, colorectal cancer is the third most commonly diagnosed cause of cancer and cancer deaths.

Most colorectal cancers develop from adenomatous polyps located in the colon and rectum. Over time, and in combination with various genetic, environmental and lifestyle factors, some of these noncancerous growths may become malignant. Therefore, medical imaging screening assessments play an important role in both finding and removing precancerous adenomatous polyps and treating early-stage malignancies (see Figure 4).

The ACS recommends that individuals aged 50 and older and at average risk for colorectal cancer receive a colonoscopy every 10 years or a CT colonoscopy (also called virtual colonoscopy) every 5 years. The ACS also recommends that people at average risk for colorectal cancer receive a digital rectal examination and a chemical screen to detect fecal occult blood or stool DNA as a part of their annual physical exam (see Box 4).

Having a familial history of colorectal cancer puts people at high risk for developing the disease. For these individuals, the American College of Gastroenterology suggests a first colonoscopy beginning at age 40 years or 10 years younger than the age of diagnosis for their youngest affected relative. The college recommends repeat colonoscopies every 5 years for these individuals.

The overall lifetime risk of colorectal cancer is approximately 5% or 1 of every 20 people. Of these patients, 20% to 25% have a predisposing family history or illness that makes colorectal cancer more likely. Although it is not possible to eliminate risk factors associated with age, race or family history, others that relate to diet, smoking habits, obesity and physical activity are amenable to change.

Inherited gene mutations cause approximately 5% to 10% of colorectal cancer cases. Two of the most frequently encountered inherited colorectal cancers are hereditary nonpolyposis colorectal cancer, or Lynch syndrome, and familial adenomatous polyposis (FAP). Lynch syndrome, which accounts for approximately 3 of every 100 cases of colorectal cancer, is the result of changes in genes that code for DNA repair proteins. Mutant DNA repair genes located on chromosomes 2 and 3 put some individuals at high risk for colon cancer. People who have Lynch syndrome are more likely to have a family history of.
Box 4
Colorectal Cancer Risk Factors

- Colon cancer before the age of 45 years.
- Endometrial cancer.
- Other related cancers such as ovarian, kidney, stomach and liver cancer.

Testing for Lynch syndrome includes taking a detailed family history to determine whether other family members have associated early-onset cancers. Because Lynch syndrome mutation is an autosomal dominant trait, each child has a 50% chance of inheriting the disease from an affected parent. Therefore, genetic counseling plays an important role in helping patients make well-informed decisions concerning prophylactic surgical treatments, childbearing and communicating with family members.

People who receive positive Lynch syndrome results should undergo colon, urinary tract and gastrointestinal (GI) cancer screens to identify and remove any abnormal growths. The ACS recommends that women who have Lynch syndrome also undergo endometrial and ovarian cancer screens. Some people opt for surgical procedures to remove their colon, uterus or ovaries to reduce their cancer risk.

Each year, FAP is the cause of approximately 1600, or 1%, of all colorectal cancer cases. People who have FAP also are at increased risk for developing cancer of the small intestine, stomach, bones, thyroid and bile ducts. Alterations in 1 of 2 genes cause FAP. Changes in the tumor suppressor adenomatous polyposis coli (APC) gene cause the classic form of FAP. Resulting from an autosomal dominant trait, classic FAP is the outcome of inheriting a single altered APC gene. Similar to Lynch syndrome, a child has a 50% chance of inheriting a single defective APC gene from an affected parent.

Attenuated FAP is another type of inherited APC colorectal cancer. However, in this situation, the inheritance pattern is autosomal recessive and requires receiving a copy of the defective gene from both parents. Unlike classic FAP, attenuated FAP produces fewer polyps and symptoms tend to occur later in life. Because of later onset and relatively few polyps, attenuated FAP is underdiagnosed and therefore probably more common than might be expected (Lori Ballinger, MS, CGC, University of New Mexico Cancer Research and Treatment Center, oral communication, June 16, 2010).

Changes to the DNA-repairing MUTYH genes are a third cause of inherited colorectal cancer. MUTYH-associated colorectal polyp proliferation, an autosomal recessive trait, requires inheriting a damaged gene from both parents. Because attenuated FAP is autosomal recessive, children who have one parent with attenuated FAP or MUTYH-associated colorectal cancer become carriers.

Genetic testing and counseling play an important role in helping patients make important health and lifestyle decisions. Taking a detailed family history can help determine whether the patient falls within the 30% of people who have sporadic FAP. Although these individuals do not have a family history of this cancer, they can pass newly altered genes to their children. Because there is no indication for early screening, people who have sporadic FAP usually have colorectal cancer by the time they receive genetic counseling services.

When the family history and blood tests detect FAP, the genetic counselor provides information to help patients make treatment decisions and to facilitate discussion with family members. One particularly challenging issue pertains to the screening and prevention strategies for the patient’s children and other potentially affected relatives.

Many people who have FAP develop colon polyps during their teens, and more than 90% of them have polyps by age 30 years. The ACS recommends that those as young as 12 years old who are affected by FAP receive an annual flexible sigmoidoscopy or colonoscopy examination.

Unlike Lynch syndrome and noninherited colorectal cancers, people who are FAP positive have thousands
of polyps in their colon. Research has shown a 100% chance that some of these polyps will become cancerous by age 40 years. Therefore, prophylactic surgery to remove the colon and sometimes the rectum is the only way to lower the colorectal cancer risk for people who have FAP. Fortunately, some of the surgical procedures used to treat FAP preserve normal bowel function.

Surgery removes risk of colon cancer but polyps continue to grow in the surgically created pouch, rectum and small intestines. Physicians may prescribe off-label use of medications such as anti-inflammatory and anti-arthritis agents to shrink polyps as an additional treatment for many patients. Recently, the FDA approved the use of the antiarthritis cyclo-oxygenase 2 (COX-2) inhibitor celecoxib to shrink existing colorectal polyps in patients who have FAP. Research to develop medications specifically designed to shrink existing polyps or to prevent polyp growth is ongoing.

Molecular Imaging and Colon Cancer

PET combined with CT may become an alternative to endoscopic colonoscopy. The endoscopic colonoscopy procedure involves an uncomfortable bowel preparation and sedation, but the typical CT colonoscopy does not require sedation. Bowel cleansing may cause nausea and vomiting and is contraindicated for patients who have other GI tract diseases such as ulcerative colitis. The necessity to comply with an inconvenient and unpleasant preparative step makes people less willing to undergo a colorectal cancer screening procedure.

To overcome issues pertaining to dread and compliance, researchers at the University College London, are investigating combined PET-CT in patients with no bowel preparation. In a study involving 56 patients, Taylor et al had subjects undergo a PET-CT scan without bowel preparation, and then 2 weeks later undergo a traditional colonoscopy. Comparing colonoscopy results to PET-CT and CT alone showed that CT colonoscopy, with or without PET, could detect polyps 6 mm or larger. The researchers reported that all subjects preferred the PET-CT procedure. Because of the relatively low sensitivity of the PET-CT method, Taylor stated that CT colonoscopy without bowel preparation is a reasonable alternative for patients otherwise unwilling or unable to undergo the bowel cleansing portion of the procedure.

Breast Cancer

Excluding skin cancer, breast cancer is the most common cancer among women living in the United States. Researchers estimated that in 2007, more than 178,800 women received a diagnosis of invasive breast cancer and another 62,000 received a diagnosis of localized ductal and lobular carcinomas.

Cancer surveillance statistics reveal important trends in breast cancer demographics and incidence rates. For example, white women older than 40 years have a higher incidence of breast cancer than African American women in the same age group. However, African American women have a higher incidence rate before age 40 years and are more likely to die from breast cancer at every age. This information helps clinical researchers target specific at-risk populations and develop improved breast cancer detection, treatment and monitoring protocols.

Research shows that age, genetics, lifestyle, income level and access to mammograms and medical care are some of the demographic factors that influence breast cancer incidence and survival rates. For women living in the United States, the overall lifetime risk of developing breast cancer is 1 in 8 or 12.5%.

Reviewing breast cancer surveillance data can uncover subtle influences on breast cancer incidence rates.

