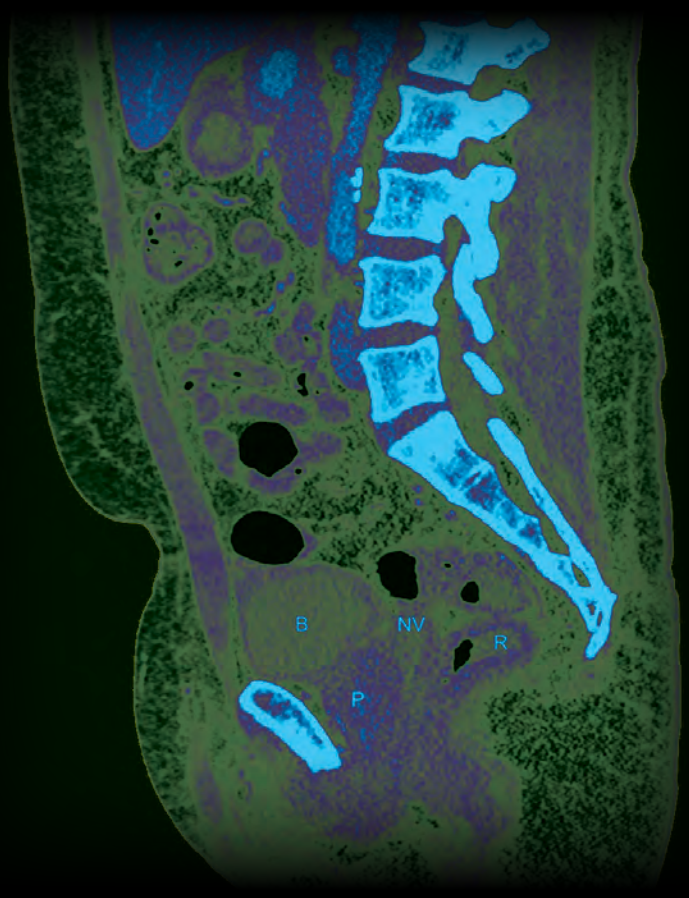
July / August 2022
Volume 51, Number 4

Applied Radiology

AppliedRadiology®

50 YEARS

The Journal of Practical Medical Imaging and Management



SA–CME
Abdominal and Pelvic Imaging of Transgender Patients

Pulmonary Embolism Response Teams: An Integrated Approach to Patient Care

Non-neoplastic Cystic Lesions of the Central Nervous System, Part 1: Developmental Cysts

Times are Tight: Staff Shortages Prompt New Strategies

Sellar Atypical Teratoid Rhabdoid Tumor

July / August 2022 Volume 51, Number 4

www.appliedradiology.com

multihance®
(gadobenate dimeglumine)
injection, 529 mg/mL

TRUST EARNED

What does seeing better with MultiHance® mean?[1-4*]

MultiHance® demonstrated significantly improved visualization and contrast enhancement of CNS lesions when compared with Gadavist® at 0.1 mmol/kg.[1†]

- The 0.1 mmol/kg dose of MultiHance demonstrated consistently better lesion visualization for all readers compared to all tested MR contrast agents.[1-4]
- 3 blinded independent readers reported superiority for MultiHance in significantly (*P*=.0001) more patients for all evaluated end points. The opinions of the 3 readers were identical for 61.9%–73.5% of the patients, resulting in values of 0.414–0.629 for inter-reader agreement.

The individuals who appear are for illustrative purposes. All persons depicted are models and not real patients.
Please see Brief Summary of Prescribing Information including Boxed Warning on adjacent page.
*MRI imaging of the CNS in adult and pediatric patients to visualize lesions with abnormal BBB or abnormal vascularity of the brain, spine and associated tissues or to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease.

MultiHance® (gadobenate dimeglumine) injection, 529 mg/mL and
MultiHance® Multipack™ (gadobenate dimeglumine) injection, 529 mg/mL

Indications and Usage:
MultiHance® (gadobenate dimeglumine) injection, 529 mg/mL is a gadolinium-based contrast agent indicated for intravenous use in:
- Magnetic resonance imaging (MRI) of the central nervous system (CNS) in adults and pediatric patients (including term neonates) to visualize lesions with abnormal blood-brain barrier or abnormal vascularity of the brain, spine, and associated tissues and
- Magnetic resonance angiography (MRA) to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease

IMPORTANT SAFETY INFORMATION:

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle and internal organs.
- **The risk for NSF appears highest among patients with:**
  - **chronic, severe kidney disease (GFR < 30 mL/min/1.73m^2), or**
  - **acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended MultiHance dose and allow a sufficient period of time for elimination of the drug from the body prior to re-administration.**

CONTRAINDICATIONS
MultiHance is contraindicated in patients with known allergic or hypersensitivity reactions to gadolinium-based contrast agents.

WARNINGS AND PRECAUTIONS
Nephrogenic Systemic Fibrosis: NSF has occurred in patients with impaired elimination of GBCAs. Higher than recommended dosing or repeated dosing appears to increase risk.
Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of MultiHance administration and resolved with prompt emergency treatment. Consider the risk for hypersensitivity reactions, especially in patients with a history of hypersensitivity reactions or a history of asthma or other allergic disorders.
Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver, and spleen. At equivalent doses, retention varies among the linear agents. Retention is lowest and similar among the macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established, but they have been established in the skin and other organs in patients with impaired renal function. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.
Acute Renal Failure: In patients with renal insufficiency, acute renal failure requiring dialysis or worsening renal function have occurred with the use of GBCAs. The risk of renal failure may increase with increasing dose of the contrast agent. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests.
Extravasation and Injection Site Reactions: Extravasation of MultiHance may lead to injection site reactions, characterized by local pain or burning sensation, swelling, blistering, and necrosis. Exercise caution to avoid local extravasation during intravenous administration of MultiHance.
Cardiac Arrhythmias: Cardiac arrhythmias have been observed in patients receiving MultiHance in clinical trials. Assess patients for underlying conditions

or medications that predispose to arrhythmias. The effects on QTc by MultiHance dose, other drugs, and medical conditions were not systematically studied.
Interference with Visualization of Certain Lesions: Certain lesions seen on non-contrast images may not be seen on contrast images. Exercise caution when interpreting contrast MR images in the absence of companion non-contrast MR images.

ADVERSE REACTIONS
The most commonly reported adverse reactions are nausea (1.3%) and headache (1.2%).

USE IN SPECIFIC POPULATIONS
Pregnancy: GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. Use only if imaging is essential during pregnancy and cannot be delayed.
Lactation: There is no information on the effects of the drug on the breastfed infant or the effects of the drug on milk production. However, limited literature reports that breastfeeding after MultiHance administration to the mother would result in the infant receiving an oral dose of 0.001%-0.04% of the maternal dose.
Pediatric Use: MultiHance is approved for intravenous use for MRI of the CNS to visualize lesions with abnormal blood brain barrier or abnormal vascularity of the brain, spine, and associated tissues in pediatric patients from birth, including term neonates, to less than 17 years of age. Adverse reactions in pediatric patients were similar to those reported in adults. No dose adjustment according to age is necessary in pediatric patients two years of age and older. For pediatric patients, less than 2 years of age, the recommended dosage range is 0.1 to 0.2 mL/kg. The safety of MultiHance has not been established in preterm neonates.

Please see full Prescribing Information and Patient Medication Guide for additional important safety information for/regarding MultiHance (gadobenate dimeglumine) injection, 529 mg/mL at https://www.braccoimaging.com/us-en/products/magnetic-resonance-imaging/multihance

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

MultiHance is manufactured for Bracco Diagnostics Inc. by BIPSO GmbH – 78224 Singen (Germany) and by Patheon Italia S.p.A., Ferentino, Italy.
MultiHance is a registered trademark of Bracco International B.V.
MultiHance Multipack is a trademark of Bracco International B.V.
All other trademarks and registered trademarks are the property of their respective owners.

References: 1. Seidl Z, Vymazal J, Mechi M, et al. Does higher gadolinium concentration play a role in the morphologic assessment of brain tumors? Results of a multicenter intraindividual crossover comparison of gadobutrol versus gadobenate dimeglumine (the MERIT Study). *AJNR Am J Neuroradiol.* 2012;33(6):1050-1058. **2.** Maravilla KR, Maldjian JA, Schmalfuss IM, et al. Contrast enhancement of central nervous system lesions: multicenter intraindividual crossover comparative study of two MR contrast agents. *Radiology.* 2006;240(2):389-400. **3.** Rowley HA, Scialfa G, Gao PY, et al. Contrast-enhanced MR imaging of brain lesions: a large-scale intraindividual crossover comparison of gadobenate dimeglumine versus gadodiamide. *AJNR Am J Neuroradiol.* 2008;29(9):1684-1691. **4.** Vaneckova M, Herman M, Smith MP, et al. The benefits of high relaxivity for brain tumor imaging: results of a multicenter intraindividual crossover comparison of gadobenate dimeglumine with gadoterate meglumine (The BENEFIT Study). *AJNR Am J Neuroradiol.* 2015 Sep;36(9):1589–1598.

Bracco Diagnostics Inc.
259 Prospect Plains Road, Building H
Monroe Township, NJ 08831 USA
Phone: 609-514-2200
Toll Free: 1-877-272-2269 (U.S. only)
Fax: 609-514-2446

BRACCO

Bracco Diagnostics

multihance®
(gadobenate dimeglumine)
injection, 529 mg/mL

Rx ONLY
Please see full prescribing information.
A brief summary follows.

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs.

Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating systemic fibrosis affecting the skin, muscle and internal organs.

- The risk for NSF appears highest among patients with:
  - chronic, severe kidney disease (GFR <30 mL/min/1.73m2), or
  - acute kidney injury.
- Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.
- For patients at highest risk for NSF, do not exceed the recommended MultiHance dose and allow a sufficient period of time for elimination of the drug from the body prior to re-administration. [see ***Warnings and Precautions (5.1)***]

1 INDICATIONS AND USAGE

1.1 MRI of the Central Nervous System (CNS)

MultiHance is indicated for intravenous use in magnetic resonance imaging (MRI) of the central nervous system (CNS) in adults and pediatric patients (including term neonates), to visualize lesions with abnormal blood-brain barrier or abnormal vascularity of the brain, spine, and associated tissues.

1.2 MRA of Renal and Aorto-ilio-femoral Vessels

MultiHance is indicated for use in magnetic resonance angiography (MRA) to evaluate adults with known or suspected renal or aorto-ilio-femoral occlusive vascular disease.

4 CONTRAINDICATIONS MultiHance is contraindicated in patients with known allergic or hypersensitivity reactions to gadolinium-based contrast agents [see ***Warnings and Precautions (5.2)]***.

5 WARNINGS AND PRECAUTIONS

5.1 Nephrogenic Systemic Fibrosis (NSF) Gadolinium-based contrast agents (GBCAs) increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast enhanced MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR <30 mL/min/1.73m^2) as well as patients with acute kidney injury. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30-59 mL/min/1.73m^2) and little, if any, for patients with chronic, mild kidney disease (GFR 60-89 mL/min/1.73m^2). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs. Report any diagnosis of NSF following MultiHance administration to Bracco Diagnostics (1-800-257-5181) or FDA (1-800-FDA-1088 or www.fda.gov/medwatch).

Screen patients for acute kidney injury and other conditions that may reduce renal function.

Features of acute kidney injury consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess renal function in the setting of acute kidney injury. For patients at risk for chronically reduced renal function (e.g., age > 60 years, diabetes mellitus or chronic hypertension), estimate the GFR through laboratory testing.

Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA and the degree of renal impairment at the time of exposure. Record the specific GBCA and the dose administered to a patient. For patients at highest risk for NSF, do not exceed the recommended MultiHance dose and allow a sufficient period of time for elimination of the drug prior to re-administration. For patients receiving hemodialysis, physicians may consider the prompt initiation of hemodialysis following the administration of a GBCA in order to enhance the contrast agent's elimination. The usefulness of hemodialysis in the prevention of NSF is unknown [see ***Dosage and Administration (2) and Clinical Pharmacology (12)***].

5.2 Hypersensitivity Reactions Anaphylactic and anaphylactoid reactions have been reported, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of MultiHance administration and resolved with prompt emergency treatment. Prior to MultiHance administration, ensure the availability of personnel trained and medications to treat hypersensitivity reactions. If such a reaction occurs stop MultiHance and immediately begin appropriate therapy. Additionally, consider the risk for hypersensitivity reactions, especially in patients with a history of hypersensitivity reactions or a history of asthma or other allergic disorders. Observe patients for signs and symptoms of a hypersensitivity reaction during and for up to 2 hours after MultiHance administration.

5.3 Gadolinium Retention Gadolinium is retained for months or years in several organs. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (e.g. brain, skin, kidney, liver, and spleen. The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, gadolinium retention varies among the linear agents with Omniscan (gadodiamide) and Optimark (gadoversetamide) causing greater retention than other linear agents [Eovist (gadoxetate disodium), Magnevist (gadopentetate dimeglumine), MultiHance (gadobenate dimeglumine)]. Retention is lowest and similar among the macrocyclic GBCAs [Dotarem gadoterate meglumine), Gadavist (gadobutrol), ProHance (gadoteridol)].

Consequences of gadolinium retention in the brain have not been established. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function [see ***Warnings and Precautions (5.1)***]. There are rare reports of pathologic skin changes in patients with normal renal function. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention [see ***Adverse Reactions (6.2)***]. While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.

5.4 Acute Renal Failure In patients with renal insufficiency, acute renal failure requiring dialysis or worsening renal function have occurred with the use of gadolinium-based contrast agents. The risk of renal failure may increase with increasing dose of the contrast agent. Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests. Consider follow-up renal function assessments for patients with a history of renal dysfunction.

5.5 Extravasation and Injection Site Reactions Extravasation of MultiHance may lead to injection site reactions, characterized by local pain or burning sensation, swelling, blistering, and necrosis. In animal experiments, local reactions including eschar and necrosis were noted even on Day 8 post perivenous injection of MultiHance. Exercise caution to avoid local extravasation during intravenous administration of MultiHance. If extravasation occurs, evaluate and treat as necessary if local reactions develop.

5.6 Cardiac Arrhythmias Cardiac arrhythmias have been observed in patients receiving MultiHance in clinical trials [see ***Adverse Reactions (6.1)***]. Assess patients for underlying conditions or medications that predispose to arrhythmias.

A double-blind, placebo-controlled, 24-hour post dose continuous monitoring, crossover study in 47 subjects evaluated the effect of 0.2 mmol/kg MultiHance on ECG intervals, including QTc. The average changes in QTc values compared with placebo were minimal (<5 msec). QTc prolongation between 30 and 60 msec were noted in 20 subjects who received MultiHance vs. 11 subjects who received placebo. Prolongations ≥ 61 msec were noted in 6 subjects who received MultiHance and in 3 subjects who received placebo. None of these subjects had associated malignant arrhythmias. The effects on QTc by MultiHance dose, other drugs, and medical conditions were not systematically studied.

5.7 Interference with Visualization of Certain Lesions Certain lesions seen on non-contrast images may not be seen on contrast-images. Exercise caution when interpreting contrast MR images in the absence of companion non-contrast MR images.

6 ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the label:

- Nephrogenic systemic fibrosis [see ***Warnings and Precautions (5.1)***]
- Hypersensitivity reactions [see ***Warnings and Precautions (5.2)***]

6.1 Clinical Trials Experience

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

Adult In clinical trials with MultiHance, a total of 4967 adult subjects (137 healthy volunteers and 4830 patients) received MultiHance at doses ranging from 0.005 to 0.4 mmol/kg. There were 2838 (57%) men and 2129 (43%) women with a mean age of 56.5 years (range 18 to 93 years). A total of 4403 (89%) subjects were Caucasian, 134 (3%) Black, 275 (6%) Asian, 40 (1%) Hispanic, 70 (1%) in other racial groups, and for 45 (1%) subjects, race was not reported.

The most commonly reported adverse reactions in adult subjects who received MultiHance were nausea (1.3%) and headache (1.2%). Most adverse reactions were mild to moderate in intensity. One subject experienced a serious anaphylactoid reaction with laryngeal spasm and dyspnea [see ***Warnings and Precautions (5.2)***]. Serious adverse reactions consisting of convulsions, pulmonary edema, acute necrotizing pancreatitis, and anaphylactoid reactions were reported in 0.1% of subjects in clinical trials.

Adverse reactions that occurred in at least 0.5% of 4967 adult subjects who received MultiHance are listed below (Table 2), in decreasing order of occurrence within each system.

TABLE 2: ADVERSE REACTIONS REPORTED IN ≥ 0.5% OF ADULT SUBJECTS WHO RECEIVED MULTIHANCE IN CLINICAL TRIALS

Number of subjects dosed	4967
Number of subjects with any adverse reaction	517 (10.4%)
Gastrointestinal Disorders	
Nausea	67 (1.3%)
General Disorders and Administration Site Disorders	
Injection Site Reaction	54 (1.1%)
Feeling Hot	49 (1.0%)
Nervous System Disorders	
Headache	60 (1.2%)
Dysgeusia	33 (0.7%)
Paresthesia	24 (0.5%)
Dizziness	24 (0.5%)

The following adverse reactions occurred in less than 0.5% of the 4967 adult subjects who received MultiHance. Serious adverse reactions described above are not repeated below.

Blood and Lymphatic System Disorders: Basophilia; **Cardiac Disorders:** Atrioventricular block first degree; **Eye Disorders:** Eye pruritus, eye swelling, ocular hyperemia, visual disturbance; **Gastrointestinal Disorders:** Abdominal pain or discomfort, diarrhea, dry mouth, lip swelling, paraesthesia oral, tongue edema, vomiting; **General Disorders and Administration Site Conditions:** Chest pain or discomfort, chills, malaise; **Immune System Disorders:** Hypersensitivity; **Investigations:** Nonspecific changes in laboratory tests (including hematology, blood chemistry, liver enzymes and urinalysis), blood pressure and electrocardiogram parameters (including PR, QRS and QT intervals and ST-T segment changes). **Musculoskeletal and Connective Tissue Disorders:** Myalgia; **Nervous System Disorders:** Parosmia, tremor; **Respiratory, Thoracic and Mediastinal Disorders:** Dyspnea, laryngospasm, nasal congestion, sneezing, wheezing; **Skin and Subcutaneous Tissue Disorders:** Hyperhidrosis, pruritus, rash, swelling face, urticaria.