■ 1980-1987 — incidence rates increased by 3.7% per year.
■ 1987-2001 — incidence rates increased by 0.5% per year.
■ 2001-2004 — incidence rates decreased by 3.5% per year.

There are many ways to account for the increase between the years 1980 and 2001. Life-long environmental exposures, obesity, delayed childbearing, widespread use of hormone replacement therapy (HRT) and an aging population may partially explain the increase. Most epidemiologists believe, however, that the effective use of mammography to detect cancers 1 to 3 years before a woman is symptomatic is responsible for making breast cancer seem more widespread.

The reasons for the recent downturn in breast cancer incidence are less clear. Some researchers have cited economic factors leading to a decrease in the number of women aged 40 years and older who report having a mammogram within the past 2 years. Others noted that the 2002 publication of results from the Women’s Health Initiative, linking HRT to increased risk for breast cancer, may have caused many women to stop or never initiate HRT.
Screening mammography and early breast cancer detection improve survival. For example, the 5-year survival rate of 94% for women who have tumors < 2 cm drops to 66% for women whose tumors are > 5 cm. For most women, the annual mammogram is an effective way to detect tumors many years before physical symptoms, such as a painless mass, redness, dimpling and nipple discharge, develop. However, for women who have dense breast tissue, the annual mammogram may not detect early-stage tumors. Some women who have dense breasts also may have inherited the BRCA-1 or BRCA-2 gene mutations associated with early-onset breast cancer. For them, other imaging options are especially important.

Differences in tissue composition can affect the radiographic appearance of the female breast. Fatty areas are radiographically lucent and therefore appear black on radiographic images. Epithelia, fibrous connective tissues and tumors, all radiographically dense, appear light or white on radiographic images. Reduced contrast makes it difficult to detect tumors in radiographically dense breasts.

At first glance, one might assume that high-density tissue camouflages small tumors and thereby delays diagnosis. Camouflage certainly is an important factor, but researchers at the Ontario Cancer Institute in Canada have found that women who have dense breasts also have an intrinsic risk of breast cancer that is 2 to 6 times that of women of the same age who have radiographically lucent breasts. Genetics, as well as the cellular characteristics of the dense breasts, appear to be important contributing factors.

Research by Norman Boyd, MD, DSc, and Ontario Cancer Institute colleagues has shown a strong correlation between the percentage of dense breast tissue and as yet undetermined inherited causes. Comparing the breast densities of more than 800 fraternal and maternal twin pairs living in North America and Australia showed that factors such as menopausal status, weight, number of live births and environmental influences accounted for only 20% to 30% of the age-adjusted variation in observed breast density. Why women with dense breasts are more prone to breast cancer is a perplexing question. Researchers at the Mayo Clinic in Rochester, Minnesota, are taking a unique approach to discovering the subtle cellular differences between dense and fatty breasts. Karthik Ghosh, MD, a Mayo Clinic breast cancer researcher and clinician, examined core-needle biopsies taken from healthy women without a history of breast disease. By microscopically observing dense and nondense areas taken from the same breast, Ghosh and her team found that high-density areas contained more epithelia and stroma and less fat than nondense areas. Although it is not yet possible to link this observation to breast cancer causality, Ghosh stated that breast tumors tend to originate in epithelia. Therefore, having more epithelial cells may be an important breast cancer risk factor.

In a parallel Mayo Clinic study, researchers found that dense breasts contain more aromatase, a naturally occurring enzyme that converts androgen hormones into estrogen, than nondense breasts. Estrogen is a risk factor associated with breast cancer development. The combination of these cellular and enzymatic findings may be an explanation for the effect of dense breast tissue on increased breast cancer risk.

Each year, of the approximately 200 000 women living in the United States who receive a breast cancer diagnosis, 5% to 10% have an inherited form of the disease. Alterations in BRCA genes that normally suppress tumor growth greatly increase a woman’s risk for developing breast and ovarian cancers before menopause.

Medical researchers estimate that 1 of every 800 people in the general population carries altered cancer-predisposing BRCA-1 and BRCA-2 genes. It is estimated that 85% of women who carry either the BRCA-1 or the BRCA-2 mutations develop a cancerous breast lesion during their lifetime.

Nearly 6% of men who carry altered BRCA genes, and especially the BRCA-2 alteration, have breast cancer by age 70 years. Men who carry the altered BRCA-2 gene also are at added risk for prostate cancer.

Genetic testing and genetic counseling are the first steps for women whose close relatives (male or female) have received a diagnosis of breast, ovarian or prostate cancer. This is especially important if the cancer occurred before the age of 50. Having a family member who received a positive BRCA-1 or BRCA-2 test result is another reason to consider undergoing a blood test for altered BRCA genes.

For women found to carry either altered gene, regular breast examination including the following is the first line of defense:

- Monthly self-examination.
- Clinical breast examination every 6 months beginning at age 25 years.
- Annual mammogram beginning at age 25 to 30 years.

Other options for at-risk women include:

- Ovarian cancer screening.
- Prophylactic mastectomy.
- Prophylactic oophorectomy.
- Lifestyle changes such as a low-fat, high complex carbohydrate diet and exercise.

There is some evidence indicating that tamoxifen, which blocks the effects of estrogen on breast tissue, may reduce cancer risk for some BRCA-positive women.\textsuperscript{56}

**Molecular Breast Imaging for Breast Cancer**

For most women, mammography still is the most effective breast imaging modality. However, imaging techniques such as ultrasound and MR imaging can improve the ability to identify changes in breast tissue, differentiate between fluid-filled cysts and tumors and screen suspicious areas for tumors. Molecular breast imaging, a relatively new modality that combines structural and physiological assessments, holds promise as a screening and diagnostic tool for women who have metastatic breast cancer or who have dense breasts.

Since 2004, the Centers for Medicare and Medicaid Services (CMS) has approved coverage for FDG-PET scanning under the following circumstances:
- As an adjunct to standard imaging modalities to stage breast cancer in patients who have distant metastases.
- Restaging patients with local-regional recurrence of metastasis.
- As an adjunct for monitoring tumor response to treatment for locally advanced metastatic breast cancer before an anticipated change in therapy.\textsuperscript{62}

Ongoing research efforts are developing and testing new molecular imaging compounds to eventually give clinicians the ability to choose the most tumor-specific strategies and monitor responses to treatment. Molecular breast imaging compounds under consideration are those that target DNA replication and cell division, programmed cell death or apoptosis and various cell surface receptors (see Table 3).\textsuperscript{62}

Cancer cells tend to proliferate or divide more rapidly than noncancerous cells. Recently, the compound 3'-deoxy-3'-(18) F-fluorothymidine (\textsuperscript{18}F-FLT) has been considered as a new cell proliferation marker. The parent compound, thymidine, is a structural component of DNA. Therefore, uptake of \textsuperscript{18}F-FLT provides a physiological measure of DNA synthesis and cell division. Research in mouse breast tumors has shown that FLT holds potential as a reliable PET imaging agent for demonstrating responses to antiproliferative treatments for breast cancer.\textsuperscript{65}

Estrogen receptor molecules are proteins that respond to estrogen. Estrogen target tissues include the brain, heart, uterus, bone, liver and breast. Hormone molecules circulating in blood bind to tissue-specific estrogen receptors and increase DNA replication and cell division. Under normal conditions, estrogen stimulates the cell division needed to prepare the uterus for implantation and pregnancy, maintain healthy bones and prepare the breast for lactation. Research has shown that environmental and noncyclic estrogen exposures can increase cancer risk.

Although estrogen does not directly cause breast cancer, the hormone stimulates cell proliferation in tumors that contain estrogen receptors (ERs). Anti-estrogen therapy using estrogen-receptor blocking drugs such as tamoxifen and raloxifene is a typical treatment for ER+ tumors.\textsuperscript{64}

Typically, immunohistochemistry, which requires a biopsy and staining of paraffin-imbedded sections with anti-ER antibodies, is the method used to assess breast tumors for the presence or absence of estrogen receptors (see Figure 5). The level of observed estrogen receptor expression is a source of important prognostic information and indicates the likelihood of a favorable response to hormone therapy.\textsuperscript{65}

Peterson et al showed that PET scanning with \textsuperscript{18}F-fluoroestradiol (FES) has the potential to become a reliable tracer for the evaluation and management

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<th>Table 3</th>
<th>Molecular Breast Imaging: PET Tracers\textsuperscript{62}</th>
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<td><strong>Tracer</strong></td>
<td><strong>Target</strong></td>
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<tr>
<td>Fluoro-L-thymidine F 18 (FLT)</td>
<td>DNA replication and cell division</td>
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<tr>
<td>Annexin V derivatives</td>
<td>Programmed cell death</td>
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<tr>
<td>Fluoroestradiol F 18 (FES)</td>
<td>Estrogen receptor</td>
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\textsuperscript{PET = positron emission tomography.}
of ER-responsive breast cancer. In a small study involving 17 patients (16 women and 1 man) with primary or metastatic breast cancer, $^{18}$F-FES showed excellent agreement with ER expression as measured by 3 different in vitro score methods, including immunohistochemistry (see Figure 6). The researchers stated that FES-PET has several advantages over more traditional assessment methods that include:

- Noninvasive assessment and minimized potential for spreading tumor cells along the path made by the biopsy needle.
- In vitro “real-time” measurement.
- Assessment of the patient’s entire tumor burden that may include metastatic tumors and difficult-to-biopsy tumors.

A new use for sestamibi shows promise as an effective molecular breast imaging agent specifically for detecting lesions in dense breasts. To overcome the difficulty of adapting conventional gamma cameras for breast imaging studies, Mayo Clinic researchers, in collaboration with Gamma-Medica Ideas (Northridge, California) and GE Healthcare (Chalfont St Giles, United Kingdom), have developed a dual-head gamma camera system (Carrie Hruska, assistant professor of radiologic physics at the Mayo Clinic in Rochester, Minnesota, oral communication, December, 2009). Their camera system is sensitive enough to detect tumors < 10 mm in diameter. Some of the advantages of a dual-headed camera include:

- Ability to detect lesions located opposite a single detector.
- Ability to estimate lesion depth and size.
- Increased comfort — 15 lbs compression force vs 45 lbs compression force needed for traditional mammography.

Although the researchers observed $^{99m}$Tc sestamibi throughout the breast, cancerous areas preferentially absorbed the imaging agent (see Figure 7). Some benign conditions such as fibroadenomas occasionally produced false-positive results. However, scientists noted that the false-positive rate was less than the 10% associated with conventional mammography.

Surgery later identified 82 cancers in 54 patients. Of these, the dual-headed camera technology detected 76 cancers, representing a 93% success rate. Researchers believe that missed lesions were < 4 mm in diameter or resulted from poorly positioned breasts.

**Prostate Cancer**

In the United States, approximately 1 in every 6 men will receive a prostate cancer diagnosis sometime during
A digital rectal exam allows the clinician to feel for changes in prostate size and for the presence of hard or lumpy areas. A blood test for prostate specific antigen (PSA) is a first step in distinguishing a benign condition from a cancerous one.

Research shows that the benefits of regular prostate cancer screening on long-term patient outcomes are inconclusive. However, the ACS encourages health care professionals to offer their male patients aged 50 years and older the option of receiving a yearly digital rectal exam and PSA test. In situations in which there is increased prostate cancer risk, such as African American men and men who have a first-degree relative diagnosed with prostate cancer before age 60 years, testing may begin at age 40 years (Dr Fancovic, oral communication, January 15, 2009).

Benign prostatic hyperplasia (BPH), believed to be the result of changes in sensitivity to testosterone, is a problem that most men older than 50 years experience to varying degrees. Increased cell division begins in the prostate transition zone — a ring of tissue that encircles the urethra — and grows inward. As this area enlarges, it squeezes the urethra and impedes urination. Urine retention, dribbling and back pain are some of the symptoms that cause men to visit a physician for evaluation and treatment. By itself, an enlarged prostate is not harmful, and if the enlarged prostate did not cause urination difficulties, BPH might never require treatment.

Figure 6. Images illustrating the correlation between fluoroestradiol (FES) F18 uptake and subsequent response to hormonal therapy. Coronal images of FES uptake (left column) and fluorodeoxyglucose (FDG) F 18 uptake before therapy (middle column), along with FDG uptake after hormonal therapy (right column) are shown for 2 patients. Patient 1 (top row) was previously treated with adjuvant tamoxifen and had a sternal recurrence of breast cancer 4 years after primary tumor treatment. Her lesion demonstrated high pretherapy FES uptake (arrow; image also shows liver and bowel uptake, both normal findings). FDG images taken before and after 6 weeks of letrozole treatment showed a significant decline in FDG uptake, with subsequent excellent clinical response. Patient 2 (bottom row) had newly diagnosed metastatic breast cancer that had not previously been treated. Her primary tumor was ER+ by immunohistochemistry and showed FES uptake (not shown). However, her pretherapy FES images showed no uptake at bone metastases documented by multiple imaging modalities, including FDG-PET. The patient received multiple hormonal treatments with no response of the bone metastases, indicated by the post-therapy FDG-PET exam, despite response by the primary tumor. The patient ultimately had progression of bony metastases and succumbed to her disease. Image courtesy of the University of Washington, Seattle Cancer Care Alliance.

There are medical and surgical treatment options for BPH. Medical treatments include taking α-blockers such as tamsulosin to relax the smooth muscle within the prostate and bladder neck or 5-α-reductase inhibitors such as finasteride to reduce prostate size by inhibiting the production of testosterone within the prostate. Surgical treatment involves transurethral resection of the prostate to reduce size and thereby eliminate or lessen symptoms.
the cancer diagnosis, patients must undergo a TRUS-guided transrectal prostate biopsy. A spring-loaded 18-gauge biopsy needle is placed in the rectum to remove prostate cores that are approximately 1.2 mm in diameter and 12 to 15 mm long (Myra Zucker, PA, University of New Mexico Hospital, Albuquerque, New Mexico, oral communication, January 6, 2009).

To make a reliable diagnosis, the prostate biopsy sampling pattern must be one likely to find any abnormalities. Although there is a wide range of biopsy protocols, a systematic 12-core TRUS-guided procedure through the rectum and into the prostate is becoming the accepted standard (see Figure 8).

With the exception of finding prostatic intraepithelial neoplasia (PIN), the histopathology study differentiates between benign and cancerous pathologies. PIN is a precancerous condition discovered in up to 16% of men who undergo a TRUS-guided biopsy. Low grade, or grade I, PIN shows few cytological changes. High-grade, or grade III, PIN demonstrates cytological changes approaching those associated with prostate cancer. Research shows that PIN incidence increases with age and often develops into prostate cancer over time (see Figure 9).

Unlike BPH, prostate cancer grows outward and may not produce symptoms or discomfort for months or years. Eventually the malignant growth invades nearby tissues and organs. With time, the cancer may spread to bones and other parts of the body. Elevated PSA blood levels signal that further testing is needed.

PSA is a protein made by prostate gland cells. Semen contains the most PSA; however, a small amount also is found in blood. Normally, men have < 4 nanograms PSA per milliliter of blood. A PSA between 4 and 8 ng/mL may indicate either BPH or prostate cancer. PSA levels > 8 ng/mL suggest prostate cancer. PSA levels tend to increase with age and as a result of a recent digital exam or ejaculation, without presence of prostate cancer. Prostate infections also increase the amount of PSA detected in blood.

Transrectal ultrasound (TRUS) of the prostate may clarify the cause for digital rectal examination findings and high PSA blood levels. However, to confirm

Figure 7. A comparison between a digital mammogram and a molecular breast image (technetium 99m sestamibi, left cranio-caudal projections) from a patient enrolled in a screening study to compare the 2 modalities in asymptomatic women at increased risk of breast cancer. The mammogram was interpreted as negative. The molecular breast image showed a lesion in the left breast. The patient had a 13-mm invasive lobular carcinoma. Image courtesy of the Mayo Clinic, Rochester, MN.