Pediatric In clinical trials of MultiHance in MRI of the CNS, 217 pediatric subjects received MultiHance at a dose of 0.1 mmol/kg. A total of 112 (52%) subjects were male and the overall mean age was 8.3 years (range 4 days to 17 years). A total of 168 (77%) subjects were Caucasian, 12 (6%) Black, 12 (6%) Asian, 24 (11%), Hispanic, and 1 (<1%) in other racial groups.

Adverse reactions were reported for 14 (6.5%) of the subjects. The frequency and the nature of the adverse reactions were similar to those seen in the adult patients. The most commonly reported adverse reactions were vomiting (1.4%), pyrexia (0.9%), and hyperhidrosis (0.9%). No subject died during study participation. A serious adverse reaction of worsening of vomiting was reported for one (0.5%) patient with a brain tumor (glioma) for which a causal relationship to MultiHance could not be excluded.

Pediatric Patients In clinical trials of MultiHance in MRI of the CNS, 307 pediatric subjects received MultiHance at a dose of 0.1 mmol/kg. A total of 160 (52%) subjects were male and the overall mean age was 6.0 years (range, 2 days to 17 years). A total of 211 (69%) subjects were Caucasian, 24 (8%) Black, 15 (5%) Asian, 39 (13%), Hispanic, 2 (<1%) in other racial groups, and for 16 (5%), race was not reported. Adverse reactions were reported for 14 (4.6%) of the subjects. The frequency and the nature of the adverse reactions were similar to those seen in the adult patients. The most commonly reported adverse reactions were vomiting (1.0%), pyrexia (0.7%), and hyperhidrosis (0.7%). No subject died during study participation.

6.2 Post-marketing Experience

The following adverse reactions have been identified during post approval use of MultiHance. Because these 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.

Immune System Disorders: Anaphylactic, anaphylactoid and hypersensitivity reactions manifested with various degrees of severity up to anaphylactic shock, loss of consciousness and death. The reactions generally involved signs or symptoms of respiratory, cardiovascular, and/or mucocutaneous abnormalities.

General Disorders and Administration Site Conditions: Extravasation of MultiHance may lead to injection site reactions, characterized by local pain or burning sensation, swelling, blistering, and necrosis [***see Warnings and Precautions (5.4)***]. Adverse events with variable onset and duration have been reported after GBCA administration [***see Warnings and Precautions (5.3)***]. These include fatigue, asthenia, pain syndromes, and heterogeneous clusters of symptoms in the neurological, cutaneous, and musculoskeletal systems.

Skin: Gadolinium associated plaques.

7 DRUG INTERACTIONS

7.1 Transporter-Based Drug-Drug Interactions MultiHance and other drugs may compete for the canalicular multispecific organic anion transporter (MOAT also referred to as MRP2 or ABCC2). Therefore MultiHance may prolong the systemic exposure of drugs such as cisplatin, anthracyclines (e.g. doxorubicin, daunorubicin), vinca alkaloids (e.g. vincristine), methotrexate, etoposide, tamoxifen, and paclitaxel. In particular, consider the potential for prolonged drug exposure in patients with decreased MOAT activity (e.g. Dubin Johnson syndrome).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Risk Summary GBCAs cross the placenta and result in fetal exposure and gadolinium retention. The human data on the association between GBCAs and adverse fetal outcomes are limited and inconclusive (see Data). In animal reproduction studies, gadobenate dimeglumine has been shown to be teratogenic in rabbits following repeated intravenous administration during organogenesis at doses up to 6 times the recommended human dose. There were no adverse developmental effects observed in rats with intravenous administration of gadobenate dimeglumine during organogenesis at doses up to three times the recommended human dose (see Data). Because of the potential risks of gadolinium to the fetus, use MultiHance only if imaging is essential during pregnancy and cannot be delayed. The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and is 15 to 20%, respectively.

Data *Human Data* Contrast enhancement is visualized in the human placenta and fetal tissues after maternal GBCA administration. Cohort studies and case reports on exposure to GBCAs during pregnancy have not reported a clear association between GBCAs and adverse effects in the exposed neonates. However, a retrospective cohort study, comparing pregnant women who had a GBCA MRI to pregnant women who did not have an MRI, reported a higher occurrence of stillbirths and neonatal deaths in the group receiving GBCA MRI. Limitations of this study include a lack of comparison with non-contrast MRI and lack of information about the maternal indication for MRI. Overall, these data preclude a reliable evaluation of the potential risk of adverse fetal outcomes with the use of GBCAs in pregnancy. *Animal Data* Gadolinium Retention GBCAs administered to pregnant non-human primates (0.1 mmol/kg on gestational days 85 and 135) result in measurable gadolinium concentration in the offspring in bone, brain, skin, liver, kidney, and spleen for at least 7 months. GBCAs administered to pregnant mice (2 mmol/kg daily on gestational days 16 through 19) result in measurable gadolinium concentrations in the pups in bone, brain, kidney, liver, blood, muscle, and spleen at one month postnatal age.

Reproductive Toxicology Gadobenate dimeglumine has been shown to be teratogenic in rabbits when administered intravenously at 2 mmol/kg/day (6 times the recommended human dose based on bodysurface area) during organogenesis (day 6 to 18) inducing microphthalmia/small eye and/or focal retinal fold in 3 fetuses from 3 separate litters. In addition, MultiHance intravenously administered at 3 mmol/kg/day (10 times the recommended human dose based on body surface area) has been shown to increase intrauterine deaths in rabbits. There was no evidence that MultiHance induced teratogenic effects in rats at doses up to 2 mmol/kg/day (3 times the recommended human dose based on body surface area), however, rat dams exhibited no systemic toxicity at this dose. There were no adverse effects on the birth, survival, growth, development and fertility of the F1 generation at doses up to 2 mmol/kg in a rat peri- and post-natal (Segment III) study.

10 OVERDOSAGE

Clinical consequences of overdosage with MultiHance have not been reported. Treatment of an overdosage should be directed toward support of vital functions and prompt institution of symptomatic therapy. In a Phase 1 clinical study, doses up to 0.4 mmol/kg were administered to patients. MultiHance has been shown to be dialyzable [see ***Clinical Pharmacology (12.3)***].

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action Gadobenate dimeglumine is a paramagnetic agent and, as such, develops a magnetic moment when placed in a magnetic field. The large magnetic moment produced by the paramagnetic agent results in a large local magnetic field, which can enhance the relaxation rates of water protons in its vicinity leading to an increase of signal intensity (brightness) of tissue.

In magnetic resonance imaging (MRI), visualization of normal and pathological tissue depends in part on variations in the radiofrequency signal intensity that occur with 1) differences in proton density; 2) differences of the spin-lattice or longitudinal relaxation times (T1); and 3) differences in the spin-spin or transverse relaxation time (T2). When placed in a magnetic field, gadobenate dimeglumine decreases the T1 and T2 relaxation time in target tissues. At recommended doses, the effect is observed with greatest sensitivity in the T1-weighted sequences.

12.2 Pharmacodynamics Unlike other tested paramagnetic contrast agents (See Table 3), MultiHance demonstrates weak and transient interactions with serum proteins that causes slowing in the molecular tumbling dynamics, resulting in strong increases in relaxivity in solutions containing serum proteins. The improved relaxation effect can contribute to increased contrast-to-noise ratio and lesion-to-brain ratio, which may improve visualization.

TABLE 3: RELAXIVITY (mM^{-1}s^{-1}) OF GADOLINIUM CHELATES

	Human plasma	
	r_1	r_2
Gadobenate	9.7[1]	12.5[1]
Gadopentetate	4.9[1]	6.3[1]
Gadodiamide	5.4[2]	---
Gadoteridol	5.4[1]	---

r_1 and r_2 relaxivities indicate the efficiency in shortening T1 and T2 relaxation times, respectively.
[1] In heparinized human plasma, at 39°C.
[2] In citrated human plasma, at 37°C.
--- Not available

Disruption of the blood-brain barrier or abnormal vascularity allows enhancement by MultiHance of lesions such as neoplasms, abscesses, and infarcts. Uptake of MultiHance into hepatocytes has been demonstrated.

12.3 Pharmacokinetics Three single-dose intravenous studies were conducted in 32 healthy male subjects to assess the pharmacokinetics of gadobenate dimeglumine. The doses administered in these studies ranged from 0.005 to 0.4 mmol/kg. Upon injection, the meglumine salt is completely dissociated from the gadobenate dimeglumine complex. Thus, the pharmacokinetics is based on the assay of gadobenate ion, the MRI contrast effective ion in gadobenate dimeglumine. Data for plasma concentration and area under the curve demonstrated linear dependence on the administered dose. The pharmacokinetics of gadobenate ion following intravenous administration can be best described using a two-compartment model.

Distribution Gadobenate ion has a rapid distribution half-life (reported as mean ± SD) of 0.084 ± 0.012 to 0.605 ± 0.072 hours. Volume of distribution of the central compartment ranged from 0.074 ± 0.017 to 0.158 ± 0.038 L/kg, and estimates of volume of distribution by area ranged from 0.170 ± 0.016 to 0.282 ± 0.079 L/kg. These latter estimates are approximately equivalent to the average volume of extracellular body water in man. *In vitro* studies showed no appreciable binding of gadobenate ion to human serum proteins.

Elimination Gadobenate ion is eliminated predominately via the kidneys, with 78% to 96% of an administered dose recovered in the urine. Total plasma clearance and renal clearance estimates of gadobenate ion were similar, ranging from 0.093 ± 0.010 to 0.133 ± 0.270 L/hr/kg and 0.082 ± 0.007 to 0.104 ± 0.039 L/hr/kg, respectively. The clearance is similar to that of substances that are subject to glomerular filtration. The mean elimination half-life ranged from 1.17 ± 0.26 to 2.02 ± 0.60 hours. A small percentage of the administered dose (0.6% to 4%) is eliminated via the biliary route and recovered in feces.

Metabolism There was no detectable biotransformation of gadobenate ion. Dissociation of gadobenate ion *in vivo* has been shown to be minimal, with less than 1% of the free chelating agent being recovered alone in feces.

Pharmacokinetics in Special Populations

Renal Impairment: A single intravenous dose of 0.2 mmol/kg of MultiHance was administered to 20 subjects with impaired renal function (6 men and 3 women with moderate renal impairment [urine creatinine clearance >30 to <60 mL/min] and 5 men and 6 women with severe renal impairment [urine creatinine clearance >10 to <30 mL/min]). Mean estimates of the elimination half-life were 6.1 ± 3.0 and 9.5 ± 3.1 hours for the moderate and severe renal impairment groups, respectively as compared with 1.0 to 2.0 hours in healthy volunteers.

Hemodialysis: A single intravenous dose of 0.2 mmol/kg of MultiHance was administered to 11 subjects (5 males and 6 females) with end-stage renal disease requiring hemodialysis to determine the pharmacokinetics and dialyzability of gadobenate. Approximately 72% of the dose was recovered by hemodialysis over a 4-hour period. The mean elimination half-life on dialysis was 1.21 ± 0.29 hours as compared with 42.4 ± 24.4 hours when off dialysis.

Hepatic Impairment: A single intravenous dose of 0.1 mmol/kg of MultiHance was administered to 11 subjects (8 males and 3 females) with impaired liver function (Class B or C modified Child-Pugh Classification). Hepatic impairment had little effect on the pharmacokinetics of MultiHance with the parameters being similar to those calculated for healthy subjects.

Gender, Age, Race: A multiple regression analysis performed using pooled data from several pharmacokinetic studies found no significant effect of sex upon the pharmacokinetics of gadobenate. Clearance appeared to decrease slightly with increasing age. Since variations due to age appeared marginal, dosage adjustment for geriatric population is not recommended. Pharmacokinetic differences due to race have not been systematically studied.

Pediatric: A population pharmacokinetic analysis incorporated data from 25 healthy subjects (14 males and 11 females) and 15 subjects undergoing MR imaging of the central nervous system (7 males and 8 females) betweenages of 2 and 16 years. The subjects received a single intravenous dose of 0.1 mmol/kg of MultiHance. The geometric mean Cmax was 62.3 µg/mL (n=16) in children 2 to 5 years of age, and 64.2 µg/mL (n=24) in children older than 5 years. The geometric mean AUC 0-∞ was 77.9 µg-h/mL in children 2-5 years of age (n=16) and 82.6 µg-h/mL in children older than 5 years (n=24). The geometric mean half-life was 1.2 hours in children 2 to 5 years of age and 0.93 hours in children older than 5 years. There was no significant gender-related difference in the pharmacokinetic parameters in the pediatric patients. Over 80% of the dose was recovered in urine after 24 hours. Pharmacokinetic simulations indicate similar AUC and Cmax values for MultiHance in pediatric subjects less than 2 years when compared to those reported for adults; no age-based dose adjustment is necessary forthis pediatric population.

17 PATIENT COUNSELING INFORMATION

17.1 Nephrogenic Systemic Fibrosis Instruct patients to inform their physician if they:

• have a history of kidney and/or liver disease, or • have recently received a GBCA.

GBCAs increase the risk for NSF among patients with impaired elimination of the drugs. To counsel patients at risk for NSF: • Describe the clinical manifestations of NSF • Describe procedures to screen for the detection of renal impairment.

Instruct the patients to contact their physician if they develop signs or symptoms of NSF following MultiHance administration, such as burning, itching, swelling, scaling, hardening and tightening of the skin; red or dark patches on the skin; stiffness in joints with trouble moving, bending or straightening the arms, hands, legs or feet; pain in the hip bones or ribs; or muscle weakness.

17.2 Common Adverse Reactions

Inform patients that they may experience:

• reactions along the venous injection site, such as mild and transient burning or pain or feeling of warmth or coldness at the injection site • side effects of feeling hot, nausea, and headache.

17.3 General Precautions

Instruct patients scheduled to receive MultiHance to inform their physician if they:

• are pregnant or breast feeding • have a history of renal disease, heart disease, seizure, asthma or allergic respiratory diseases • are taking any medications • have any allergies to any of the ingredients of MultiHance.

Rx only US Patent No. 4,916,246 Manufactured for Bracco Diagnostics Inc. Monroe Township, NJ 08831 By Patheon Italia S.p.A. - 03013 Ferentino (Italy) Revised October 2018 18-061418B

[†]Multicenter double-blind randomized intraindividual crossover study design of 123 patients with known or suspected brain tumors. Each patient received 0.1-mmol/kg doses of MultiHance and Gadavist in 2 identical MR imaging examinations. Contrast agents were administered by IV using manual bolus injection (n=118) or a power injector (n=4). Both agents were administered at 0.1 mmol/kg of body weight, corresponding to 0.2 mL/kg for MultiHance and 0.1 mL/kg for Gadavist. The interval between the 2 MR imaging examinations was >48 hours to avoid carryover effects but <14 days to minimize the chance of measurable disease progression or lesion evolution. All images were evaluated by 3 blinded, independent experienced radiologists who were unaffiliated with the study centers. Each reader evaluated the patient images separately and independently. Images were evaluated qualitatively for diagnostic information and scored for: 1) lesion border delineation, 2) disease extent, 3) visualization of lesion internal morphology, and 4) lesion contrast enhancement compared with surrounding normal tissue. All assessments used a 3-point scales from 1 (examination 1 superior) through 0 (examinations equal) to 1 (examination 2 superior).

Gadavist® (gadobutrol) is a registered trademark of Bayer Healthcare. **Reference:** Seidl Z, Vymazal J, Mechl M, et al. Does higher gadolinium concentration play a role in the morphologic assessment of brain tumors? Results of a multicenter intraindividual crossover comparison of gadobutrol versus gadobenate dimeglumine (the MERIT Study). *AJNR Am J Neuroradiol.* 2012 Jun-Jul;33(6):1050–1058.

AppliedRadiology® 50 YEARS
The Journal of Practical Medical Imaging and Management

Anderson Publishing, Ltd
180 Glenside Avenue,
Scotch Plains, NJ 07076
Tel: 908-301-1995
Fax: 908-301-1997
info@appliedradiology.com

Editorial Advisory Board

Applied Radiology®

The Journal of Practical Medical Imaging and Management

July / August 2022
Vol 51 No 4

Applied Radiology (ISSN 0160-9963, USPS 943180) is published in print 6 times a year, January, March, May, July, September, and November, by Anderson Publishing Ltd at 180 Glenside Ave., Scotch Plains NJ 07076. Periodicals postage paid at Scotch Plains, NJ and additional mailing offices. Free subscriptions for US-based qualified radiology professionals. Subscriptions for the US and its territories and possessions: $115 per year, $225 for two years. Foreign and Canadian subscriptions $215 for one year payable in US funds, international money orders, or by credit card only. Postmaster: Please send address changes to Applied Radiology, PO Box 317, Lincolnshire, IL 60069-0317 (847-564-5942) or email AppliedRadiology@Omeda.com.

Promoting One's Promotion

Erin Simon Schwartz, MD, FACR

Dr Schwartz is the Editor-in-Chief of Applied Radiology. She is the Chief of the Division of Neuroradiology and holds the Robert A Zimmerman Chair in Pediatric Neuroradiology in the Department of Radiology at The Children's Hospital of Philadelphia. She is also a Professor of Radiology, Perelman School of Medicine, University of Pennsylvania. She can be reached at erin@appliedradiology.com.

If you read my bio each issue (and why would you if I didn't call attention to it?), you'll notice a change this month. As of July 1, I am officially now a full Professor.

It's a funny thing, getting promoted in academia. And it feels even funnier to be promoting my promotion. But it's exactly the sort of thing we *should* be doing. Sharing our achievements so that we can be celebrated, which encourages others to do the same, and allows us to celebrate them in turn.

However, it does not come naturally for me, as I suspect it doesn't for many people. Especially for women. So many of us were taught to keep our heads down, keep working, and wait to be recognized for our successes – big and small. That eventually someone would notice. This would be fine if everyone did it. But they don't.