There are no established treatment guidelines for men whose biopsies reveal PIN. The general recommendation is a follow-up biopsy within 3 to 6 months and every 1 to 2 years afterward, along with regular PSA testing. Studies show that most patients who have Grade II or Grade III PIN develop prostate cancer within 10 years.72

As with PIN, histological appearance is the basis for scoring prostate cancer. The Gleason score evaluates 2 different cell patterns and how much each differs from normal prostate tissue. Based on a 1 (most like normal tissue) to 5 (most different from normal tissue) ranking system, the Gleason score is the total of 2 cell pattern scores. Therefore, Gleason scores range from 2 to 10. A high Gleason score indicates a high-grade tumor that is more likely to spread than one that receives a lower score.71

Staging, using a bone scan as well as MR or CT imaging, is another important aspect of the patient's diagnostic work-up. Staging helps determine whether the tumor already has invaded nearby tissues or has spread to other parts of the body (see Table 4).

Prostate cancer treatment depends on many factors that include the patient's age, overall health and symptoms. The Gleason score, the number of biopsy cores that contain cancer cells and tumor stage are other important treatment considerations.

Active surveillance is a realistic option when the risks of treatment outweigh the benefits. During the surveillance period, the patient receives regular PSA testing, and after 1 year, another biopsy to assess Gleason score changes. A significant increase in either PSA blood levels or the Gleason score often is reason to begin active treatment. Prostate cancer treatment options may include:

- Surgery to remove the prostate.
- Cryosurgery to freeze and kill prostate tissue.
- Transurethral resection to relieve symptoms.
- External radiation therapy to kill cancer cells and reduce tumor volume.
- Internal radiation therapy to kill cancer cells and reduce tumor volume.
- Medical hormone therapy to block the action or synthesis of testosterone.
- Surgical hormone therapy to remove the testicles.
- Chemotherapy to treat metastatic prostate cancer that no longer responds to hormones.

Patient willingness to accept the quality-of-life changes that may occur as a result of treatment is
Recently completed “proof of concept” Trofex (Molecular Insight Pharmaceuticals, Cambridge, Massachusetts) phase I studies show the merit of the \(^{123}\)I strategy. According to Molecular Insight’s CEO John Babich, PhD, the test compounds MIP-1072 and MIP-1095 produce a strong signal in soft tissues, lymph nodes and bone, thus making it possible to give patients quantitative and objective information concerning the amount and location of recently diagnosed and recurrent prostate cancers (oral communication, January 13, 2009). Having this information will help clinicians and patients balance quality-of-life concerns with decisions concerning timing, risks and benefits of initiating medical or surgical treatment.

**Conclusion**

Molecular imaging has the potential to improve the diagnosis and treatment of a wide spectrum of diseases and conditions. However, physiology-based analysis makes molecular imaging fundamentally different from structural modalities such as radiography, MR and CT scanning. The ability to visualize, characterize and measure biological processes at the molecular and cellular levels helps researchers to dissect and understand the genesis of various disease processes and helps clinicians make a diagnosis long before patients report symptoms.

This raises the possibility that molecular imaging, rather than the patient history, physical exam and assorted laboratory tests, eventually may be the evaluation tool used to assess risk for diseases such as diabetes, heart disease and cancer. While this scenario certainly raises many practical questions and concerns, the

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**Table 4**

**Prostate Cancer Staging**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Cancer not felt during a digital rectal exam and not observed by ultrasound. Cancer is found by chance during surgery for BPH. Gleason score less than 4.</td>
</tr>
<tr>
<td>II</td>
<td>May be felt during digital rectal exam or observed by ultrasound. Gleason score 4 or greater. Tumor contained within the prostate.</td>
</tr>
<tr>
<td>III</td>
<td>Tumor extends beyond the prostate and may have invaded the seminal vesicles. Cancer has not spread to the lymph nodes.</td>
</tr>
<tr>
<td>IV</td>
<td>Tumor may have invaded the bladder, rectum and beyond the seminal vesicles. The tumor may have spread to the lymph nodes, bones, or other organs.</td>
</tr>
</tbody>
</table>


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For some men, the possibility of incontinence, impotence or the potential discomforts associated with hormonal ablation far outweigh the benefits of treatment (John W Babich, PhD, Molecular Insight Pharmaceuticals Inc, Cambridge, Massachusetts, oral communication, January 20, 2009). Resistance to treatment makes sensitive and specific molecular imaging techniques especially important.

**Prostate Cancer and Molecular Imaging**

Molecular imaging studies can make the decision to begin active prostate cancer treatment less ambiguous. ProstaScint (EUSA Pharma, Langhorn, Pennsylvania) is an In 111-tagged monoclonal antibody used for gamma camera imaging. The monoclonal antibody recognizes and binds to prostate-specific membrane antigen (PSMA), a glycoprotein produced by prostatic epithelial cells. Because prostate cancer cells make more PSMA than normal or BPH prostate cells, the ProstaScint agent is used to:

- Stage newly diagnosed patients at high risk for metastases.
- Diagnose metastases in patients who have undergone prostatectomies and who have rising PSA levels.

In combination with structural imaging, the specially tagged antibodies can help to identify lymph nodes containing metastatic prostate cancer cells 1 to 3 years before they are detectable by CT or MR alone.\(^{15}\)

Molecular Insight Pharmaceuticals Inc, a biopharmaceutical company in Cambridge, Massachusetts, that specializes in molecular medicine, is taking a slightly different approach to developing a prostate cancer molecular imaging probe. Recognizing that PMSA also is an enzyme, the company is testing \(^{123}\)I-labeled small molecules, rather than antibodies, that have an affinity for PMSA enzyme binding sites (see Figure 10).
more immediate challenges are making the technology compatible with existing instrumentation, linking research findings to patient care, and making molecular imaging easy for practitioners to use.

References


Figure 10. Patient with prostate cancer. The top image is a CT scan; the bottom is a CT scan with the nuclear medicine image (Trofex, Molecular Insight Pharmaceuticals, Cambridge, Massachusetts) overlaid in color. The Trofex scan illuminates the cancer invading the patient’s vertebrae (yellow/white spot on the spine). Image courtesy of Molecular Insight Pharmaceuticals Inc, Cambridge, MA.


Janet Yugoda Shagam, PhD, is a medical and science writer and a regular contributor to Radiologic Technology. In addition to freelance writing, Dr Shagam teaches writing workshops at the University of New Mexico in Albuquerque, the University of New Mexico School of Medicine and the Max Planck Institute in Göttingen, Germany. She is a member of the National Association of Science Writers.

The author wishes to thank Myra Zucker, PA, for providing gross and histological images, and Lori Ballinger, MS, CGC, and Edward Fancovic, MD, for helpful discussions.

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Directed Reading Continuing Education Quiz

Cancer-focused Molecular Imaging

To receive Category A+ continuing education credit for this Directed Reading, read the preceding article and circle the correct response to each statement. Choose the answer that is most correct based on the text. Transfer your responses to the answer sheet on Page 86 and then follow the directions for submitting the answer sheet to the American Society of Radiologic Technologists. You also may take Directed Reading quizzes online at www.asrt.org. Effective October 1, 2002, new and reinstated members are ineligible to take DRs from journals published prior to their most recent join date unless they have purchased a back issue from ASRT. Your access to Directed Reading quizzes for Continuing Education credit is determined by your area of interest. For access to other quizzes, go to www.asrt.org/store.

*Your answer sheet for this Directed Reading must be received in the ASRT office on or before this date.

1. New ways to identify molecular markers of many diseases and conditions are the result of new:
   a. immunohistochemistry staining techniques.
   b. sophisticated deoxyribonucleic acid (DNA) mapping and sequencing techniques.
   c. positron emission tomography (PET) technology and education.
   d. radioisotope-labeled lectins.

2. Research shows that ______ are the underlying cause of cancer.
   a. poor eating habits
   b. high pollution levels
   c. DNA-directed changes
   d. lifestyle risks such as smoking

3. Another name for recombinant DNA technology is:
   a. genomics.
   b. genetic engineering.
   c. proteomics.
   d. DNA sequencing.