It's primarily women who wait to be acknowledged, and primarily men who share their successes, especially with their chairs/leadership. Now, before you object, "But I know of a man who didn't …" and "I know of a woman who did … ," of course, there are exceptions to the norm. But it's still the norm.

I share this because we need to change the norm. There's a story I tell of the time I was planning a continuing education conference for a radiology society years ago. Several men reached out, sharing that they had expertise in a particular topic and would like to be invited to speak at the conference. Similarly, people have reached out to offer their services as reviewers for *Applied Radiology* or to request an invitation to join the editorial board. To be fair, when I don't personally know the requestor, I can only base my assumption of gender on their name or by googling for images of them. However, I have never received one of these requests from someone I knew to be female.

Nationally, only 16% of fulltime medical school faculty women are full professors, and 24% are associate professors. At my institution, in 2020-2021 (most recent data available) women made up 49% of the medical school class, 62% of instructors/lecturers, and 54% of all assistant professors. But women comprise only 40% of the associate professors and 30% of the full professors.[1] Penn clearly does better than the national average, with entire programs devoted to the recruitment and retention of female faculty members, but the disparity between junior and senior faculty representation remains too great.

I am proud to add my +1 to the n of new female full professors, but we still have a long way to go.

Reference

1) https://www.focusprogram.org/benchmarks-gender-statistics-18-19. Accessed June 13, 2022.

Abdominal and Pelvic Imaging of Transgender Patients

Description

The abdominal radiologist plays an important role in providing care for transgender and gender-diverse patients, regardless of whether these patients choose to pursue gender-affirming hormone therapy or surgery. Radiologists must be aware of the various treatment options and associated anatomic and pathologic changes in transgender patients to ensure accurate imaging interpretation. This activity is designed to educate radiologists about caring for transgender patients by reviewing relevant imaging findings of hormonal therapies, nonoperative procedures, and gender-affirming surgeries with a focus on abdominal and pelvic imaging. Creating an inclusive environment for transgender patients is also discussed.

Learning Objectives

Upon completing this activity, the reader should be able to:

- Identify abdominal and pelvic imaging findings of gender-affirming hormone therapy.
- Recognize abdominal and pelvic imaging findings of non-operative and operative gender-affirming procedures.
- Explain how to improve their imaging center's inclusivity to ensure positive patient experiences

Accreditation/ Designation Statement

This activity has been planned and implemented in accordance with the accreditation requirements and policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of IAME and Anderson Publishing. IAME is accredited by the ACCME to provide continuing medical education for physicians. IAME designates this activity for a maximum of 1 AMA PRA Category 1 Credits™.

These credits qualify as SA-CME credits.

Authors

Elainea N Smith, MD,
Mohammad Ghosheh MBBS
Kristin K Porter, MD PhD

Affiliations: University of Alabama Birmingham, Birmingham, Alabama (Drs Smith, Porter); King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia (Dr Ghosheh).Disclosures: Drs Smith and Ghosheh: none. Dr Porter is a stockholder of Pfizer, Inc.

Target Audience

- Radiologists
- Related Imaging Professionals

System Requirements

For assistance accessing this course online or printing a certificate, email CustomerService@AppliedRadiology.org.

Instructions

This activity is designed to be completed within the designated time period. To successfully earn credit, participants must complete the activity during the valid credit period. To receive SA–CME credit, you must:

1. Review this article in its entirety.
2. Visit *www.appliedradiology.org/SAM2*.
3. Log into your account or create an account (new users).
4. Complete the post-test and review the discussion and references.
5. Complete the evaluation.
6. Print your certificate.

Estimated time for completion:
1 hour

Date of release and review:
July 1, 2022
Expiration date: June 30, 2024

Disclosures

Neither the authors, Elainea N Smith, MD; Mohammad Ghosheh MBBS; Kristin K Porter, MD PhD; nor Joseph Jalkiewicz, planner of this activity, have any relevant relationships with ineligible companies. No one else at Anderson Publishing or IAME who controlled the content of this activity has relationships with ineligible companies.

Abdominal and Pelvic Imaging of Transgender Patients

Elainea N Smith, MD; Mohammad Ghosheh, MBBS; Kristin K Porter, MD, PhD

The abdominal radiologist plays an important role in providing care for transgender and gender diverse patients, regardless of whether these patients choose to pursue gender affirming hormone therapy or surgery. If a patient does pursue gender affirming surgery, imaging plays an integral role in both preoperative and postoperative management.[1]

The term "transgender" describes a person whose gender identity is incongruent with their sex assigned at birth.[2] In 2016, it was estimated that approximately 1.4 million people in the United States identified as transgender[3] – approximately 1 in 250 adults, which has significantly increased in the past decade.[4] Not every person with gender incongruence will pursue hormonal therapy or gender-affirming surgery. In 2015, only approximately 25% of national transgender survey respondents had undergone gender-affirming surgery.[5] This rate is expected to increase as Medicare and Medicaid in the United States now cover gender-affirming surgical procedures, and many third-party payers are beginning to increase coverage as well.[6]

Radiologists must be aware of the various treatment options and associated anatomic and pathologic changes in transgender patients to ensure accurate imaging interpretation.[6] This article aims to discuss relevant imaging findings of hormonal therapies, nonoperative procedures, and gender-affirming surgeries, with a focus on abdominal and pelvic imaging. Additionally, it is critical for imaging centers to create an inclusive environment for these patients as they expand care; thus, this article will also explore potential pitfalls and strategies to overcome them.

Affiliations: University of Alabama Birmingham, Birmingham, Alabama (Drs Smith, Porter); King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia (Dr Ghosheh).
Disclosures: None. Prior Publication/Presentation: None.

Imaging Findings of Hormonal Therapies

At least 80% of transgender people have taken or want to take gender-affirming hormone therapy, according to the National Transgender Discrimination Survey Report on Health and Health Care.[7] Transgender women may take an estrogen with an androgen blocker, with or without a progestogen, to feminize their bodies while suppressing or minimizing male secondary sex characteristics. Transgender men may take testosterone to masculinize their bodies. Additionally, gender nonbinary, gender nonconforming, or gender-diverse individuals may take hormones to develop or minimize masculine or feminine sexual secondary characteristics. The abdominal and pelvic imaging findings in patients undergoing hormone therapy are dependent on the hormone regimen and length of treatment.

Feminizing Hormone Therapy

Imaging findings may be associated with desired effects and deleterious side effects of hormone therapy. For example, feminizing hormones may result in reduced testicular size, subcutaneous fat redistribution, and muscle-mass reduction. Rare harmful side effects that may be evaluated with imaging include venous thromboembolism (exacerbated by smoking and mitigated by transdermal estradiol administration) and liver dysfunction or fulminant hepatitis.[8]

Studies have found that prostate cancer risk is lower in transgender women receiving androgen-deprivation and estrogen treatment.[9] Given that population-based, prostate-specific antigen (PSA) screening is not globally recommended, that there is a low incidence of prostate cancer in transgender women, and

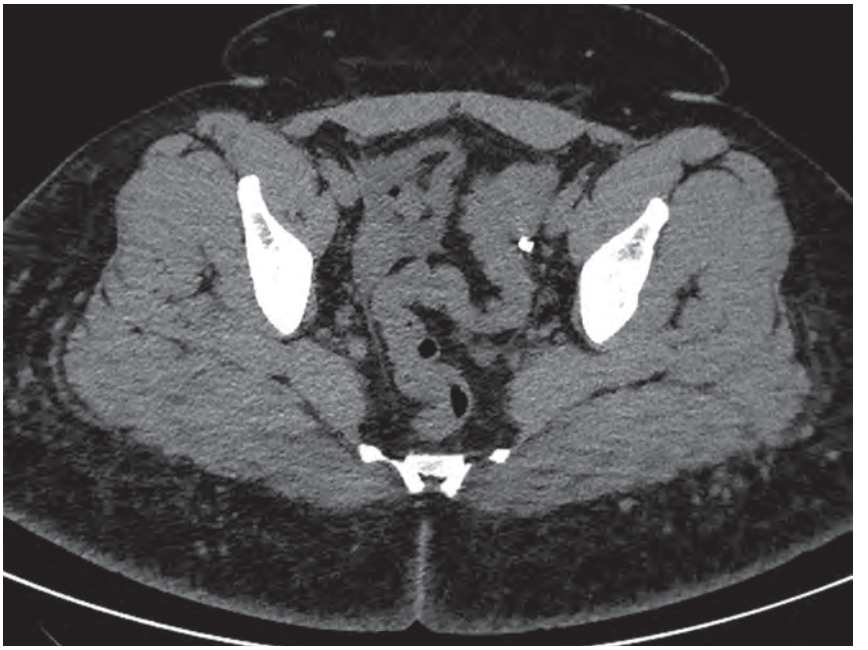
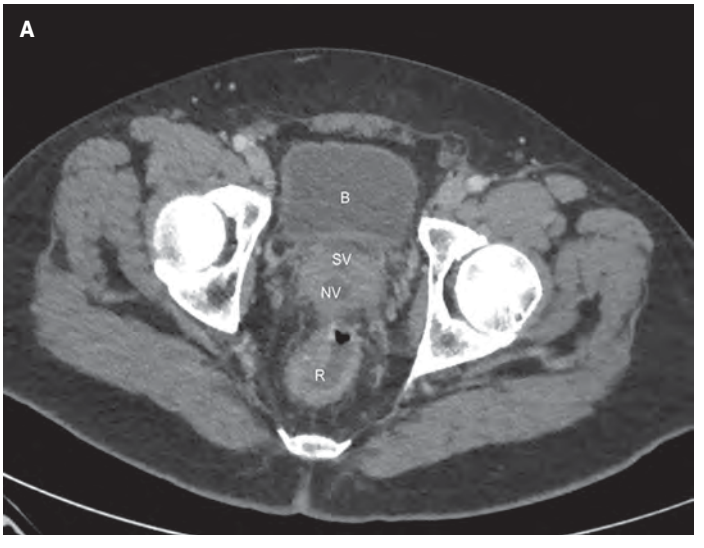


Figure 1. Axial CT pelvis of a patient who underwent subcutaneous gluteal silicone injections for augmentation demonstrates numerous soft tissue-density granulomas in the gluteal fat.



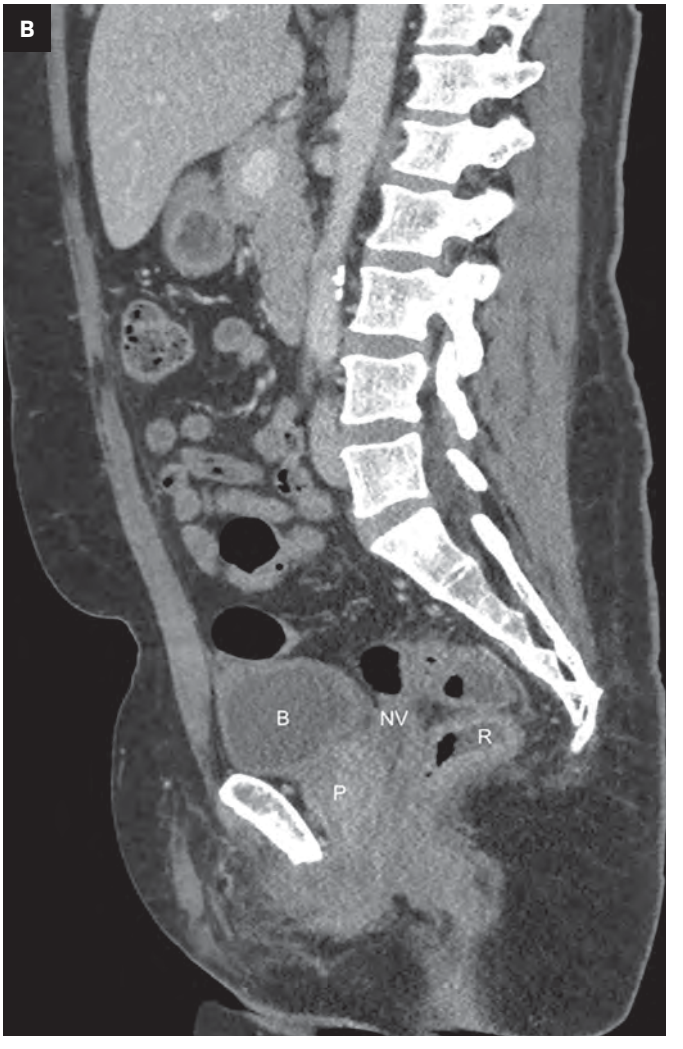


Figure 2. The expected postoperative CT appearance of a neovagina in a transgender woman in the axial (A) and sagittal (B) planes. In some patients, imaging may be performed with vaginal trainer in place to readily identify the neovagina. In this patient the neovagina is mostly collapsed aside from a small volume of simple fluid. B = bladder; SV = seminal vesicles; NV = neovagina; R = rectum; P = prostate.

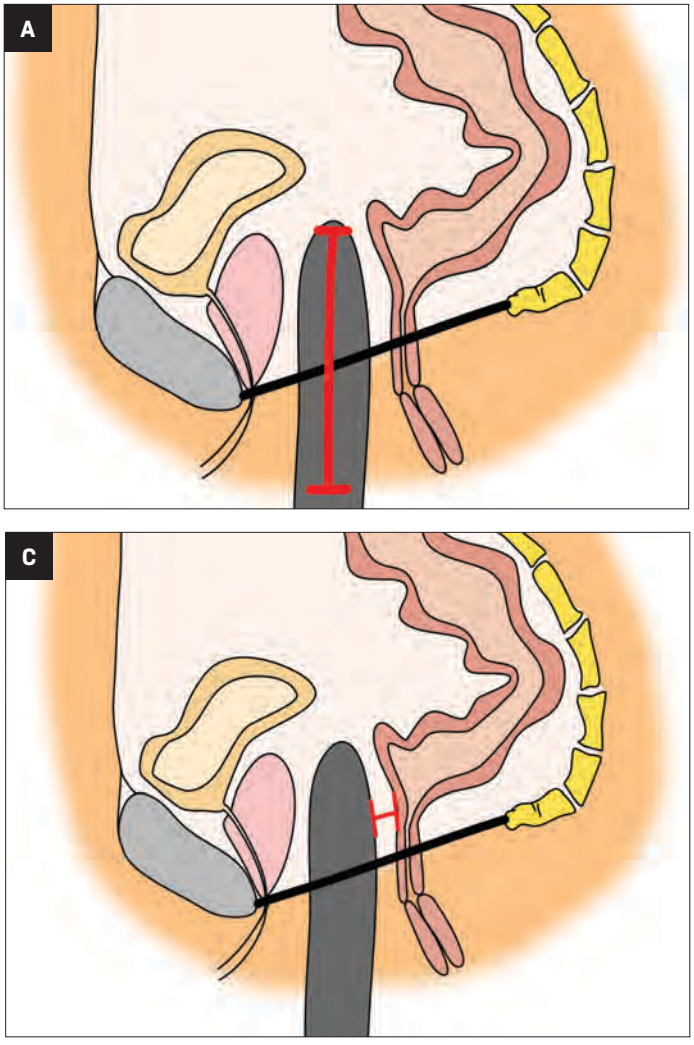


Figure 3. In postvaginoplasty patients, it is important to report the neovaginal depth (A, red line), the angle of inclination between the long axis of the neovagina and a mid-sagittal line between the inferior edge of the pubic symphysis and the tip of the last coccygeal segment (B, curved red line), and thickness of the rectovaginal septum (C, red line).

that there is a lack of PSA reference values in this population, routine PSA screening is not recommended. However, maintaining an awareness of the presence of the prostate gland in these patients and the possibility of prostate cancer, which may be seen on imaging, is important for radiologists. In patients who have undergone vaginoplasty, transvaginal ultrasound (US) may be the best imaging modality for prostate examination and preferred over digital rectal examination. Similarly, prostatitis and epididymitis may occur and should remain considerations in transgender women with elevated PSA and/or pelvic pain. Routine testicular cancer screening is also not recommended for transgender women who have not undergone orchiectomy, as they are not at increased risk. However, if there is suspicion for a testicular tumor, scrotal US should be performed.[10]

Masculinizing Hormone Therapy

Masculinizing hormone therapy may result in increased muscle mass, subcutaneous fat redistribution, and clitoral growth. Idiopathic pelvic pain is an uncommon side effect after initiation of testosterone therapy; and, while cessation of menses is expected to occur within 6 months,[10] over half of these patients experience persistent uterine bleeding. There is no consensus regarding an increased risk of endometrial hyperplasia and cancer in patients receiving masculinizing hormone therapy; thus, screening for endometrial cancer is not currently recommended.[10] Pelvic US may be indicated for evaluation of persistent or abnormal uterine bleeding; however, due to potential significant emotional and physical discomfort, clinicians may elect to pursue computed tomography (CT) or magnetic resonance imaging (MRI) evaluation as a first-line imaging choice.[1]

Masculinizing hormonal therapy with testosterone in transgender men has been linked to an increase in volume and follicular count of the ovaries; radiologists should be aware that these ovarian changes may resemble polycystic ovarian syndrome on imaging.[10] In sexually active

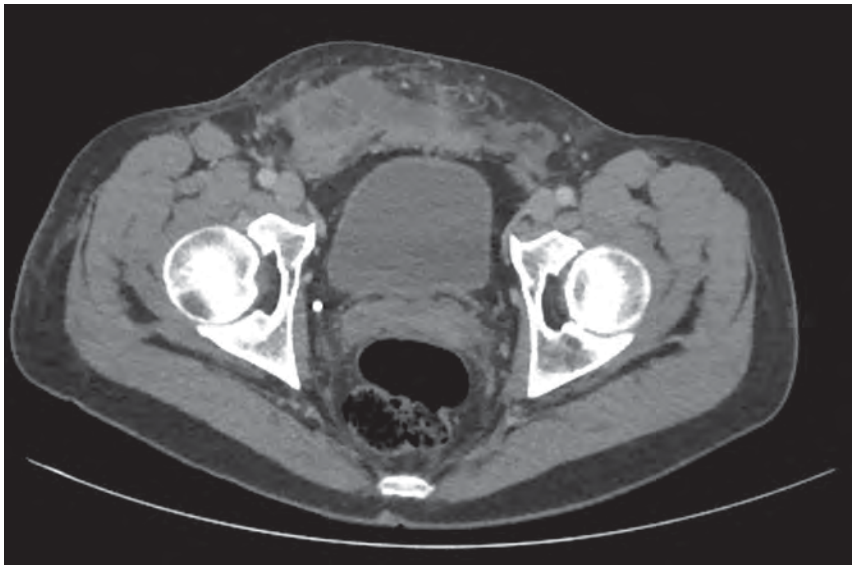


Figure 4. Postvaginoplasty patient who developed anterior pelvic wall subcutaneous abscesses, as visualized with contrast-enhanced CT abdomen and pelvis.