4. ______ is a physiology-based imaging modality.
   a. Computed tomography (CT)
   b. Magnetic resonance (MR)
   c. Radiography
   d. PET

5. Single-photon emission computed tomography:
   a. provides detailed anatomical information.
   b. is inexpensive and widely available.
   c. can locate and link radioactive hot spots to their anatomical locations when fused with MR or CT.
   d. does not require a camera.

6. Use of ______ was one of the first examples of molecular imaging.
   a. iodine I 125 to diagnose and treat thyroid disease
   b. carbon C 14 to date archeological remains
   c. strontium Sr 90 to image bones
   d. oxygen O 16 to look for brain lesions

Continued on next page
7. Individuals can modify cancer risks such as:
   a. autosomal DNA changes and air pollution.
   b. recessive DNA changes and exercise habits.
   c. race and diet.
   d. diet and smoking.

8. In 2008 in the United States, the top causes of death were _____ and _____.
   a. AIDS; tuberculosis
   b. cancer; infectious diseases
   c. industrial accidents; heart disease
   d. heart disease; cancer

9. _____ is the most frequently diagnosed cancer in the United States.
   a. Breast cancer
   b. Melanoma
   c. Nonmelanoma skin cancer
   d. Prostate cancer

10. The most common cause of all types of skin cancer is _____.
    a. smoking
    b. sun/ultraviolet ray exposure
    c. exposure to industrial solvents
    d. chronic infection

11. _____ is used to determine whether melanoma has spread.
    a. Electrodesiccation
    b. Sentinel node biopsy
    c. Mohs micrographic surgery
    d. Cryosurgery

12. At the time their cancer is diagnosed, most patients have early-stage lung cancer.
    a. true
    b. false

13. The leading cause of lung cancer in nonsmokers is:
    a. ionizing radiation.
    b. inherited forms of the disease.
    c. industrial pollution.
    d. naturally occurring radon gas.

14. According to the Directed Reading, commonly used staging criteria for nonsmall cell lung cancer include _____.
    a. sentinel node biopsy results
    b. coughing and weight loss
    c. the ability to surgically remove the tumor
    d. sputum cytology

15. American and European studies have shown that annual sputum cytology screens and _____ of asymptomatic high-risk individuals can detect early-stage lung cancer.
    a. chest radiography
    b. CT scans
    c. PET scans
    d. spirometry screens

16. The concept of overdiagnosis refers to:
    a. including false-positive results in lung cancer morbidity and mortality studies.
    b. including false-negative results in lung cancer morbidity and mortality studies.
    c. patients receiving a diagnosis of a disease not likely to progress or cause symptoms or death.
    d. finding disease in low-risk patients.

Continued on next page
17. The American Cancer Society recommends that people aged 50 years and older at average risk for colorectal cancer undergo a colonoscopy:
   a. every 7 years.
   b. only when they have symptoms such as rectal bleeding.
   c. only if they have a close family member who had colorectal cancer.
   d. every 10 years.

18. Inherited gene mutations cause approximately ______% to ______% of colorectal cancer cases.
   a. 1; 3
   b. 5; 10
   c. 11; 13
   d. 15; 20

19. The only way to lower colorectal cancer risk for people who have familial adenomatous polyposis is through ______.
   a. high doses of vitamin C
   b. prophylactic removal of the colon and sometimes the rectum
   c. high doses of steroids
   d. prophylactic radiation of the colon and rectum followed by tamoxifen therapy

20. London researchers recently studied a new PET-CT colonoscopy method to overcome dread and compliance issues related to colonoscopy by eliminating ______ from the procedure.
   a. radiation
   b. general anesthesia
   c. bowel preparation
   d. advance scheduling

21. Researchers believe that the increase in breast cancer rates between 1980 and 2001 resulted mostly from:
   a. earlier childbearing.
   b. effective use of mammography to detect early-stage cancers.
   c. exposure to radioactive fallout during childhood.
   d. publication of the Women’s Health Initiative results.

22. Research by Boyd showed a strong correlation between the percentage of dense breast tissue and ______.
   a. inheritable causes
   b. environmental exposures to toxins
   c. delayed childbearing
   d. hormone replacement therapy

23. Researchers believe that ______% of women who carry the BRCA-1 or BRCA-2 gene mutations will develop a cancerous breast lesion during their lifetime.
   a. 25
   b. 45
   c. 65
   d. 85

24. Typically, ______ is used to assess breast tumors for the presence or absence of estrogen receptors (ERs).
   a. diagnostic mammography
   b. MR imaging
   c. immunohistochemistry
   d. cytopathology

Continued on next page
25. Researchers are using the compound $^{18}$F-fluorodeoxyglucose to evaluate:
   a. rapidly dividing breast cancers.
   b. estrogen-receptor responsive breast cancer.
   c. benign prostatic hyperplasia.
   d. prostate cancer.

26. Changes in sensitivity to testosterone can cause _______.
   a. benign prostatic hyperplasia
   b. reductions in prostate-specific antigen blood levels
   c. prostatic intraepithelial neoplasia (PIN)
   d. prostate cancer

27. Which of the following statements are true regarding PIN?
   1. Low-grade PIN shows few cytological changes.
   2. PIN incidence increases with age.
   3. PIN often develops into prostate cancer over time.
   
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2 and 3

28. The Gleason score evaluates:
   a. 2 different cell patterns and how much each differs from normal prostate tissue.
   b. 2 different cell patterns and how much each differs from normal breast tissue.
   c. differences between BPH and PIN.
   d. differences between BRCA-related and ER+ breast cancer.

29. The molecular imaging probe ProstaScint is an indium 111 tagged monoclonal antibody that:
   a. targets and kills breast cancer cells.
   b. identifies genetic alterations that cause BPH.
   c. recognizes and binds to prostate-specific membrane antigen.
   d. measures PSA levels.

30. Studies of the test compounds MIP-1072 and MIP-1095 produce a strong signal in _______, thus making it possible to give patients quantitative information about the location and extent of prostate cancers.
   1. soft tissues
   2. lymph nodes
   3. bone
   
   a. 1 and 2
   b. 1 and 3
   c. 2 and 3
   d. 1, 2 and 3

For your convenience, the evaluation and answer sheet for this Directed Reading now immediately follow the quiz. Just turn to Pages 85 and 86.
Directed Reading Evaluation
Cancer-focused Molecular Imaging

10805 - 02 316359

Thank you for taking the time to complete this survey. Your opinion helps us serve you better. Your comments will remain confidential and will not affect the scoring of your Directed Reading (DR) test. Choose only ONE response for each question. Use a blue or black ink pen. Do not use felt tip markers. Completely fill in the circles.

1. What is your primary area of practice?
- Administration/Management
- Education
- Quality Management
- RIS/HIS/Information Systems
- Bone Densitometry
- Magnetic Resonance
- Radiation Therapy
- RN
- Cardiovascular-Interventional
- Mammography
- Radiography
- Sonography
- Computed Tomography
- Nuclear Medicine
- Research
- Other

2. Which of the following best describes the highest educational level you have attained?
- Student who has not yet taken Registry exam
- Associate degree
- Master's degree
- Certificate
- Bachelor's degree
- Doctoral degree (e.g., Ph.D. or Ed.D.)

3. Why did you choose to complete this DR?
- Interested in the topic
- Topic pertained to my area of practice
- Other
- DR had the right number of CE credits
- Needed CE credits immediately

4. How relevant is this DR to your practice?
- Extremely relevant
- Very relevant
- Relevant
- Somewhat relevant
- Not relevant

5. How beneficial is this DR to your professional or personal development?
- Extremely beneficial
- Very beneficial
- Beneficial
- Somewhat beneficial
- Not beneficial

6. How would you rate the level of difficulty of this DR?
- Too difficult
- Somewhat difficult
- Just the right level
- Somewhat easy
- Too easy

7. How would you rate the length of this DR?
- Too long
- Somewhat long
- Just the right length
- Somewhat short
- Too short

8. Did this DR meet your expectations?
- Yes
- No
- Partially

9. Would you recommend this DR to a colleague?
- Yes
- No

10. Overall, how valuable are the Directed Readings to you?
- Very valuable
- Considerably valuable
- Valuable
- Slightly valuable
- Not very valuable

If you have comments about this Directed Reading, please write them below or send them separately to Ellen Lipman, Director of Professional Development, ASRT, 15000 Central Ave SE, Albuquerque, NM 87123-3909 or elipman@asrt.org.
Cancer-focused Molecular Imaging

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ASRT must receive the original answer sheet before the quiz expires and before the end of the CE biennium for which you want credit.
New or rejoining members cannot take DR quizzes from journals published before their most recent join date unless they purchase access to the DR quiz.

Identification Section
We need your Social Security number to track your CE credits. Please fill in your SSN in the boxes on top; then fill in the circle corresponding to each number under the box. The circles must be filled in accurately.

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To ensure proper credit please PRINT the following information.
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City _________________________________
State___________ ZIP______________
Work Phone________________________
Home Phone_______________________

CE Answers Section
USE A BLUE OR BLACK INK PEN. Completely fill in the circles.

Get immediate Directed Reading quiz results and CE credit when you take your test online at www.asrt.org/DRQuiz.

Note: For true/false questions, A=true, B=false.

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No Photocopies Accepted
How To Grow a Technologist

Lorraine M McCurdy, BHS, R.T(R)(M), RDMS, CRA, is the imaging manager at Roper St Francis Healthcare in Charleston, South Carolina.

“My Perspective” features guest editorials on topics in the radiologic sciences. Opinions expressed by writers do not necessarily reflect those of the ASRT. Those interested in writing an editorial should e-mail communications@asrt.org.

We live in times of plenty — plenty of applicants, plenty of graduates, plenty of highly skilled technologists, and no worries about filling any open positions. But I have been a manager long enough to remember having a position open for 18 months and filling it with the first applicant who had a pulse! During times of plenty it is easy to forget that things will not always be this way and hard to remember that we have an obligation to help grow future radiologic technologists. I know that times will come again when applicants will be scarce and our hospitals and imaging centers will suffer, so in our department we have a 3-pronged approach to ensuring a future with many dedicated young people seeking health care careers.

First, we don’t limit job shadowing to 1 day a year, but have an open-door policy and open arms for anyone interested in learning about careers in imaging. At Roper St Francis Healthcare we offer one-time educational experiences to introduce students aged 14 years and older and interested adults to a particular health care career by pairing them with an employee for a period of 8 hours or less. The student “shadows” an employee as he or she performs normal activities. Students are allowed to observe, ask questions and gain first-hand knowledge of a career and the workplace environment.

If they are interested in an experience lasting longer than 8 hours, they are invited to apply through our volunteer department and attend a volunteer orientation. Each student signs a job shadow request form that lists his or her rights and responsibilities. Students understand that they must be supervised at all times by their mentor and they must respect the confidentiality of the employees and patients at Roper St Francis Healthcare. Parents or guardians must sign for students younger than 14 years old. Each mentor agrees to supervise and be responsible for his or her student during the job shadowing experience.

Second, our staff attends many career fairs at local junior and senior high schools. We have created a PowerPoint presentation (Microsoft Corporation, Redmond, Washington) describing imaging careers and it is full of interesting images and photos of our staff. Living in Charleston, South Carolina, we have some opportunities for unusual images and the students’ favorite is always the foot with a shark-sized bite out of the heel! Students who have family members in health care careers or who have experienced a health crisis in either their own lives or with a close family member always express the most interest, but we believe it is important to make sure that all students are aware that health care careers do not begin with “nurse” and end with “physician.” We tell the students that imaging careers marry an opportunity to make a difference in people’s lives and the use of really cool technology.

Especially now, when jobs are hard to come by and students see their parents, older siblings, other family members and friends struggling to find and keep worthwhile work, I think it is important to give them the message that careers in health care will be vital and necessary throughout their lives. Someone across the world may be able to interpret medical images and diagnose diseases, but technologists always will be needed to put their hands on patients.

Finally, we are extremely proud of our SCRUBS (Students Can Really Use Bedside Skills) program. Students aged 14 to 16 can enroll in either a week-long summer camp or a quarterly evening session. The imaging department sponsors one of the quarterly sessions, during which more than 50 students are separated into groups and rotated through each of our modalities. A department employee volunteers to demonstrate the modality and talk about his or her individual career. During the summer camp session, we host the students one morning and also participate in other parts of
the program. Students especially love the behind-the-scenes tours of the operations plant, kitchens and supply areas. Our facility’s educator helps teach the students cardiopulmonary resuscitation and first aid. The students all wear special scrub tops identifying them as SCRUBS camp members and they love to collect the different colors offered each year. Other quarterly sessions have included tours of the operating rooms, where the students practice sterile techniques and see samples of surgically removed tissues; visits to the nursery and labor and delivery department; and nursing skills classes.

As you can see, we dedicate many hours to the important task of creating interest in health care careers because we believe that it is vital to our future to have talented and interested students thinking about health care careers. Our staff is dedicated to mentoring and they are cheerleaders for their careers. As an added bonus, they encourage valuable support staff to think about moving up the career ladder. For example, we have an extremely talented special procedures technologist who began his career as a transporter, and a computed tomography technologist who originally worked as a clerk. Teaching and mentoring are projects our entire department has embraced and we encourage other departments to dedicate part of their valuable time to this important cause.

◆

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The American Registry of Radiologic Technologists (ARRT) recently topped 300 000 registered technologists! This column examines how we got there and when we expect to reach the next milestone.

1922 to 2010

The first individual to earn certification and registration was Sister M Beatrice Merrigan of St Anthony’s Hospital in Oklahoma City, Oklahoma, who earned her credential in November 1922. By the end of that decade there were 643 registered technologists. Growth continued at a slow rate until the first of the baby boom generation (those born between 1946 and 1964) began entering the profession in the 1960s. By the end of the 1960s, ARRT had reached the 50 000 milestone. By the end of the 1970s, the number topped 100 000. We reached the 200 000 mark by the mid 1990s. The rate of increase clearly accelerated in the second half of ARRT’s existence, as illustrated by the fact that it took about 60 years to reach the first 100 000, only 15 years to reach 200 000, and another 15 years to reach 300 000 (see Figure 1).

Will this rate of increase continue into the future? If the recent rate of increase was simply extrapolated, one might conclude that there will be 400 000 R.T.s in 2025 and 500 000 in 2040. The actual growth pattern will depend on demographic factors, technological developments, economic conditions and the regulatory environment, to name just a few of the important forces. These factors make projections more than a few years out very uncertain.

Demographics

The “graying” of the U.S. population is well publicized. The baby boomers, who compose a significant percentage of both the U.S. population and the R.T. population, have a significant effect on both. Baby boomers make up about 41% of all R.T.s. The average age of the R.T. population continues to increase, due in large part to the aging of the baby boomers. In 1991 the average age of the R.T. population was 37; in 2010 it had increased by 6 years to 43 years old.

Will the number of new R.T.s be enough to offset those who retire and drop registration? If not, the rate of growth in the R.T. population will decrease. The trend in the number of newly minted R.T.s provides an indication of future growth. After growing from 2000 to 2006, the numbers of first-time examinees leveled off and then began to fall during the past 4 years. The number of first-time radiography examinees during this period illustrates this trend, with the leveling off occurring at about 14 000 per year (see Figure 2).

As Figure 3 illustrates, the number of radiography examinees has gone through recurring cycles historically. Note particularly that although the number of examinees decreases over some periods, the overall trend in volume is up. That is, for each new cycle the highs are higher than the previous cycle’s highs and the lows are higher than the last cycle’s lows. Similar cycles are seen for
The best guess is that the number of R.T.s will continue to grow, although perhaps not at the same rate as seen in recent decades.