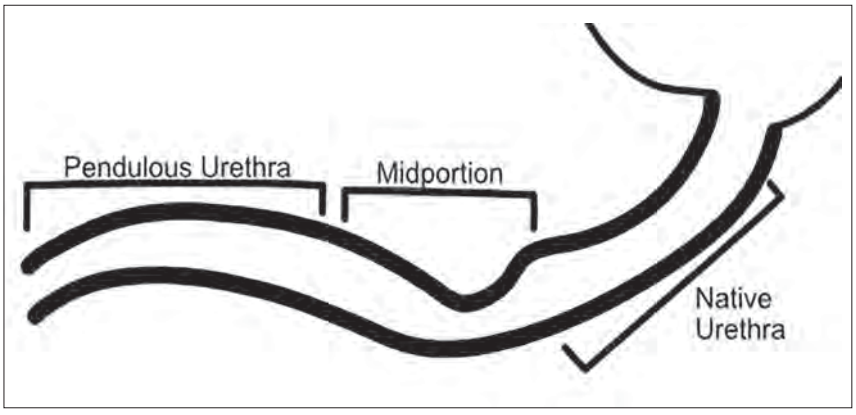


Figure 5. Neophallus urethral anatomy terminology is important when describing the locations of urethral strictures or leak.

transgender men receiving masculinizing hormone therapy and who have not undergone hysterectomy or oophorectomy, differential considerations on imaging for pelvic pain may include pregnancy, tuboovarian abscess, and pelvic inflammatory disease. Pregnancy tests prior to exposure to ionizing radiation and gadolinium administration should be considered in these patients regardless of hormone therapy administration.

Imaging Findings of Nonoperative Procedures

Silicone Injections

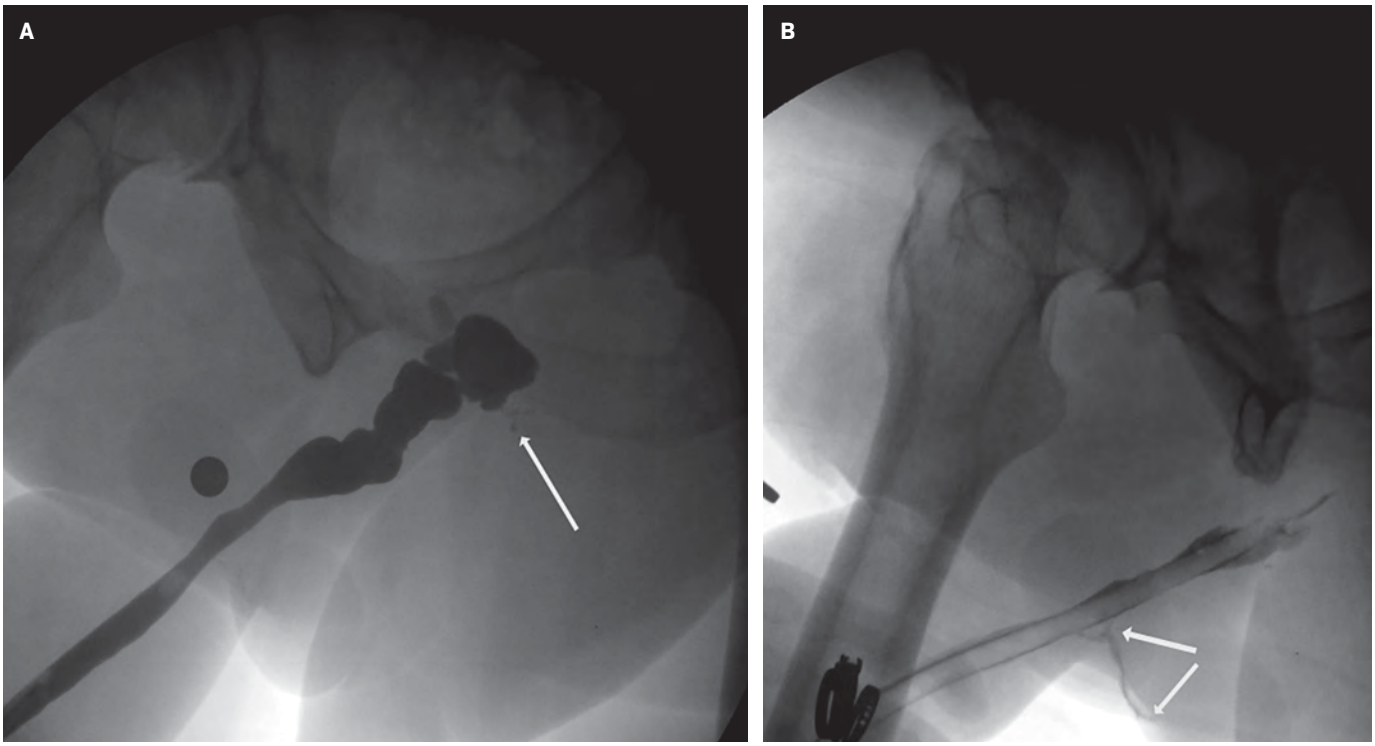
Silicone injections are now illegal in the United States; as a consequence, these procedures often are being performed in an unsupervised fashion or outside of the country. These injections are often used for breast augmentation or other soft-tissue contouring procedures.[6]

Silicone injection results in formation of soft-tissue granulomas within the subcutaneous fat, which can be visualized on imaging, including radiography and CT (Figure 1). On US, this results in the pathognomonic "snowstorm" appearance. Visualized on MRI, silicone demonstrates intermediate T1 signal intensity and increased T2 signal intensity. Silicone-selective suppression sequences can be used which result in the loss of signal in the regions of prior silicone injection. Silicone injections limit mammogram sensitivity; therefore, in this patient population, contrast-enhanced MRI is often the first-line tool for breast cancer screening.[6]

Gender-affirming Surgery

Gender-affirming surgery, which is performed to alleviate symptoms of gender dysphoria, has beneficial effects across multiple domains. Studies have demonstrated improved quality of life, sexual desire, and overall increased mood.[11] The procedure is categorized into "top surgery," which includes facial feminization or masculinization and chest reconstruction, and "bottom surgery," which includes vaginoplasty and phalloplasty.[12] For the purposes of this discussion, only abdominal imaging findings will be discussed, with a focus on bottom surgery.

Figure 6. Two patients postphalloplasty with retrograde urethrograms demonstrating postoperative leak (A, arrow) and cutaneous fistulization (B, arrows).



Feminizing Genital Surgery

Transfeminine patients often pursue gender-affirming surgery to align their external genitalia with their gender identity, as well as for receptive intercourse. Multiple components are involved, including penectomy, orchiectomy, and penoscrotal inversion or enteric vaginoplasty.[12]

Penoscrotal inversion is the most common surgical technique for vaginoplasty. After orchiectomy, penile disassembly is performed, with shortening and repositioning of the urethra. The remaining penile and scrotal skin is inverted to create a neovagina. The neovaginal flap is sometimes sutured to the sacrospinous ligament to prevent prolapse. A neoclitoris that is sensate is created from a portion of the glans penis.[6]

On CT, the neovagina appears as a collapsed tubular structure often surrounded by granulation tissue and associated fat stranding (Figure 2). In the immediate postoperative setting, the neovagina contains surgical packing material; it is essential to not label this packing as a postoperative abscess. Small perivaginal hematomas are expected. Residual erectile tissue can be visualized and is hyperenhancing; care should be taken to ensure this is not contrast extravasation in the immediate postoperative setting. In the outpatient setting, vaginal dilators may be in place. In evaluating a neovagina on imaging, including the vaginal depth, angle of inclination, and thickness of the rectovaginal septum is important (Figure 3).[6]

Postoperative complications may be seen in this patient population, with highly variable reported rates, likely owing to slight variances in operative technique. Urinary issues such as strictures requiring surgery have been reported in 13.4% of patients[11]; these are best evaluated with fluoroscopy. The average intraoperative rectal injury rate after vaginoplasty is approximately 2.4%, with 1.7% of total patients developing rectovaginal fistulization.[11] This is best evaluated with small field-of-view, contrast-enhanced pelvic MRI. Wound dehiscence is seen in approximately 12% of patients; however, the incidence of major infection is only 2.1%.[11] These complications are well-evaluated utilizing either CT or MRI, depending on the complete clinical scenario (Figure 4). In the setting of enteric vaginoplasty, which is less commonly performed today, postoperative complications often included acute peritonitis, mucorrhea, neovaginitis, malodor, rectal dysfunction, and anastomotic stricture.[11] Vaginal prolapse is also a potential postoperative complication,[12] in which case dynamic pelvic MRI is best for evaluation.

Masculinizing Genital Surgery

Masculinizing genital surgeries include hysterectomy, oophorectomy, vaginectomy, phalloplasty, metoidioplasty, and scrotoplasty — most of which are staged to reduce the

risk of significant blood loss. Two main surgical options for creating a neophallus include metoidioplasty and phalloplasty, with phalloplasty being the most complex gender-affirming surgery; it often requires a multidisciplinary team approach. The goals of creating a neophallus might include the ability to urinate while standing, maintain sensation, and potentially participate in penetrative sexual intercourse. Numerous surgical techniques exist; the most common and currently preferred technique is the radial forearm free flap. Anterolateral thigh flap, abdominal flap, and latissimus dorsi free flap are additional but less frequently utilized techniques. Metoidioplasty is a separate surgical technique in which the neophallus is created from a hormonally hypertrophied clitoris; however, this can limit neophallus length and prevent the ability to engage in sexual intercourse in some patients.[6]

Owing to the number of surgical techniques, data varies in the literature regarding postoperative complications for masculinization surgery. Overall, metoidioplasty is a less-invasive and lower-risk procedure than phalloplasty.[12] In patients undergoing phalloplasty, wound dehiscence occurs in 9.8%. This is adequately evaluated with CT to assess for the presence of underlying abscess.[11] It is essential to monitor early perfusion of the flap in the immediate postoperative setting using ultrasound with color doppler as well.[4] Minor urethral issues (including stenoses, strictures, or fistulas which resolved with treatment) occurred in 24% of patients, with major urethral complications seen in an additional 24.4% of patients.[11] These urinary complications are well-evaluated fluoroscopically with retrograde urethrograms (Figures 5 and 6). Reported rates of urethral issues in metoidioplasty are lower, with minor issues in 3.9% of patients, and major urethral issues in 11.4%. However, it was also reported that 15% of patients who underwent metoidioplasty elected to undergo a secondary phalloplasty.[11] In phalloplasty patients, donor site complications are also a consideration, and include graft necrosis, excessive scarring, paresthesias, and limitation of wrist motion. However, these are generally beyond the scope of practice for abdominal radiologists.[11]

Erectile devices can also be considered in patients who intend to engage in penetrative intercourse; they are usually placed months after the neophallus has healed. These devices demonstrate higher rates of complications in postoperative transgender patients compared to cis-gender individuals requiring prosthesis.[12] This difference is hypothesized to be secondary to earlier age of implantation and lack of supportive cavernosal fascial layers. These potential complications include mechanical device failure, malposition, and infection, and are well evaluated with CT.[4] Testicular prostheses, which are usually either silicone or saline filled, may also be placed. Complications of these prostheses include malposition, rupture, and infection, all of which are well evaluated with CT or MRI[4].

Creating an Inclusive Environment

As accessibility to gender-affirming care increases, it is essential for radiologists not only to increase their knowledge of the imaging findings but also to ensure that imaging centers improve their inclusivity to ensure positive patient experiences. The 2015 U.S. Transgender Survey found that 33% of responders had at least one negative experience in a healthcare setting related to their gender identity.[3] Grimstad, et al, surveyed over 500 transgender and nonbinary patients, and more than 70% reported having one or more negative experience during an imaging encounter.[13] These included not being asked their correct pronouns, incorrect use of pronouns, personnel discomfort, and failure to protect privacy. Additionally, almost 25% were misgendered in the radiology report.[13]

Initiating staff training covering respectful communication, including correct use of pronouns, and cultural sensitivity and gender-affirming care standards, as well as training in proper imaging techniques for these patients, are essential for medical imaging centers. Radiology residency programs should incorporate LGBTQ culture competency, as well. Gender-neutral restrooms/ changing facilities, as well as LGBTQ-affirming reading materials and signage are also essential to creating a positive and welcoming patient experience. Integrating these issues into organizational accreditation guidelines, such as those provided by the American College of Radiology, would be impactful.[13]

Conclusion

The rapid evolution of transgender healthcare across the world is allowing for greater access to care and overall improved quality of life for many with gender dysphoria.[4] As more transgender patients seek gender-affirming surgery, it is essential for abdominal radiologists to remain current on the latest surgical techniques, their potential complications, and the appropriate imaging modalities to best evaluate them. Additionally, as they seek to provide adequate imaging interpretations, abdominal radiologists should strive for excellence in the transgender patient experience. This will help to maintain their role as integral members of the multidisciplinary transgender care team and to perpetuate a culture of inclusivity within the medical field.

References

1) Stowell JT, Zavaletta VA, Carroll EF, Grimstad FW. Multidisciplinary approach to imaging for gender-affirming surgery: engaging surgeons, radiologists, and patients to ensure a positive imaging experience. *Ann Transl Med*. Apr 2021;9(7):610. doi:10.21037/atm-20-6431.

2) National LGBT Health Education Center: Glossary of LGBT Terms for Health Care Teams. Updated June 2017. Accessed March 13, 2022, https://www.lgbtqiahealtheducation.org/wp-content/uploads/2018/03/Glossary-2018-English-update-1.pdf.

3) Flores AR, Herman JL, Gates GJ, Brown TNT. How many adults identify as transgender in the United States? Updated 2016. https://williamsinstitute.law.ucla.edu/wp-content/uploads/Trans-Adults-US-Aug-2016.pdf. Accessed March 13, 2022,

4) Stowell JT, Horowitz JM, Thomas S. Gender-affirming surgical techniques, complications, and imaging considerations for the abdominal radiologist. *Abdom Radiol (NY)*. Jul 2020;45(7):2036-2048. doi:10.1007/s00261-019-02398-1.

5) James SE, Herman JL, Rankin S, Keisling M, Mottet L, Anafi M. The Report of the 2015 U.S. Transgender Survey. *Washington, DC: National Center for Transgender Equality*. 2016;

6) Stowell JT, Grimstad FW, Kirkpatrick DL, et al. Imaging findings in transgender patients after gender-affirming surgery. *Radiographics*. Sep-Oct 2019;39(5):1368-1392. doi:10.1148/rg.2019190010

7) Nguyen HB, Chavez AM, Lipner E, et al. Gender-affirming hormone use in transgender individuals: impact on behavioral health and cognition. *Current Psychiatry Reports*. 2018/10/11 2018;20(12):110. doi:10.1007/s11920-018-0973-0.

8) Deutsch MB. Overview of feminizing hormone therapy. https://transcare.ucsf.edu/guidelines/feminizing-hormone-therapy. Accessed April 4, 2022.

9) de Nie I, de Blok CJM, van der Sluis TM, et al. Prostate cancer incidence under androgen deprivation: nationwide cohort study in trans women receiving hormone treatment. *J Clin EndocrinolMetabol*. 2020;105(9):e3293-e3299. doi:10.1210/clinem/dgaa412.

10) Sowinski JS, Gunderman RB. Transgender patients: what radiologists need to know. *AJR Am J Roentgenol*. May 2018;210(5):1106-1110. doi:10.2214/AJR.17.18904.

11) Oles N, Darrach H, Landford W, et al. Gender affirming surgery: a comprehensive, systematic review of all peer-reviewed literature and methods of assessing patient-centered outcomes (Part 2: Genital Reconstruction). *Ann Surg*. Jan 1 2022;275(1):e67-e74. doi:10.1097/sla.0000000000004717.

12) Hassan O, Sun D, Jha P. Imaging in gender affirmation surgery. *Curr Urol Rep*. Jan 30 2021;22(2):14. doi:10.1007/s11934-020-01029-3.

13) Grimstad FW, Stowell JT, Gaddis M. Survey of experiences of transgender and gender nonbinary patients during imaging encounters and opportunities for improvement. *AJR Am J Roentgenol*. Nov 2020;215(5):1136-1142. doi:10.2214/ajr.19.22558

Pulmonary Embolism Response Teams: An Integrated Approach to Patient Care

Merry Ellen Barnett, MD; Sukhdeep Grewal, MD; Andrew D Mihalek, MD; Louise Man, MD; Aditya M Sharma, MBBS; Minhaj S Khaja, MD, MBA

Pulmonary embolism (PE) is the third-leading cause of cardiovascular death in the United States, with an annual mortality of approximately 100,000 people per year.[1] While anticoagulation is the primary treatment for acute pulmonary embolism, additional reperfusion strategies exist, including systemic thrombolysis, surgical embolectomy, extracorporeal membrane oxygenation (ECMO) and catheter-directed therapies.

Owing to variations in major professional society recommendations and a lack of data from robust clinical trials, the optimal management for PE remains a topic of debate.[2–5] As such, the pulmonary embolism response team (PERT) concept was created in response to rapid advances in therapeutic options and increasing recognition of the complexity involved in the management of patients afflicted by PE.[6]

The ultimate goal of the PERT is to mobilize rapid medical decision making to improve morbidity and mortality associated with intermediate- and high-risk PE. The goal of this paper is to provide a narrative review of the pulmonary embolism response process, provide an overview of state-of-the-art PE care, and to highlight the critical role of the radiologist (diagnostic and interventional) in PERT.