Demand

There can be no doubt that as the average age of the U.S. population increases, the need for health care services will grow. The Bureau of Labor Statistics (BLS) is tasked with predicting demand for various professionals based on projected demand for services. For radiologic technologists, the BLS estimated that in 2008 there were 214,700 technologists employed and projected that 251,000 technologists will be needed by 2018. This would be an increased need for 37,000 additional technologists or 17% growth. If the 17% BLS growth estimate is used, then ARRT’s 300,000 R.T.s will grow to about 350,000 by 2018, which is only halfway to the next 100,000. Because BLS’ predicted
What a clever and practical book is MRI Parameters and Positioning. This is the ideal book for the beginning magnetic resonance (MR) imaging technologist and makes a great textbook for the classroom or independent learner. It also is helpful for standardizing protocols wherever MR imaging is being performed, rather like Merrill's Atlas does for radiography. As the authors point out, “It is only through standardization that the quality of diagnostic imaging will improve.” Protocols are presented for every region of the body in a simple, concise manner. In addition, the latest in MR angiography, MR cholangiography, MR urography and MR colonography are included.

The organization of MRI Parameters and Positioning makes it easy to access information on any area of the body quickly and efficiently. Each area begins with no-nonsense patient preparation guidelines, such as “Offer the patient ear plugs or ear protectors.” These are important little instructions that we may all forget when starting out. The guidelines are followed by important but simple directives for positioning, such as “Secure the head in the head coil, cushion the legs.”

Sequences and protocols follow. I found this section unique and valuable in that it explains in detail important information for scanning. As an example, for an axial sequence of the brain and skull, readers are directed to “Plot on central sagittal plane, line through anterior and posterior margin of the corpus callosum (parallel to a line running through the anterior and posterior commissure); [complete] enough scans to delineate the brain completely from the vertex to the cerebellum usually to the line of the foramen magnum.” This knowledge makes the technologist more professional and independent in the workplace by familiarizing him or her with what is expected and needed to complete the exam, thereby minimizing wasted time.

I found the “tips and tricks” most useful, even for experienced technologists. The section includes ideas for difficult patients. For example, “In patients with increased kyphosis, place cushions under the pelvis as well; in those with neck problems, it may be necessary to raise the head somewhat and cushion it.” Great stuff! In the angiography sections, there are even suggestions for giving bolus injections, including flow rates. In addition, anatomical illustrations aid in understanding positioning and anatomy.

The appendix alone is truly a treasure. Included are parameters for different field strengths discussed in an easy-to-understand way. This is important information that can be accessed quickly, as when changing between machines of differing strength, without having to read a lengthy paragraph. Another chart displays scan parameters and their effects. For instance, if the field of view is decreased, how will that affect resolution, signal-to-noise ratio and acquisition time? Also included in the appendix is an artfully and thoughtfully presented chart of MR acronyms for the major manufacturers (Siemens, GE, Philips, Hitachi and Toshiba). For instance, Siemens calls a steady-state free precession PSIF; GE calls it SSFP; Philips refers to it as T2-FFE; and Hitachi uses the term Time-Reversed SARGE. This handy chart could be extremely helpful when changing jobs.
or manufacturers because these acronyms can be very confusing. Last but not least, the glossary explains all the different terms and acronyms thoroughly.

All in all, I strongly recommend MRI Imaging Parameters and Positioning. This handy and practical little book will help make the confusing world of MR imaging more readily understandable.

Connie McCready, BA, R.T.(R)(M)(CT)(MR)    Retired
Portland, Oregon

RADIOGRAPHIC IMAGE ANALYSIS. 3rd ed.
McQuillen-Martensen K. 2010. 570 pgs.

In the third edition of this textbook, the author does an excellent job overall of presenting information about how to produce a quality image. The text starts where it all counts — with the patient — and provides a discussion of our professional responsibility to the patient. Ms. McQuillen-Martensen reminds us of our duty to produce high-quality radiographs using proper positioning and techniques, and explains how to evaluate the images produced. She even goes a little further to list what possibly would constitute the basis for a malpractice suit. In summary, the author emphasizes the importance of producing quality radiographs and covers all facets of the process.

In each chapter, objectives and terminology used in the chapter are listed and defined. This provides a quick reference for the reader. The beginning of the text discusses image recording, density, contrast, grid ratio, source-to-image distance, markers, peak kilovolts, collimation and distortion. The author progresses to information that is required on an image, the placement of the cassette, the central ray angulation and reasons for the angulation. Radiation protection and other important factors involved in producing a radiograph are emphasized in this chapter. Also in the first chapter, the author discusses the rules or foundation for technical factors required for adequate density and contrast, and she suggests changes to correct an unacceptable film-screen image.

The author discusses digital radiography (DR) and computerized radiography (CR) and the terminological and other differences between them. Excellent drawings of histograms help evaluate whether the techniques used in these imaging systems are correct. The author compares density to image brightness and changes needed to correct technical factors. In addition, she emphasizes the same important identification information and the placement of markers on DR and CR images.

Additional chapters each contain technique charts, excellent examples of correctly positioned and incorrectly positioned images and criteria to evaluate images. Anatomy is labeled on each image, and breathing instructions are discussed. Information on pediatric and geriatric positioning has been expanded to assist the radiographer with compensatory methods to produce quality images of these patients.

This text is a powerful book with information that is valuable to anyone in radiography. If I had a criticism it would be very minute. That criticism would be offering baseline techniques for density using automatic exposure control settings with little information about actual baseline milliamperage settings.

As an educator who has taught image analysis for many years, I believe this is an excellent reference for educators as well as student radiographers. The textbook also can be used by registered radiographers and even radiology residents. The third edition of this text only improves on prior editions and provides updated information. I would recommend this book to any radiology program as a reference or textbook for courses.

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Mobile, Alabama
Skull Fracture Diagnosis: A Case Study

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An 18-year-old white male patient presented to a small Midwestern hospital at about 10 am complaining of right posterior head pain. The patient had fallen down the stairs at his residence around 2 am, then returned to bed. He woke up later that morning complaining of headache, nausea and general malaise. The patient’s mother brought him to the local emergency department (ED) for evaluation. The patient was checked into the ED and evaluated by the physician on duty. The ED physician examined the patient and ordered a CT scan of the brain without contrast to include soft tissue (ie, brain) and bony window settings (ie, skull).1

A CT scan was performed on a GE LightSpeed (GE Healthcare, Chalfont St Giles, UK). A lateral CT scout image was obtained and used to plan the study.1 Slices 1 through 10 were done at 5 mm cuts and slices 11 through 18 were done at 10 mm cuts.2 Window width settings for the soft-tissue structures were 146 and window level settings were +47. Window width setting for the bone windows was 2000 and window level setting was +600.1 The scan was done from the base of the skull through the skull cap.2,3 Figure 1 demonstrates the CT lateral scout image and scan data.2

The study began at 10:28 am and ended at 10:35 am. The patient did not complain of any difficulties and was taken by stretcher back to the ED. The CT images were evaluated by the ED physician, who assessed the CT scan as negative. Figure 2 shows slice 4 enlarged by the technologist for the ED physician’s benefit.

An immediate radiologist consult was not possible because telephone line transmission was inactive and the radiologist had not arrived yet to view the CT hard copy images.

The ED physician told the ED nurse to give the patient and his mother head injury instructions and ask them to call back immediately if there were any change in the patient’s condition.1 The patient and his mother left the ED. At around 11:15 am, they returned, with the patient complaining of posterior head pain and the mother demanding a more thorough evaluation of her son’s condition.

The technologist who had performed the CT scan mentioned to the ED physician that 2 views of the skull could be performed to correlate with the CT to improve diagnostic efficacy.5 The ED physician agreed and ordered a 2-view skull series. The radiographer produced

Figure 1. Computed tomography lateral head scan and scan data.
a right lateral projection and an anteroposterior axial Towne projection corresponding to the area of the patient’s headache in the right posterior region of the skull.\textsuperscript{5,6}

Both of these images were taken to the ED physician. The ED physician believed that the Towne projection demonstrated a linear density on the right occipital region of the skull that was absent in the left occipital region.\textsuperscript{4,7} The ED physician said this could be a fracture. The radiologist arrived at this time and looked at the CT brain scan and radiographs of the skull (see Figures 3 and 4).

The radiologist indicated that there was an approximately 9 cm linear density in the right occipital region of the skull that was demonstrated on the Towne projection and the previous CT brain study. The radiologist communicated the diagnosis to the ED physician, who then made arrangements to have the patient flown to a major trauma center for neurosurgical consultation.

It is noteworthy that while CT still is considered the “gold standard” in brain trauma imaging, plain films can be valuable in conjunction with CT for assessing patients with traumatic head injuries.\textsuperscript{5,6} ◆

**References**


Goniometers

What is a goniometer and what does it have to do with radiography? This is a question often posed by radiography students and sometimes technologists alike after hearing the word “goniometer.” Goniometry, derived from the Greek words for angle and measure, is defined as the measurement of angles. A goniometer is a device that is used to measure angles. Goniometry is a common practice in the field of occupational therapy, in which a joint’s range of motion is measured for therapeutic assessment. So you probably are still asking, “What does this have to do with radiography?”

Radiography often requires that a patient’s body or body part be manipulated for optimal visualization of anatomy. Radiographers use terms such as angle, oblique, flex and extend to describe this positioning. As a radiography instructor, I have noticed a pattern with student radiographers having difficulty with correct oblique positioning and angling of body parts. The problem arises when students are instructed to position the patient or part at a precise degree. Many students are comfortable with positioning or angling at 45° because it is fairly easy to gauge halfway between 0° and 90°. However, students are still estimating the amount, and not every student can accurately assess a 45° angle. In addition, not all positioning or angling requirements are exactly 45°. Some examples of this positioning include placing the orbitomeatal line 37° from the table, flexing the knee 20° and obliquing the patient 30° from lateral, just to name a few. It is difficult for many students to obtain this specific amount of angulation or obliquity. This results in estimating the degree of angulation, thus leading to incorrect positioning and the need for repeat exposures.

This is where the goniometer plays a critical role in helping students obtain that exact degree of angulation and eliminating the need for estimation. In addition to finding angles, most goniometers also double as rulers, which can be used for determining exact distances from anatomical landmarks and also can be used to find part thickness of smaller anatomy when calipers are not available.

Older models of goniometers were bulky and made of metal, consisting of a 180° arc and an extendable antenna (see Figure 1). These devices are very effective, but finding one in good condition is rare. They are also considerably more expensive than models that are currently manufactured. Another negative aspect is their size, which usually limits the device to the immediate x-ray room or department. Today’s goniometers used in radiography, sometimes referred to as angle finders, angle rules, or angulators, are small plastic devices that fit in one’s pocket, making them portable and easily accessible. This portability is beneficial to students who rotate through multiple

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**Figure 1.** A metal goniometer.
clinical sites during their education. In addition, this type of goniometer is relatively inexpensive and can even be customized with an institution’s name or logo (see Figure 2).

So if this is such a great tool, why aren’t more technologists using it? Over time, a technologist learns how to accurately gauge positioning angles and obliquity from experience. However, a student radiographer is just getting accustomed to positioning. Students emulate what they see technologists do in the clinical setting, and often try to position patients just by estimating. Using a goniometer gives students a way to measure and verify their positioning. With practice and proper instruction, students eventually will be able to accurately position patients without the aid of the goniometer.

The goniometer is not intended to be used as a requirement for learning, but rather as a supplemental instructional tool for students beginning the profession. If you, as an educator or clinical supervisor, notice that students are having difficulty with positioning angles, obliquity, or measurements, goniometers may prove to be an invaluable tool to help improve student learning.

◆

Figure 2. A plastic goniometer.
Writing Conclusions

The conclusion is often the most difficult part of writing a research paper. The Hamilton College handout on conclusions goes so far as to state that “...almost all writers struggle with writing conclusions” because of the fact that this section plays such an important role in an article or research paper. Many authors make the mistake of simply restating or summarizing their findings. The conclusion, which is sometimes incorporated into the discussion or may be a stand-alone section, is much more than a summary. This section should include an analysis of the findings/results, implications for practice, limitations and suggestions for future research. This column discusses the main parts that should be included in a conclusion.

Analysis of Findings/Results

One of the main mistakes authors make when writing conclusions is to summarize the information previously presented. This section should not be a summary, but an analysis or synthesis of the findings/results. Authors should reflect on the original purpose, problem statement and hypotheses (if applicable) and tie the conclusions back to these. In this section, the author discusses his or her findings in light of previously published literature. If the paper is a quantitative research paper, such as survey research, the author should compare his or her findings to similar study findings discussed in the literature review section. If the paper is a qualitative literature review, major agreements and disagreements found in the literature should be discussed.

It is important to note that no new information should be presented in the conclusion. This section provides an analysis of what has been discussed. Through this analysis, the author should demonstrate how this work adds to the body of previously published literature. This includes analyzing the literature, finding themes and drawing conclusions based on the literature, which leads to providing the reader with implications for practice.

Implications for Practice

To be able to effectively write implications for practice, an author must answer 2 questions: “So what?” and “Who cares?” By answering the question “So What?” the author is able to articulate the significance of the research. Here, the author shows the reader the importance of the work and proves that the work is useful and meaningful. Once the significance is discussed, it is important to know “Who cares?” One of the key parts of the conclusion is when the author speaks directly to his or her audience and tells them what they should do based on the findings. This is where research meets practice. The audience is given specific suggestions for changing or enhancing practice based on the findings. For instance, if an author conducts a literature review on job satisfaction for an audience of radiology administrators who are interested in retaining employees, the conclusion section should provide the administrators with a succinct list or table of specific actions to take to improve satisfaction and ultimately retain employees. While answering these questions, it is common to point out limitations in the study.

Limitations

Limitations are the possible weaknesses of the study. All research studies have some limitations and they often are dictated by time and budget. Creswell gave these examples of limitations:

- “The purposive sampling procedure decreases the generalizability of findings.”
- “In this qualitative study, the findings could be subject to other interpretations.”

Acknowledging study limitations also provides the opportunity to make
Suggestions for Future Research

The conclusions sections always should list suggestions for future research. These come from limitations of the study and also from gaps found in the literature. Through the process of writing, an author should become an expert on the topic and have a clear understanding of what has been published along with what needs to be investigated to add to the body of knowledge. Researchers often look to this section of a work to find ideas for research projects.

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**Patient Preparation**

No special preparation is necessary, but your physician may ask you to discontinue taking aspirin or a blood thinner before the procedure. Wear a 2-piece outfit and a comfortable bra that will provide firm support after your procedure. As with a mammogram, don’t use deodorant, talcum powder, lotion, ointment or perfume because they can affect the quality of the medical imaging.

Before the exam, a mammographer will explain the procedure and answer your questions. A mammographer, also known as a radiologic technologist, is a skilled medical professional with specialized education in radiation protection, patient care, and special breast positioning and imaging procedures.

Tell the mammographer if you are allergic to local anesthetic or any other medication.

**During the Examination**

The mammographer will ask you to undress from the waist up and change into a front-opening gown. Then you will lie face down on a specially designed table that has a hole for your breast to fit through, or you will sit with your breast on a mammography unit. You will be awake during the procedure.

Your breast will be compressed, and the mammographer will take a series of radiographic images to determine the exact location of the tissue in question. An anesthetic is injected to numb the area to be biopsied, and you may feel a slight sting. Next, a quarter-inch nick is made in the skin. The physician inserts a needle in the nick, using the images to guide the needle.

After a second set of images is taken to ensure that the needle is positioned correctly, the physician collects several small samples of breast tissue and then leaves a tiny clip in your breast to mark the biopsy site if necessary. The needle is removed and pressure is applied to the area to stop any bleeding. A small bandage is applied to the nick.

**Postexamination Information**

You may resume your normal activities after the exam, but you should avoid strenuous exercise for about a day. You may experience mild discomfort that can be relieved by applying an ice pack. Do not take aspirin as it may increase bleeding. You also may have a bruise, which should disappear in about 10 days. The nick where the needle was inserted may leave a tiny scar.

A pathologist will examine the breast tissue samples and report the findings to your physician. Your physician then will discuss the results with you and advise you about any other procedures that may be necessary.
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