Affiliation: University of Virginia Health, Charlottesville, Va.
Disclosures: Dr Sharma reports receiving speaking honoraria and research support from Boston Scientific and research support from Vascular Medcure. Dr Khaja reports receiving speaking honoraria and research support from Boston Scientific; speaking honoraria from Medtronic and Penumbra, and research support from the SIR Foundation.

How the PERT Works

The goal of a PERT is to facilitate rapid, multidisciplinary medical decision making for highly complex and time-sensitive clinical scenarios. The structure of the multidisciplinary PERT varies by institution but can include participants from emergency medicine, pulmonary/critical care medicine, cardiology, vascular medicine, hematology, diagnostic and interventional radiology, vascular surgery, cardiac surgery, and pharmacy. Figure 1 depicts how a PERT activation works at our institution. The PERT system is activated either by calling or paging the PERT on-call member, who then obtains relevant information and coordinates the multidisciplinary discussion. This allows patients with high-risk and select intermediate-risk PEs to receive expedited treatment.

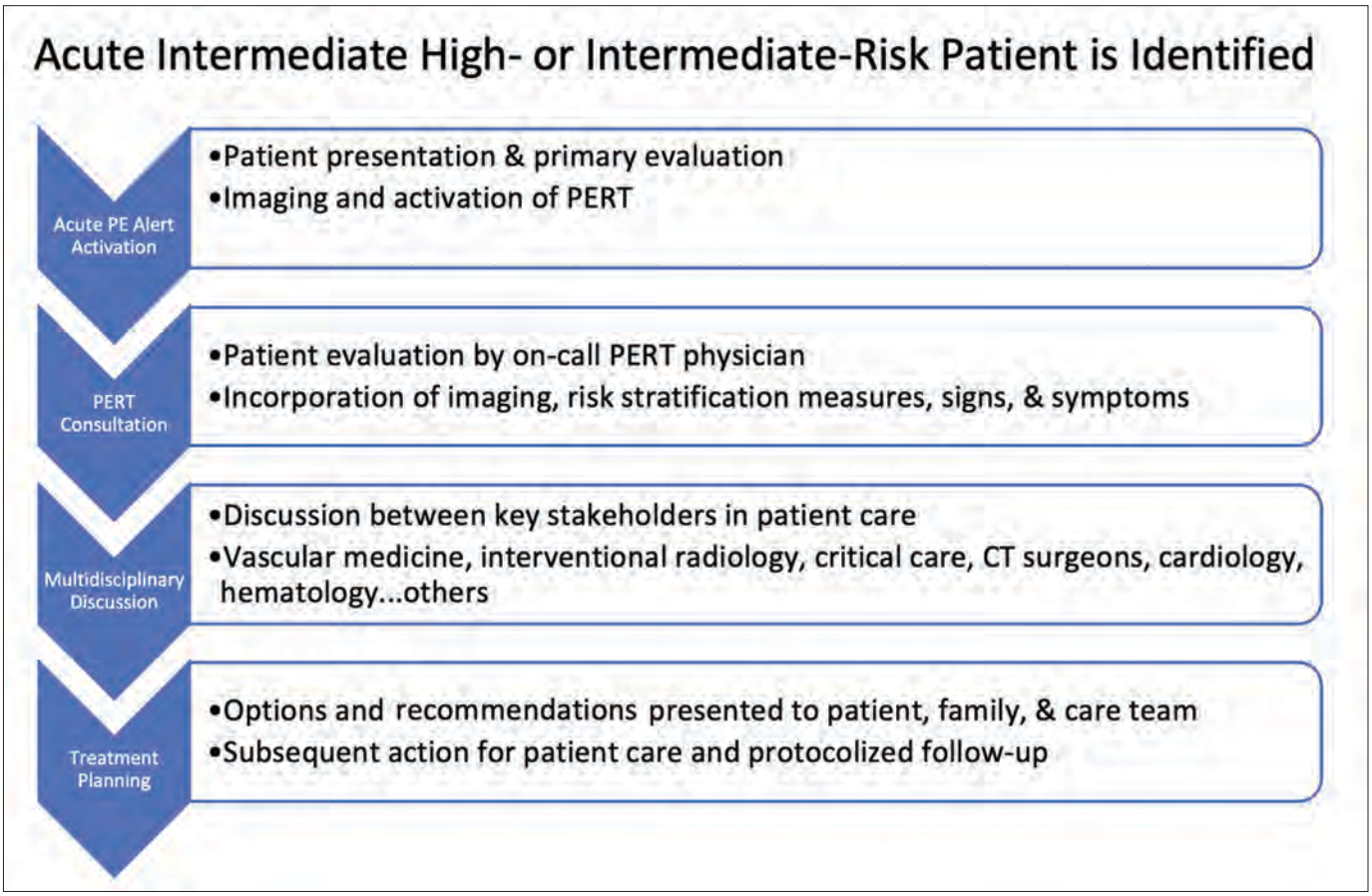
Patient Evaluation

The acute clinical presentation of PE can vary widely. Common signs and symptoms include dyspnea, pleuritic chest pain, tachycardia, presyncope, and hemoptysis. Given their ambiguous nature, risk stratification scoring models such as Wells Criteria, the pulmonary embolism rule-out criteria (PERC) rule, or the Geneva score are used to help derive the pretest probability of a PE in patients presenting in the outpatient emergent setting.[7] These scoring models, along with the use of the d-dimer test, establish the need for further radiographic testing.

Imaging and Risk Stratification

With sensitivity of 83% and specificity of 95% as reported in the PIOPED II study, computed tomography pulmonary angiography (CTPA) is the imaging modality of choice in diagnosing acute PE.[8] Findings will include either occlusive or nonocclusive filling defects in the central, lobar, segmental, and/or sub-segmental pulmonary artery branches, depending on the quality of the study. CTPA can determine whether a clot is acute or chronic and oftentimes is

Figure 1. A depiction of PERT activation.



able to identify right ventricular (RV) dysfunction (discussed below). Acute clots will often form acute angles with the arterial wall, and the arterial branch may be enlarged compared to patent vessels.[9] Additionally, CTPA will also be able to detect alternative diagnoses other than acute PE, if present. In patients with poor renal function or allergies to iodinated contrast, ventilation/perfusion (V/Q) imaging may be performed. Modified PIOPED II criteria specify one of three interpretations: PE present, nondiagnostic, or negative. PE is diagnosed when two or more large, mismatched segmental perfusion defects are present. A normal perfusion scan can exclude PE.[8]

Once a PE is confirmed on imaging, patients are risk-stratified to identify the probability of early mortality and to determine appropriate treatment. Right ventricular failure is the primary cause of short-term death in acute PE. Imaging findings of right heart dysfunction (often denoted "right heart strain") include flattening or paradoxical bowing of the intraventricular septum, right ventricular enlargement, and contrast reflux into the inferior vena cava and hepatic veins.[10] Right ventricular enlargement is defined by a ratio of RV diameter to LV diameter greater than 0.9.[11] The RV/LV ratio can be measured on axial images or multiplanar reconstruction images in the four-chamber axial view. Measurements should be made from endocardial margins, including papillary and trabecular muscles.[12] Performed correctly, the different measurement techniques have not shown significant differences in predicting 30-day mortality from acute PE. Figures 2 and 3 depict normal and abnormal RV/LV ratios. However, a CT finding of right heart enlargement has been shown to predict early death (at 30 days) in patients presenting with acute PE.[13]

Clinical markers of poor RV health, including tachycardia, hypotension, tachypnea, and hypoxemia, are incorporated into clinically validated scoring systems such as the PE Severity Index (PESI) to predict 30-day mortality.[14] The European Society of Cardiology (ESC) has used the PESI score in combination with cardiac biomarkers (troponin, B-type natriuretic peptide [BNP], lactate, and creatine) and advanced cardiac imaging (echocardiography) to provide a unified stratification sys-

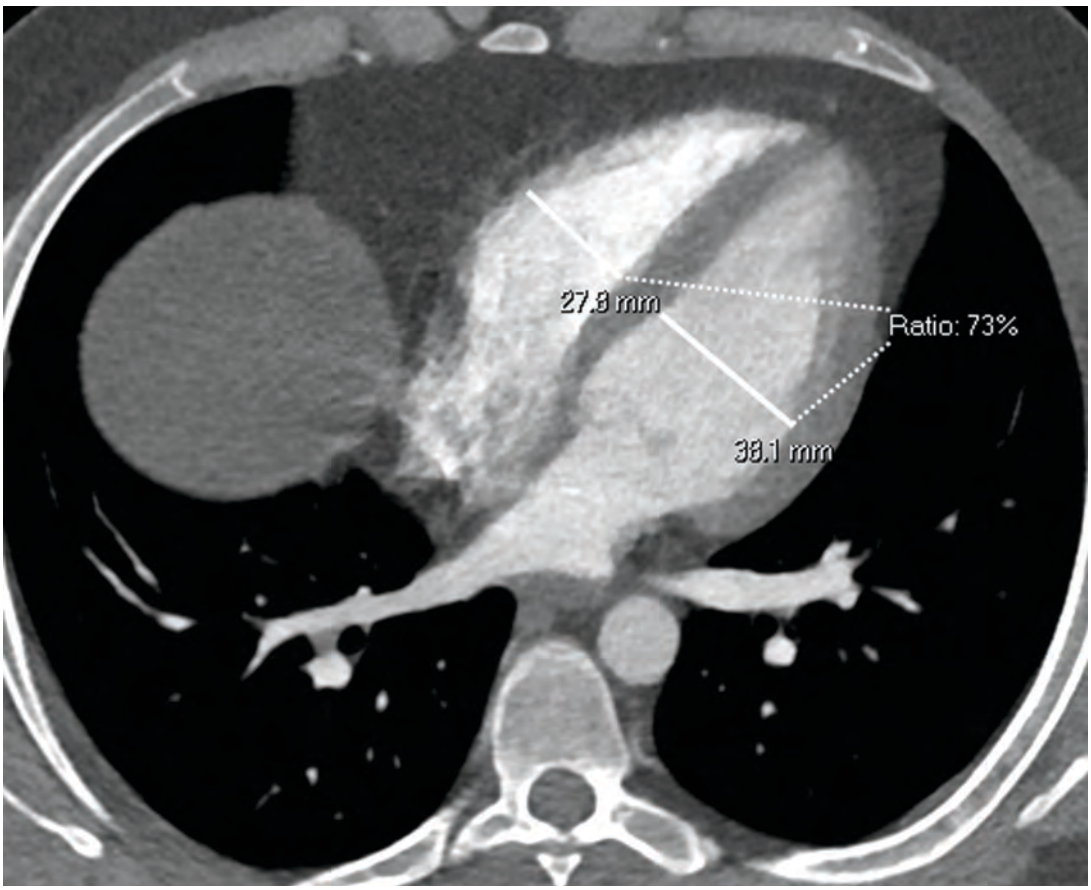
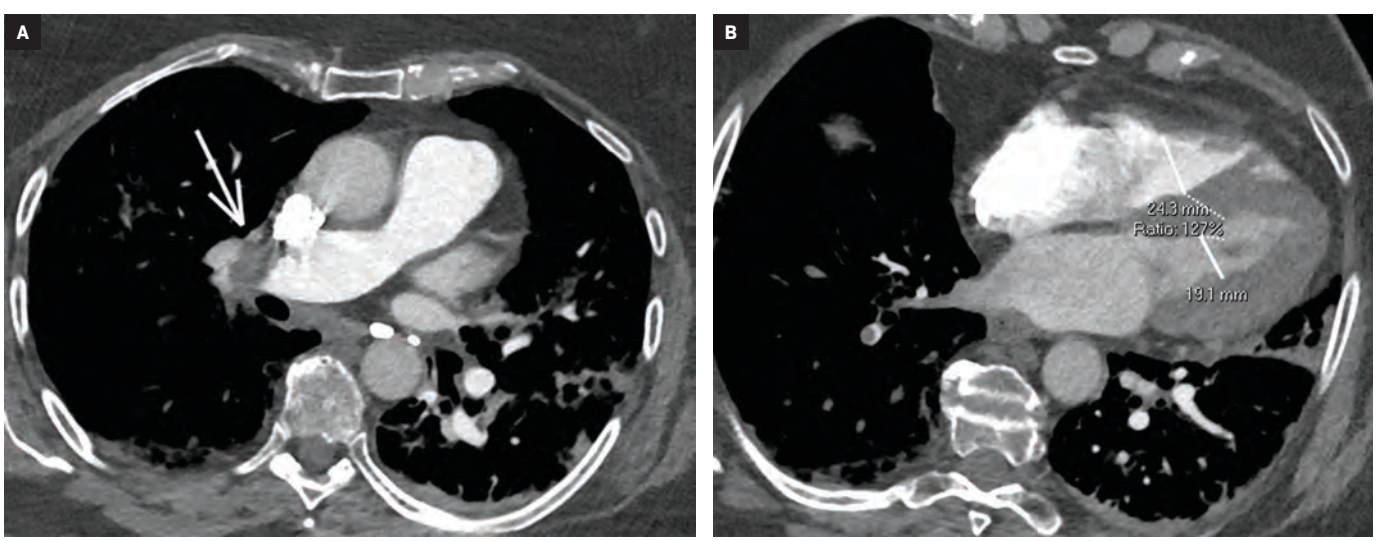


Figure 2. Normal RV/LV ratio measuring 0.73.

Figure 3. (A) Nearly occlusive right pulmonary artery filling defect (arrow). (B) CT findings of right-heart strain, including increased RV/LV ratio measuring 1.23, with slight flattening of the intraventricular septum.



tem that offers treatment options.[2] According to the ESC model, any patient who exhibits hemodynamic instability is considered "high risk" for early mortality. Hemodynamic instability is defined by cardiac arrest, persistent systolic blood pressure less than 90 mmHg for greater than 15 minutes, use of vasopressors to achieve a systolic blood pressure ≥ 90 mmHg with evidence of end-organ hypoperfusion, or a systolic blood pressure drop ≥ 40 mmHg from the patient's baseline. High-risk patients are offered hemodynamic support and considered for reperfusion therapies as appropriate.[15] Patients who are otherwise hemodynamically

In Planning for Brain Metastases Treatment, Imaging may be the Missing Link in Cost Containment[1]

When faced with a patient presenting with metastatic brain cancer, determining whether to use up-front stereotactic radiosurgery (SRS) vs. first treating with whole brain radiotherapy (WBRT) is a significant clinical decision.

WBRT: The whole story on cognitive impairment

While whole brain radiotherapy (WBRT) has been the main treatment option for many years, experts agree that it often results in cognitive deterioration and a negative impact on quality of life. This mental decline has a devastating impact on patients and their families and adds ongoing costs for the healthcare systems managing these symptoms.

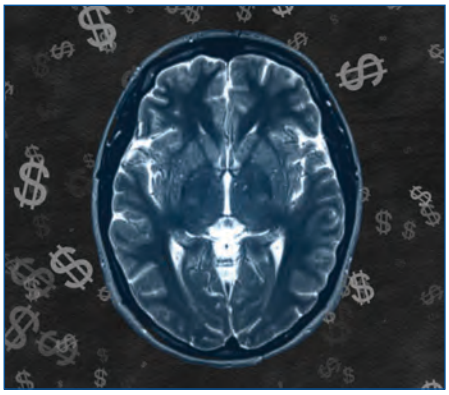
Using WBRT instead of SRS in some patients is estimated to decrease the total costs of brain metastasis management, though with increased toxicity.

SRS: Fewer side effects but greater risk of missed tumors

The cost of upfront SRS is the greatest contributor to cost of brain metastasis management.[1] SRS is often more expensive than WBRT. What's more, multiple applications of SRS can increase the cost of treatment greatly.

Stereotactic radiosurgery (SRS) has far fewer side effects, but upfront use of SRS is expensive and can carry the risk of missed tumors, requiring repeat procedures such as salvage SRS.[1]

Number of lesions and lesion size are key factors to be considered when determining the treatment plan for these patients. It follows that increased diagnostic information and accuracy could be beneficial in directing the proper therapy and improving overall long-term patient outcomes and containing costs. Getting the diagnosis right the first time is crucial to ensure proper treatment begins quickly, and high cost/high stakes procedures such as SRS need precise surgical planning.



Getting the diagnosis right the first time is crucial to ensure proper treatment begins quickly.

What does optimal visualization mean for outcomes and cost?

For surgical planning with SRS, radiologists need the best visualization achievable to accurately count the number and size of the lesions. These metrics are the key predictors of the need for SRS,[1] WBRT, or a combination of both.

By selecting the ideal contrast agent and equipment protocols, neuroradiologists can identify the proximate numbers of metastases for upfront treatment and reduced salvage treatment occurrences.

The role of radiology

As medical care for oncology patients continues to evolve, it will be increasingly important to assess the cost of various interventions given the often-limited life expectancy of cancer patients, the rising costs of cancer therapy, and the increasing prevalence of cancer in an aging population.

Through seeing all the tumors and tumor borders as clearly as technology allows, radiology can play a part in ensuring that proper treatment can begin quickly, while containing costs through optimized patient care. Efforts to carefully manage treatment approaches require improvements in protocol design, contrast administration in imaging, and utilizing multimodal imaging approaches.

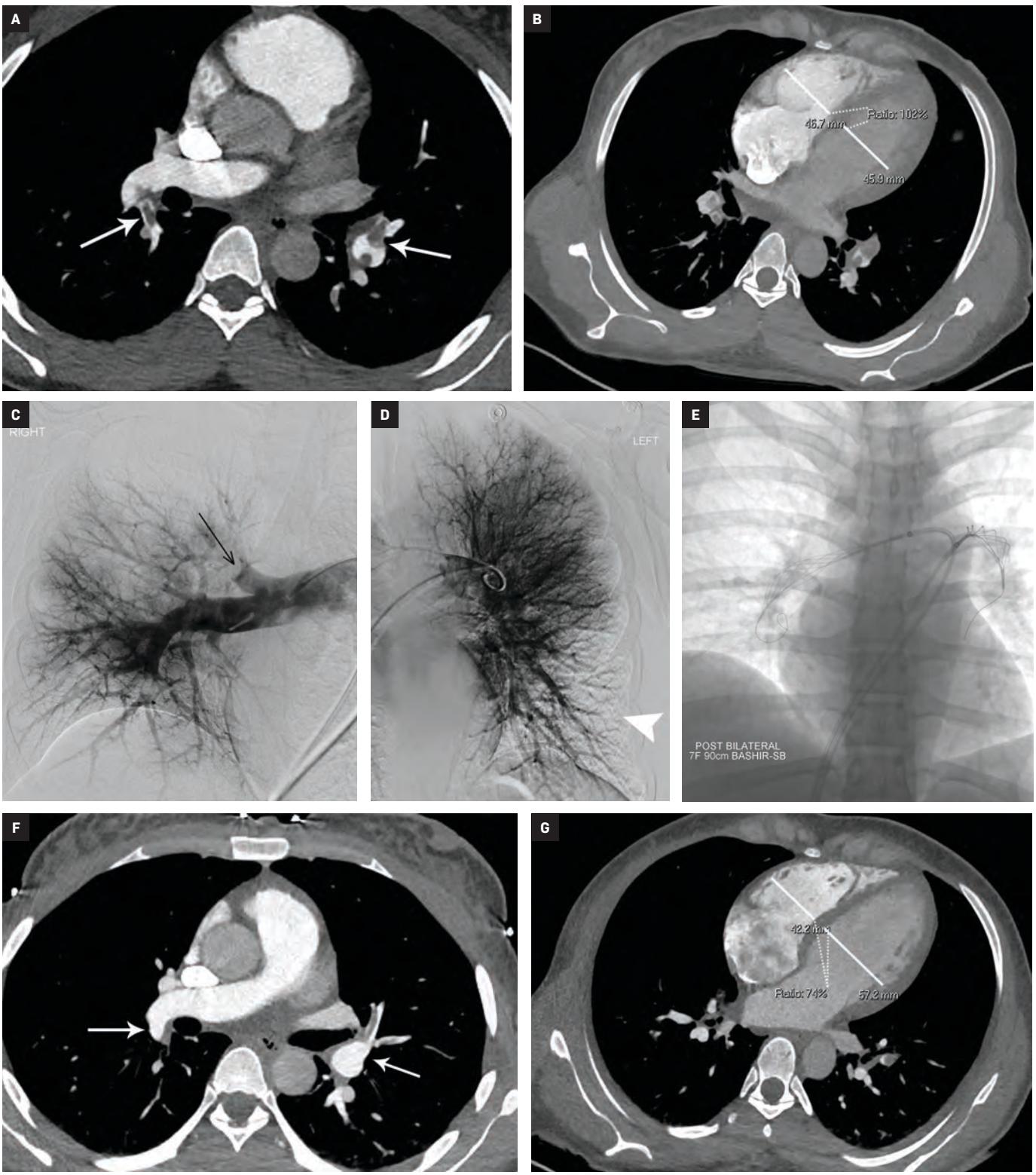
In this era of precision medicine, radiology departments' contribution to this improved standard of care will have significant short and long-term implications by reducing cost of care, providing a more proximate diagnosis, and ensuring optimal patient outcomes. ■

Reference: 1. Shenker, R. F., McTyre, E. R., Taksler, D et al. Analysis of the drivers of cost of management when patients with brain metastases are treated with upfront radiosurgery. *Clin Neurol Neurosurg.* 2019 Jan;176:10-14.

BRACCO
LIFE FROM INSIDE

For more information on MRI contrast agents, precision medicine, and reducing cost of care please visit braccomr.com

Figure 4. An adult presents with acute intermediate high-risk pulmonary embolism. (A) CTPA demonstrates filling defects in the right lower-lobar superior segmental artery and left lower-lobar and segmental arteries (arrows). (B) Right-heart strain demonstrated by elevated RV/LV ratio of 1.02. (C) Right pulmonary angiogram demonstrates multifocal filling defects, including abrupt cutoff of the right upper-lobar artery (arrow). (D) Left lower pulmonary angiogram demonstrates decreased perfusion to the left lower lobe (arrowhead). (E) Placement of bilateral Bashir endovascular catheters (Thrombolex, New Britain, PA) for overnight tPA infusion. (F,G) Repeat CTPA on post-procedure day 2 demonstrates improved thrombus burden in the bilateral central pulmonary arteries (arrows). Normalized RV/LV ratio measures 0.74.



stable are stratified into the low-risk or intermediate-risk categories.[2]

Patient Management

Anticoagulation is the mainstay of acute PE therapy. Initial preference for anticoagulation is highlighted using low-molecular weight heparin (LMWH) or fondaparinux, owing to improved 30-day mortality, decreased risk of hemorrhage, and decreased recurrence of thrombotic events. Unfractionated heparin remains an option in patients with contraindications to LMWH.[16,17]

Whether a patient receives advanced therapies in addition to anticoagulation depends on their risk stratification. High-risk patients should receive appropriate hemodynamic and respiratory support and be considered for reperfusion therapies such as systemic thrombolysis, catheter-directed treatment, and surgical embolectomy.

Systemic thrombolysis involves the administration of recombinant tissue-type plasminogen activator (rtPA) to improve pulmonary artery obstruction, pulmonary artery pressure, and pulmonary vascular resistance. rtPA use in high-risk PE patients is associated with improved mortality.[18,19] Absolute contraindications to systemic thrombolysis include history of hemorrhagic stroke, recent ischemic stroke, intracranial neoplasm, recent major trauma, and active bleeding. Relative contraindications to systemic lysis include hypertension (systolic BP > 180 mmHg), recent non-intracranial bleeding, recent surgery/invasive procedures, ischemic stroke > 3 months previous, or age > 75.

Appropriate hemodynamic and respiratory support can include high-flow oxygen, mechanical ventilation, vasopressors, inotropes, and mechanical circulatory support. Veno-arterial extracorporeal membrane oxygenation (VA-ECMO) is helpful in patients with circulatory collapse and/or cardiac arrest with or without additional therapies.[20] However, data from randomized controlled trials is lacking to support the efficacy and safety of general ECMO use.[15,21]

A consensus statement from the PERT Consortium suggests surgical embolectomy in high-risk patients with contraindications to, or failure of, systemic or catheter directed thrombolysis or thrombectomy. A similar recommendation is suggested for intermediate-risk patients with significant comorbidities that could lead to clinical deterioration.[22] Right-heart thrombi and thrombus-in-transit are other scenarios where surgical embolectomy may be considered as first-line therapy.[23] Perioperative mortality in the past could be as high as 11%, but with improved patient selection and surgical techniques, mortality has fallen significantly.

The goals of interventional therapies in patients considered intermediate risk or high risk for early mortality are to avoid hemodynamic collapse and expedite symptom resolution. The risks and benefits of thrombolysis are more closely considered in intermediate-risk PE and counterbalanced by untoward outcomes. A variety of endovascular methods can be used to treat acute PE; they include catheter-directed thrombolysis, aspiration and mechanical thrombectomy, and a combination of interventions.

Several single-arm studies of specific devices have shown a reduction in RV/LV ratio at 24 and 48 hours, which is considered a surrogate endpoint. [24-28] High-quality randomized data showing a reduction in mortality and progression of disease to chronic thromboembolic disease is lacking.

An early randomized study of CDT versus unfractionated heparin (n=59) found a significant reduction in RV/LV ratio at 24 hours in the CDT group. Ninety-day RV/LV ratio was also better in the CDT group, although not significant.[29] A meta-analysis of ultrasound-assisted CDT for PE found a reduction in pulmonary artery systolic pressure, RV/LV ratio, and an improvement in the cardiac index in over 2,000 patients.[25] Multidisciplinary PERT teams are helpful in weighing the risks and benefits of each treatment.

The Radiologist's Role on the PERT

Diagnostic radiologists are truly the gatekeepers of advanced PE interventions and other treatment modalities. Their appropriate and prompt identification of acute PE and additional parameters such as right-heart strain can lead to the administration of all appropriate interventions in a timely manner, as discussed in the "Risk Stratification" section. We have found that consistently including the RV/ LV ratio on CTPA and writing "consider paging PERT" on the report is very helpful for prompt treatment plan discussion by the PERT.[30] Given the advances in and increased use of endovascular catheter-based interventions, the role of interventional specialists is also paramount in managing patients with PE.

Conclusion

Historically, the management of patients with acute pulmonary embolism, especially those at intermediate-high risk, has been haphazard, resulting in delay of potentially life-saving PERT programs have been shown to improve survival and other clinically relevant outcomes. [30-33] To achieve improved outcomes, a team-based approach involving clinicians from the initial patient encounter (emergency physicians), consultants (vascular medicine, hematologists, and critical care physicians), diagnostic and interventionalist radiologists, and cardiothoracic surgeons, is required at

times. Developing these programs can streamline patient care and result in better outcomes in PE patients at high risk for early mortality.

References

1) Wendelboe AM, Raskob GE. Global burden of thrombosis. *Circ Res.*2016;118(9):1340-1347.

2) Konstantinides SV, Meyer G, Becattini C, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS): The Task Force for the diagnosis and management of acute pulmonary embolism of the European Society of Cardiology (ESC). *Eur Heart J*. 2020;41(4):543-603.

3) Giri J, Sista AK, Weinberg I, et al. Interventional therapies for acute pulmonary embolism: current status and principles for the development of novel evidence: A scientific statement from the American Heart Association. *Circulation*. 2019;140(20):e774-e801.

4) Jaff MR, McMurtry MS, Archer SL, et al. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation*. 2011;123(16):1788-1830.

5) Stevens SM, Woller SC, Baumann Kreuziger L, et al. Executive Summary: Antithrombotic therapy for VTE disease: Second update of the CHEST guideline and expert panel report. *Chest*. 2021;160(6):2247-2259.

6) Provias T, Dudzinski DM, Jaff MR, et al. The Massachusetts General Hospital Pulmonary Embolism Response Team (MGH PERT): creation of a multidisciplinary program to improve care of patients with massive and submassive pulmonary embolism. *Hosp Pract 1995*. 2014;42(1):31-37.

7) Raja AS, Greenberg JO, Qaseem A, et al. Evaluation of patients with suspected acute pulmonary embolism: best practice advice from the clinical guidelines committee of the American College of Physicians. *Ann Intern Med*. 2015;163(9):701-711.

8) ostman HD, Stein PD, Gottschalk A, Matta F, Hull R, Goodman L. Acute pulmonary embolism: sensitivity and specificity of ventilation-perfusion scintigraphy in PIOPED II study. *Radiology*. 2008;246(3):941-946.

9) Wittram C, Maher MM, Yoo AJ, Kalra MK, Shepard JA, McLoud TC. CT angiography of pulmonary embolism: diagnostic criteria and causes of misdiagnosis. *Radiographics*. 2004;24(5):1219-1238.

10) Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med*. 2006;354(22):2317-2327.

11) Sista AK, Kuo WT, Schiebler M, Madoff DC. Stratification, imaging, and management of acute massive and submassive pulmonary embolism. *Radiology*. 2017;284(1):5-24.

12) Lu MT, Demehri S, Cai T, et al. Axial and reformatted four-chamber right ventricle-to-left ventricle diameter ratios on pulmonary CT angiography as predictors of death after acute pulmonary embolism. *AJR Am J Roentgenol*. 2012;198(6):1353-1360.

13) Schoepf UJ, Kucher N, Kipfmueller F, Quiroz R, Costello P, Goldhaber SZ. Right ventricular enlargement on chest computed tomography: a predictor of early death in acute pulmonary embolism. *Circulation*. 2004;110(20):3276-3280.

14) Dudzinski DM, Giri J, Rosenfield K. Interventional treatment of pulmonary embolism. *Circ Cardiovasc Interv*. 2017;10(2):e004345.

15) Elbadawi A, Mentias A, Elgendy IY, et al. National trends and outcomes for extra-corporeal membrane oxygenation use in high-risk pulmonary embolism. *Vasc Med*. 2019;24(3):230-233.

16) Robertson L, Jones L. Fixed dose subcutaneous low molecular weight heparins versus adjusted dose unfractionated heparin for the initial treatment of venous thromboembolism. *Cochrane Database Syst Rev*. 2017.;2(2):CD001100. doi: 10.1002/14651858.CD001100.pub4.

17) Smith SB, Geske JB, Maguire JM, Zane NA, Carter RE, Morgenthaler TI. Early anticoagulation is associated with reduced mortality for acute pulmonary embolism. *Chest*. 2010;137(6):1382-1390.

18) Marti C, John G, Konstantinides S, et al. Systemic thrombolytic therapy for acute pulmonary embolism: a systematic review and meta-analysis. *Eur Heart J*. 2015;36(10):605-614.

19) Kline JA, Nordenholz KE, Courtney DM, et al. Treatment of submassive pulmonary embolism with tenecteplase or placebo: cardiopulmonary outcomes at 3 months: multicenter double-blind, placebo-controlled randomized trial. *J Thromb Haemost JTH*. 2014;12(4):459-468.

20) Strobel R, Khaja M, Peruri A, et al. Veno-arterial extracorporeal membrane oxygenation and thrombectomy for massive pulmonary embolism. *Heart Surg Forum*. 2022;25(2):E241-E242.

21) Kaso ER, Pan JA, Salerno M, et al. Venoarterial extracorporeal membrane oxygenation for acute massive pulmonary embolism: A meta-analysis and call to action. *J Cardiovasc Transl Res*. 2022;15(2):258-267.

22) Rivera-Lebron B, McDaniel M, Ahrar K, et al. Diagnosis, treatment and follow up of acute pulmonary embolism: Consensus practice from the PERT Consortium. *Clin Appl Thromb Hemost*. 2019;25:1076029619853037.

23) Keeling WB, Sundt T, Leacche M, et al. Outcomes after surgical pulmonary embolectomy for acute pulmonary embolus: a multi-institutional study. *Ann Thorac Surg*. 2016;102(5):1498-1502.

24) Sista AK, Horowitz JM, Tapson VF, et al. Indigo aspiration system for treatment of pulmonary embolism: results of the EXTRACT-PE trial. *JACC Cardiovasc Interv*. 2021;14(3):319-329.

25) Pei DT, Liu J, Yaqoob M, et al. Meta-analysis of catheter directed ultrasound-assisted thrombolysis in pulmonary embolism. *Am J Cardiol*. 2019;124(9):1470-1477.

26) Tu T, Toma C, Tapson VF, et al. A prospective, single-arm, multicenter trial of catheter-directed mechanical thrombectomy for intermediate-risk acute pulmonary embolism: The FLARE study. *JACC Cardiovasc Interv*. 2019;12(9):859-869.

27) iazza G, Hohlfelder B, Jaff MR, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: The SEATTLE II study. *JACC Cardiovasc Interv*. 2015;8(10):1382-1392.

28) Aggarwal V, Giri J, Nallamothu BK. Catheter-based therapies in acute pulmonary embolism: the good, the bad, and the ugly. *Circ Cardiovasc Interv*. 2020;13(6):e009353.

29) Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation*. 2014;129(4):479-486.

30) Myc LA, Solanki JN, Barros AJ, et al. Adoption of a dedicated multidisciplinary team is associated with improved survival in acute pulmonary embolism. *Respir Res*. 2020;21(1):159.

31) Wright C, Elbadawi A, Chen YL, et al. The impact of a pulmonary embolism response team on the efficiency of patient care in the emergency department. *J Thromb Thrombolysis*. 2019;48(2):331-335.

32) Wright C, Goldenberg I, Schleede S, et al. Effect of a multidisciplinary pulmonary embolism response team on patient mortality. *Am J Cardiol*. 2021;161:102-107.

33) Kabrhel C, Rosovsky R, Channick R, et al. A multidisciplinary pulmonary embolism response team: initial 30-month experience with a novel approach to delivery of care to patients with submassive and massive pulmonary embolism. *Chest*. 2016;150(2):384-393.

Non-neoplastic Cystic Lesions of the Central Nervous System
Part 1: Developmental Cysts

Orest Kayder, MD; Hamed Kordbacheh, MD; Sai Srikar Kilaru, MD; Imad Zak, MD, FACR

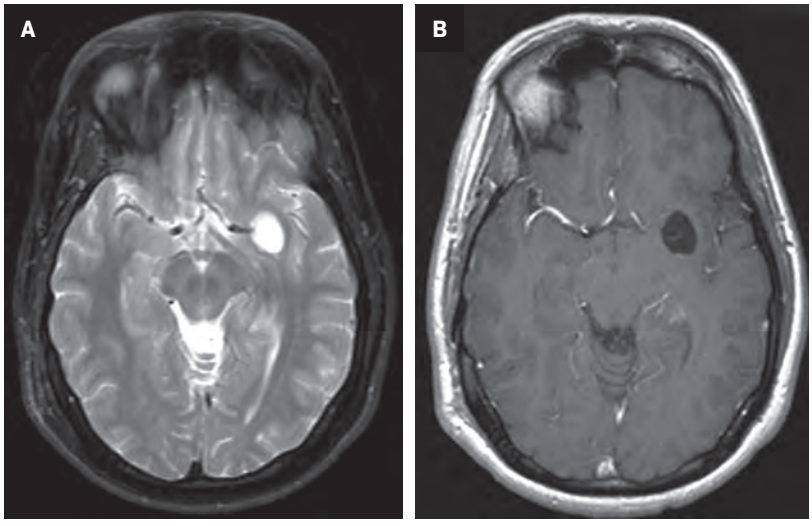
Editor's note: This is the first part of a two-part series. The second part will appear in the September/October 2022 issue of Applied Radiology.

A variety of developmental and acquired intracranial cysts are frequently encountered on imaging. Knowledge of their imaging characteristics, localization, and clinical behavior improves diagnostic accuracy. In this first part of a two-part series, we review non-neoplastic, developmental cystic lesions, including prominent perivascular/Virchow-Robin spaces, epidermoid, dermoid, colloid cyst, arachnoid cyst, and Rathke cleft cysts. Epidemiologic and pathophysiologic features, clinical presentation, diagnosis, and radiologic characteristics for each will be discussed.

Prominent Perivascular (Virchow-Robin) Spaces

Perivascular spaces (PVS) are not true lesions. As the name implies, they are a result of blood vessels penetrating the brain parenchyma attaining a peripheral pial and arachnoid covering; thus, they contain variable amounts of cerebrospinal fluid (CSF) in a potential small subarachnoid space.[1] These are not specific to one age group and the incidence has been reported to increase with age.[1] Perivascular spaces are potential conduits for leptomeningeal spread of tumors and infections.[2] Prominent or giant PVS exceeding 15 mm can be seen in the inferomedial temporal lobes, pons, and deep nuclei.[1] Most large PVSs are found incidentally; however, they may be seen in patients suffering from headache and other neurological symptoms (Figure 1).

Figure 1. Giant perivascular space in a middle-aged patient presenting with vertigo. Incidental large unilocular CSF-intensity cystic region in the deep left cerebral hemisphere on axial T2 (A). (B) Postcontrast axial T1 shows the PVS following CSF signal and without contrast enhancement.



A knowledge of the imaging appearances and typical locations of these cyst-like structures should avoid raising unnecessary concerns. Magnetic resonance imaging (MRI) is the preferred modality to confirm giant PVS, but they can also be diagnosed with computed tomography (CT.) On both modalities these structures behave similarly to CSF and show no contrast enhancement in the wall.[1,3]

Affiliations: Detroit Medical Center and Wayne State University School of Medicine, Detroit, Michigan (Drs Kayder, Kordbacheh); Wayne State University School of Medicine, Detroit, Michigan (Dr Kilaru); John D Dingell VA Medical Center and Wayne State University School of Medicine, Detroit, Michigan (Zak).
Disclosures: None. Prior publication/presentation: None of the figures have been used previously in a publication or national/international presentation. No part of this manuscript has been published previously.

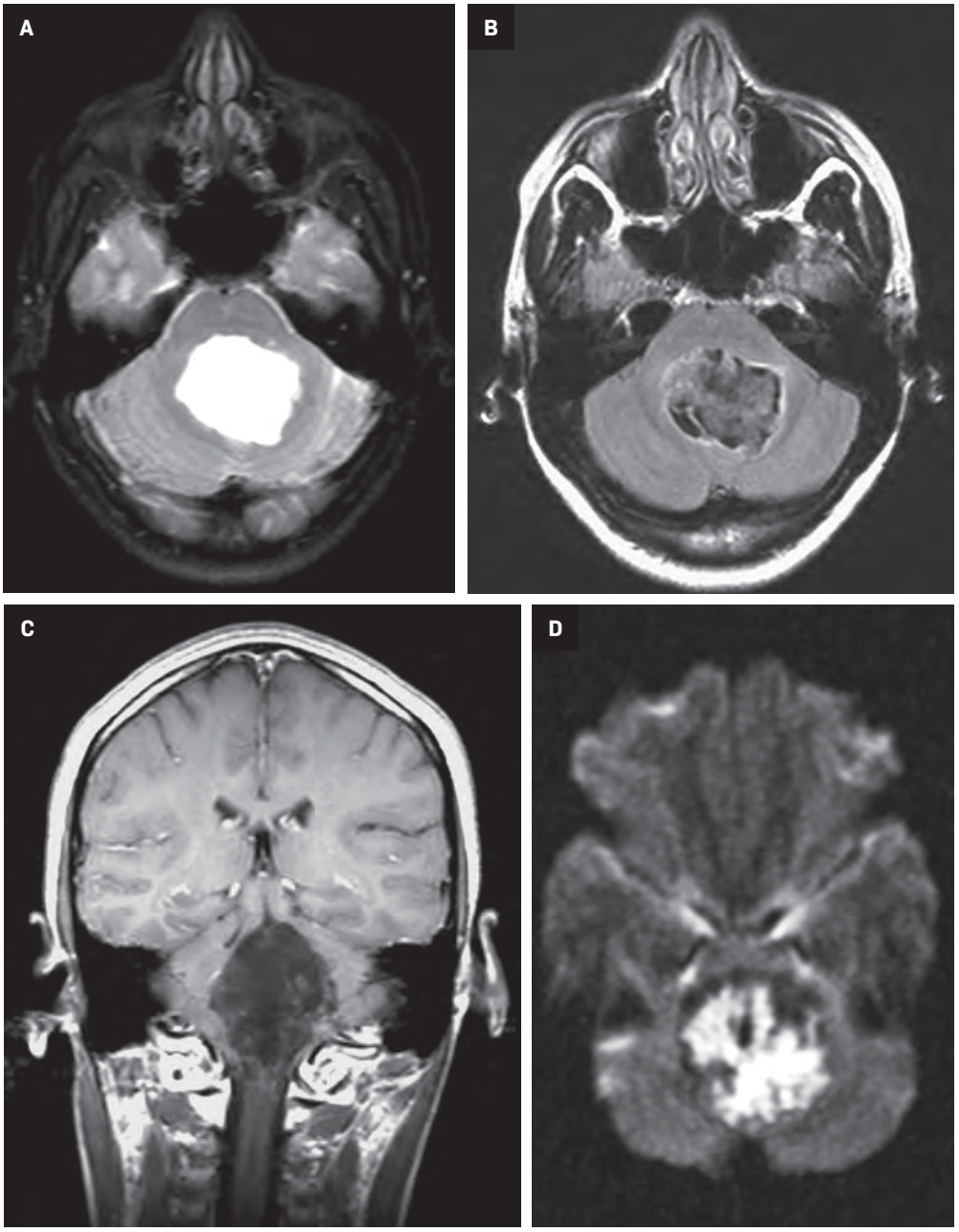


Figure 2. Epidermoid in an adult presenting with headache. (A) axial T2, (B) axial FLAIR, (C) coronal postcontrast T1, and (D) DWI show a large, complex, nonenhancing lesion with diffusion restriction lesion filling the fourth ventricle.

Epidermoid Cysts

Epidermoid cysts account for approximately 1-2% of all intracranial tumors.[4] Men and women are affected equally, with peak incidence in the third and fourth decades. They result from displacement of ectodermal elements during neural tube closure.[5] These tumors are usually located in the parasellar region and cerebellopontine angle and less frequently in the suprasellar cistern, cerebral and cerebellar hemispheres. Epidermoids expand slowly with benign histopathologic features. Malignant transformation of epidermoid is extremely rare. Most patients become symptomatic during adulthood.[4] Signs and symptoms generally result from mass effect on adjacent structures and include headache, cranial nerve deficits, and seizures.

Extradural epidermoids are less frequent than intradural ones, usually occur in the temporal bones, and appear as well-defined lesions with scalloped margins. Epidermoids are hypodense on CT, similar to or slightly higher than CSF, with minimal to no peripheral enhancement. Up to 25% of epidermoids show calcification on CT. Findings on MRI depend on maturation of the cysts but generally epidermoids are hypointense on T1 images and hyperintense on T2 images.[6] Distinguishing epidermoid from arachnoid cysts can be challenging with CT; MRI is more

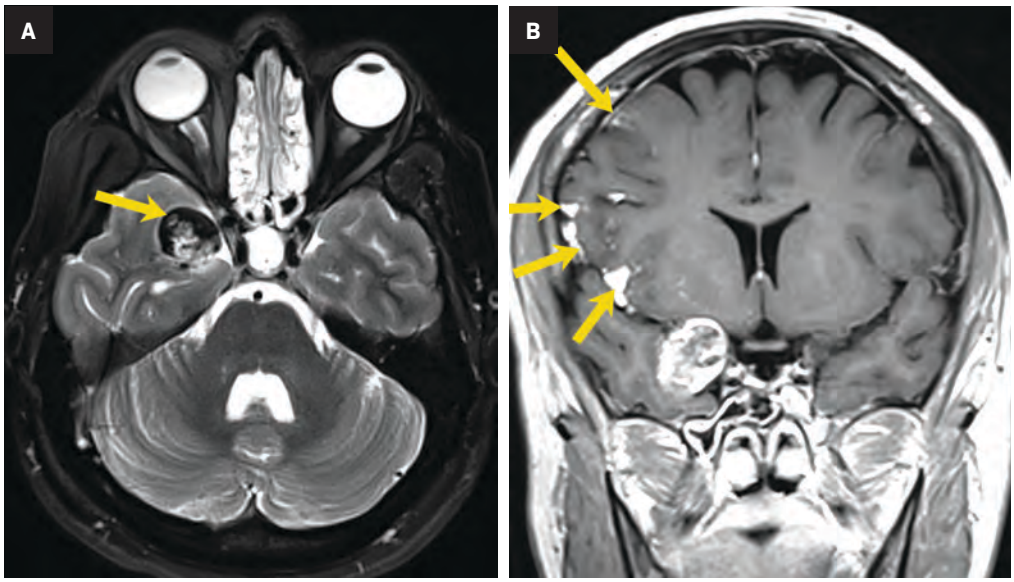


Figure 3. Dermoid in an adult presenting with headache and dizziness. (A) axial fat-suppressed T2 shows a typical, extra-axial, fat-containing dermoid in the medial right middle cranial fossa (arrow). (B) coronal postcontrast T1 shows intrinsically T1 hyperintense fat droplets (arrows) in the sylvian fissure and cerebral convexity sulci, indicating rupture and spillage of contents into the subarachnoid space.

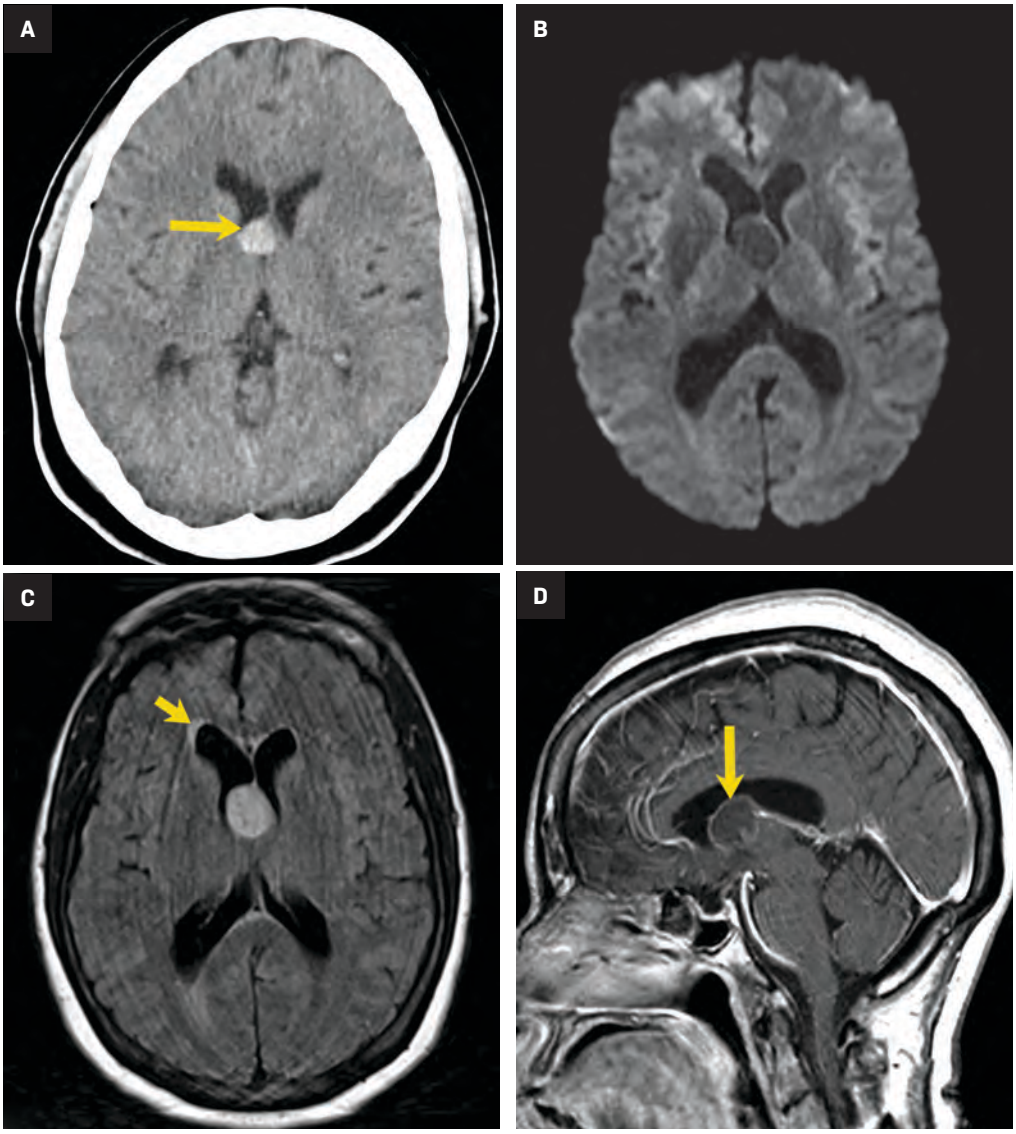


Figure 4. Colloid cyst in an adult presenting with headache, dizziness, and blurring of vision. (A) axial CT shows a round, cystic lesion with hyperdense content between the foramina of Monro (arrow). (B) Axial DWI shows no diffusion restriction whereas (C) axial FLAIR shows hyperintense contents representing proteinaceous material. Notice the transependymal CSF flow capping the anterior horn of the right lateral ventricle on FLAIR (arrowhead), concerning for early obstruction. (D) Sagittal T1 postcontrast image shows typical location of colloid cyst in the roof of the third ventricle anteriorly.

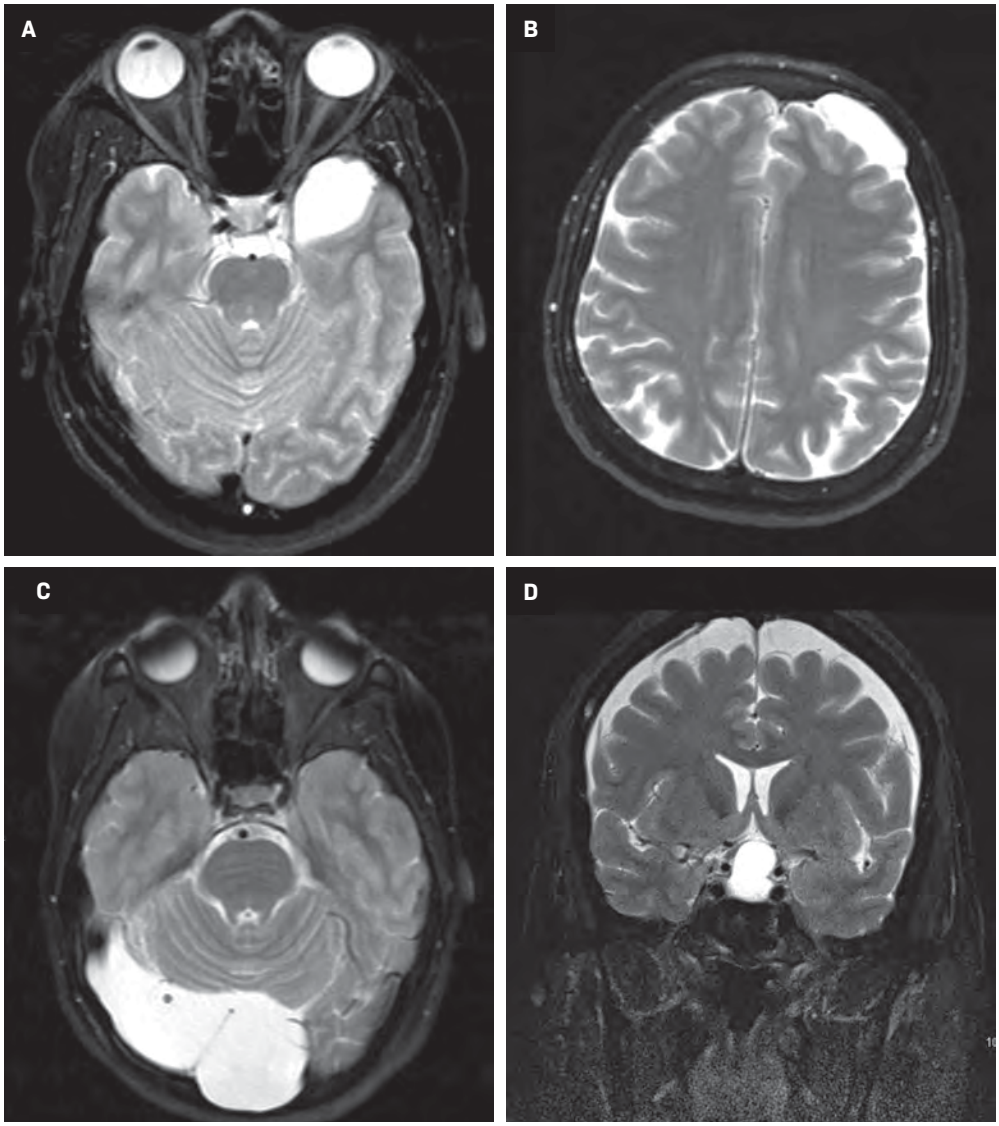


Figure 5. Arachnoid cyst in four different patients. Representative T2 images with extra-axial cysts in (A) medial left middle cranial fossa, (B) left anterior cranial fossa, (C) posterior fossa, (D) sellar/suprasellar regions.

useful, as epidermoids are brighter than CSF on fluid attenuation inversion recovery (FLAIR) and, unlike arachnoid cysts, which demonstrate facilitated diffusion owing to their cystic nature, epidermoids typically have reduced diffusion on diffusion weighted imaging (DWI) with low apparent diffusion coefficient (ADC) values (Figure 2).

Dermoid Cysts

Intracranial dermoids are rare, accounting for 1% of all intracranial lesions.[7] Men are affected more commonly than women, and patients are younger than those with epidermoids at presentation. Unlike epidermoids, these lesions tend to occur in the supratentorial midline or paramedian locations. The typical location for a dermoid is in the suprasellar cistern or in the temporosylvian region.[7] Most patients with dermoids are asymptomatic. Symptoms usually result from mass effect on adjacent structures or chemical meningitis upon rupture of the cyst and leakage into the subarachnoid space.

Dermoid cysts have characteristic imaging appearances. They present as well-defined, lobulated midline lesions on CT with fat density and calcification in the wall. Contrast enhancement is uncommon in dermoids. Lesions are hyperintense on T1 images with signal void that corresponds to calcification. Dermoids do not show enhancement with gadolinium on MRI. Dermoid signal varies from hypo- to hyperintense on T2 images (Figure 3). Classically, when a dermoid ruptures, fat droplets will appear scattered in the subarachnoid spaces and/or intraventricularly, best seen as hyperintense on T1 images; chemical meningitis can result in leptomeningeal enhancement.

Colloid Cysts

Colloid cysts are benign growths that occur primarily in the wall of the third ventricle. These cysts are

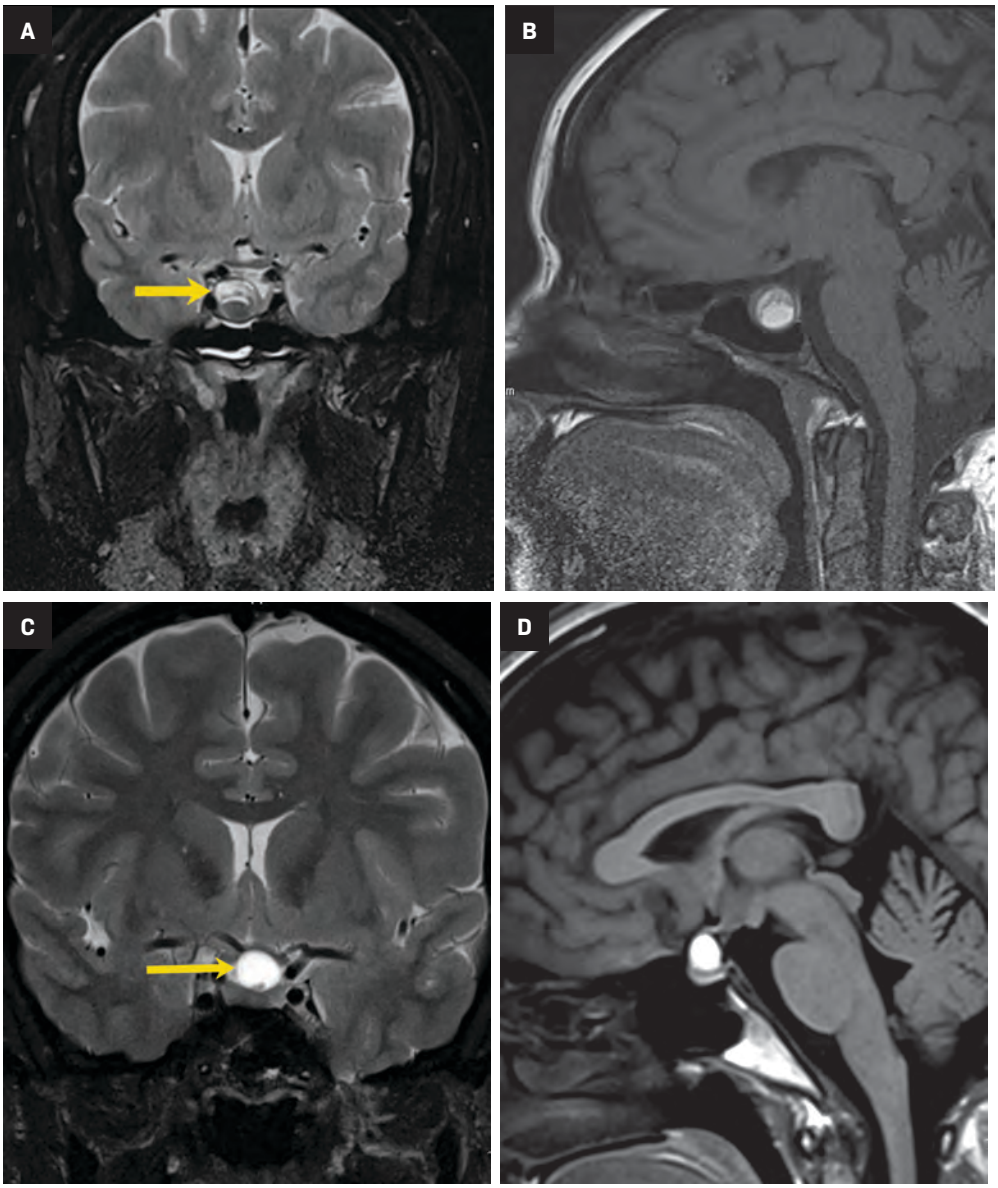


Figure 6. Rathke cleft cysts. (A, B) in an adult with pituitary enlargement incidentally detected on a head CT obtained for trauma. (A) Coronal T2 shows intrasellar cytic lesion of heterogeneously low signal intensity (arrow) whereas (B) sagittal T1 image shows predominately high signal intensity. (C, D) MRI in an adult with a history of paresthesia shows a suprasellar cystic lesion of high signal intensity on both (C) T2 and (D) T1 images.

the result of abnormal folding of the neuroepithelial paraphysis during development.[8] Colloid cysts are lined by columnar epithelium that secretes mucin. They account for up to 2% of all primary brain tumors,[8] typically present between the third and fifth decades of life, and are more common in men.[9]

Asymptomatic colloid cysts are seen incidentally on imaging. Although benign, they can cause acute obstruction of the foramen of Monro, leading to hydrocephalus and herniation, especially after acute intracystic hemorrhage (Figure 4). Symptomatic colloid cysts present with severe headaches and vomiting and may also cause seizures, especially in cases diagnosed in the first two decades of life.[10] Patients might also present with intermittent headaches that tend to improve when supine.[9]

Colloid cysts can be seen on CT and MRI. On CT, they are easily seen as well-defined, hyperdense, round lesions, but they can also be subtle when they are small hypodense or isodense lesions (Figure 4). Their intensity on MRI is dependent on their contents. Colloid cysts typically appear hyperintense on T1 and hypointense to isointense on T2 when compared to brain tissue. Colloid cysts may not be well seen on FLAIR sequences because of the dark signal of the cyst blending with adjacent CSF.[11] The DWI signal also varies with the contents of the cyst (Figure 4).

Arachnoid Cysts

Arachnoid cysts are non-neoplastic intracranial lesions that contain cerebrospinal fluid (Figure 5). These cysts are lined by arachnoid cells and have a prevalence of 1.4% in the adult population. The prevalence of

these cysts is slightly higher, 2.6%, in the pediatric population. While most arachnoid cysts are considered developmental, some may develop subsequent to head injury and infection.[12] Arachnoid cysts have been reported in various locations of the brain, including but not limited to the cerebral convexities, posterior fossa and, most commonly, the middle cranial fossa.[13]

Most patients with arachnoid cysts are asymptomatic. Symptoms may arise depending on the location and size of the cyst and in the event of complications such as acute intracystic hemorrhage. Symptoms most often consist of headache but may also include seizures or focal neurological deficits.[14]

Arachnoid cysts are seen on CT and MRI as well-defined, extra-axial entities that are isodense/isointense to CSF.[10] Fluid–fluid level can be seen in hemorrhagic cysts. Arachnoid cysts typically do not enhance.[15]

Rathke Cleft Cysts

Rathke cleft cysts are non-neoplastic lesions that originate from remnants of the Rathke pouch. Owing to their epithelial origin, they are lined by columnar or cuboidal epithelium.[16] They typically contain gelatinous fluid but can also contain hemorrhagic, mucinous, or inflammatory contents.[17] Rathke cleft cysts are the most common lesions found incidentally in the sella and parasellar region, with an estimated incidence up to 11% postmortem.[16]

Most Rathke cleft cysts are usually asymptomatic. When they are symptomatic, headache is the most common presenting symptom, but others may include visual disturbances resulting from compression of the optic chiasm. Hormonal disturbances may occur as a result of pituitary and hypothalamic compression.[18] Hormonal abnormalities may include hyperprolactinemia, cortisol deficiency, diabetes insipidus, syndrome of inappropriate antidiuretic hormone secretion, and hypogonadism.[17]

On CT, the density of Rathke cleft cysts varies according to their contents. Cysts may appear hyperdense, isodense, or hypodense.[19] These noncalcified lesions have well-defined margins and typically do not show contrast enhancement.[20] Their typical appearance on MRI reflects high proteinaceous content with T1 hyperintensity and T2 hypointensity (Figure 7).[18] However, the signal intensity varies with the nature of the fluid contents.[19,20] Intracystic hemorrhage may result in hyperintense signal on both T1 and T2 imaging. On postcontrast MRI, there should be no nodular enhancement, a feature that may differentiate these benign cysts from craniopharyngioma. Rarely, curvilinear enhancement is seen in the wall of the cyst.[19]

Conclusion

Intracranial cysts are seen in a broad spectrum of pathology with overlapping anatomic and imaging characteristics. However, proper knowledge of their clinical presentation, anatomic location, and imaging appearances, particularly on MRI, can help narrow the differential diagnosis and facilitate patient care.

References

1) Bilginer B, Narin F, Hanalioglu S, Oguz KK, Akalan N. Virchow-Robin spaces cyst. *Childs Nerv Syst*. 2013;29(12):2157-2162.

2) Gordon M, Parmar H, Ibrahim M. Spread of infection to Virchow-Robin spaces in a patient with Streptococcus pneumoniae meningitis. *J Comput Assist Tomogr*. 2009;33(4):562-564.

3) Uchino A, Takase Y, Nomiyama K, Egashira R, Kudo S. Acquired lesions of the corpus callosum: MR imaging. *Eur Radiol*. 2006;16(4):905-914.

4) Patibandla MR, Yerramneni VK, Mudumba VS, Manisha N, Addagada GC. Brainstem epidermoid cyst: An update. *Asian J Neurosurg*. 2016;11(3):194-200.

5) Chowdhury FH, Haque MR, Sarker MH. Intracranial epidermoid tumor; microneurosurgical management: An experience of 23 cases. *Asian J Neurosurg*. 2013;8(1):21-28.

6) Kato K, Ujiie H, Higa T, et al. Clinical presentation of intracranial epidermoids: a surgical series of 20 initial and four recurred cases. *Asian J Neurosurg*. 2010;5(1):32-40.

7) Caldarelli M, Colosimo C, Di Rocco C. Intra-axial dermoid/epidermoid tumors of the brainstem in children. *Surg Neurol*. 2001;56(2):97-105.

8) Lawrence JE, Nadarajah R, Treger TD, Agius M. Neuropsychiatric manifestations of colloid cysts: a review of the literature. *Psychiatr Danub*. 2015;27 Suppl 1:S315-320.

9) pears RC. Colloid cyst headache. *Curr Pain Headache Rep*. 2004;8(4):297-300.

10) Musa G, Simfukwe K, Gots A, Chmutin G, Chmutin E, Chaurasia B. Clinical and radiological characteristics in fatal third ventricle colloid cyst. Literature review. *J Clin Neurosci*. 2020;82(Pt A):52-55.

11) Jenkinson MD, Mills S, Mallucci CL, Santarius T. Management of pineal and colloid cysts. *Pract Neurol*. 26 2021;21(4):292-299.

12) Mustansir F, Bashir S, Darbar A. Management of arachnoid cysts: a comprehensive review. *Cureus*. 10 2018;10(4):e2458.

13) Al-Holou WN, Terman S, Kilburg C, Garton HJ, Muraszko KM, Maher CO. Prevalence and natural history of arachnoid cysts in adults. *J Neurosurg*. 2013;118(2):222-231.

14) Karnazes AC, Kei J, Le MV. Image diagnosis: arachnoid cyst. *Perm J*. 2015;19(2):e110-111.

15) Dutt SN, Mirza S, Chavda SV, Irving RM. Radiologic differentiation of intracranial epidermoids from arachnoid cysts. *Otol Neurotol*. 2002;23(1):84-92.

16) Larkin S, Karavitaki N, Ansorge O. Rathke's cleft cyst. *Handb Clin Neurol*. 2014;124:255-269.

17) Cabuk B, Selek A, Emengen A, Anik I, Canturk Z, Ceylan S. Clinicopathologic characteristics and endoscopic surgical outcomes of symptomatic Rathke's cleft cysts. *World Neurosurg*. 2019;132:e208-e216.

18) Crenshaw WB, Chew FS. Rathke's cleft cyst. *AJR Am J Roentgenol*. Jun 1992;158(6):1312.

19) Nishioka H, Haraoka J, Izawa H, Ikeda Y. Magnetic resonance imaging, clinical manifestations, and management of Rathke's cleft cyst. *Clin Endocrinol (Oxf)*. 2006;64(2):184-188.

20) Kucharczyk W, Peck WW, Kelly WM, Norman D, Newton TH. Rathke cleft cysts: CT, MR imaging, and pathologic features. *Radiology*.1987;165(2):491-495.

Times Are Tight: Staff Shortages Prompt New Strategies

Kerri Reeves

Kerri Reeves is a contributing editor based in Ambler, PA.

Healthcare has been the second largest industry sector hit by the "Great Resignation," with tens of thousands of workers abandoning their posts or the field altogether.[1] Radiology, experiencing shortages across various positions and modalities, is struggling to both maintain staffing levels and bring in new talent.

"Staffing is a major issue, and it exists at multiple levels for a hospital," says Levon Nazarian, MD, FAIUM, FACR, American Institute of Ultrasound in Medicine (AIUM) president and professor of radiology at Sidney Kimmel Medical College of Thomas Jefferson University in Philadelphia. "No practice of any kind is exempt from this problem—from the smallest private group with four staff members to the biggest academic center with 150, everybody is experiencing the same problem."

The reasons for shortages in radiology—and radiation oncology—vary across geographical regions, imaging modalities, work environments, and positions. For technologists, educational challenges are impacting the supply of trained professionals, while the COVID-19 pandemic has shifted the career outlook for many imaging professionals and physicians.

"We're seeing workforce shortages that are widespread, and they're coming for multiple reasons," says Eric M Rubin, MD, FACR, chair of the American College of Radiology (ACR) Human Resources Commission, and partner in Southeast Radiology LTD in suburban Philadelphia. "We're experiencing an increasing overall workload as the impact of the Baby Boomer generation is in full force. We're seeing an increase in the need for subspeciality reads in radiology, and also an increasingly fluid workforce where people are more likely to switch jobs. We do recognize that groups are struggling right now to properly staff and get the daily work done," he says.

Association data

While shortages in radiology are being reported nationwide, professional organizations are looking for data-driven evidence to provide a deeper understanding of the job market and its influencing factors. Both the ACR, through its workforce survey, and the American Society of Radiation Oncology (ASTRO), through its Workforce Task Force, are performing "deep dives" into data analysis to evaluate the staffing and hiring landscape; final results are not yet available.

The ACR put a pause on compiling data in 2020 due to the pandemic and has completely revamped its survey to glean deeper insights, Dr Rubin reports.

The American Society of Radiologic Technologists (ASRT) notes that the pandemic has likely impacted its most recent Radiologic Sciences Staffing and Workplace Survey results. The survey showed a slight decrease in vacancy rates for most medical imaging disciplines in 2021. Radiography is the only modality that experienced a long-term decline in the average number of budgeted full-time equivalents (FTEs) per department, the ASRT says. Data show that in 2003, the average was 10.1 FTEs in radiography, with 9.3 budgeted FTEs in

"We used to have people waiting in line for jobs here. That's just not the case now."

Nancy Godby, MS-MHA, MA, RT(R)(M), ARRT, CHC

2021. Statistics for average budgeted FTEs for five other modalities for 2021 vs 2003 are:

- Computed tomography, 6.2, up from 3.4;
- Magnetic resonance imaging, 4.7, up from 1.7;
- Mammography, 4.9, up from 2.1;
- Nuclear medicine, 3.6, up from 1.8; and,
- Sonography, 5.0, up from 2.6

The U.S. Bureau of Labor Statistics (BLS) projects that radiologic and MRI technologist employment will grow 9% by 2030, about as fast as the average for all occupations, estimating 20,800 openings for these positions each year, on average.[2] The BLS statistics point to a trend that more technologists will be needed to meet growing demand for imaging services.

Educational Challenges

Nancy Godby, MS-MHA, MA, RT(R)(M), ARRT, CHC, director of radiology at Cabell (WVa) Huntington Hospital, notes her greatest staffing challenge is in radiography and says she's had difficulty attracting talent since July of 2021. Huntington's universities only offer four-year imaging programs.

"I've been reaching out to leaders of our local universities to encourage them to do a needs assessment in the community," Godby says. "Yes, we need all the higher modality imaging professionals, but we also really need people who want to be X-ray techs."

"We used to have people waiting in line for jobs here. That's just not the case now," Godby adds, noting her reliance on agency technologists and mandatory overtime to meet demand for imaging services.

In radiation oncology, a lack of programs is contributing to shortages of physicists and dosimetrists and, to a lesser extent, radiation therapists, says Bruce G Haffty, MD, FACR, FASTRO, FASCO, chair of ASTRO's workforce subcommittee, associate vice chancellor of Cancer Programs at Rutgers Biomedical and Health Sciences, and professor and chair of the department of radiation oncology at Robert Wood Johnson and NJ Medical School, Rutgers Cancer Institute of NJ.

"For physicists we're seeing a shortage and a potential undersupply because we're not getting enough of them certified," Dr Haffty says. He noted that the recent requirement for residency has left some physicists behind, and that training options for dosimetrists are limited.

"Word on the street is they are harder to come by. We could also do a bit better [at] training more [radiation] therapists," he says.

On the physician side, Dr Haffty says, ASTRO's Workforce Task Force has been commissioned to study supply and demand over the next five to 10 years using Medicare data and various treatment projections.

"There's concern that there's a relative oversupply of radiation oncologists, but we really need an unbiased and expert group to do an analysis so we can understand that better," he says.

Pandemic perceptions

While certain subspecialties like mammography and interventional radiology have been experiencing shortages for years, remote-working options sparked by the pandemic exacerbated them, says Dr Rubin.

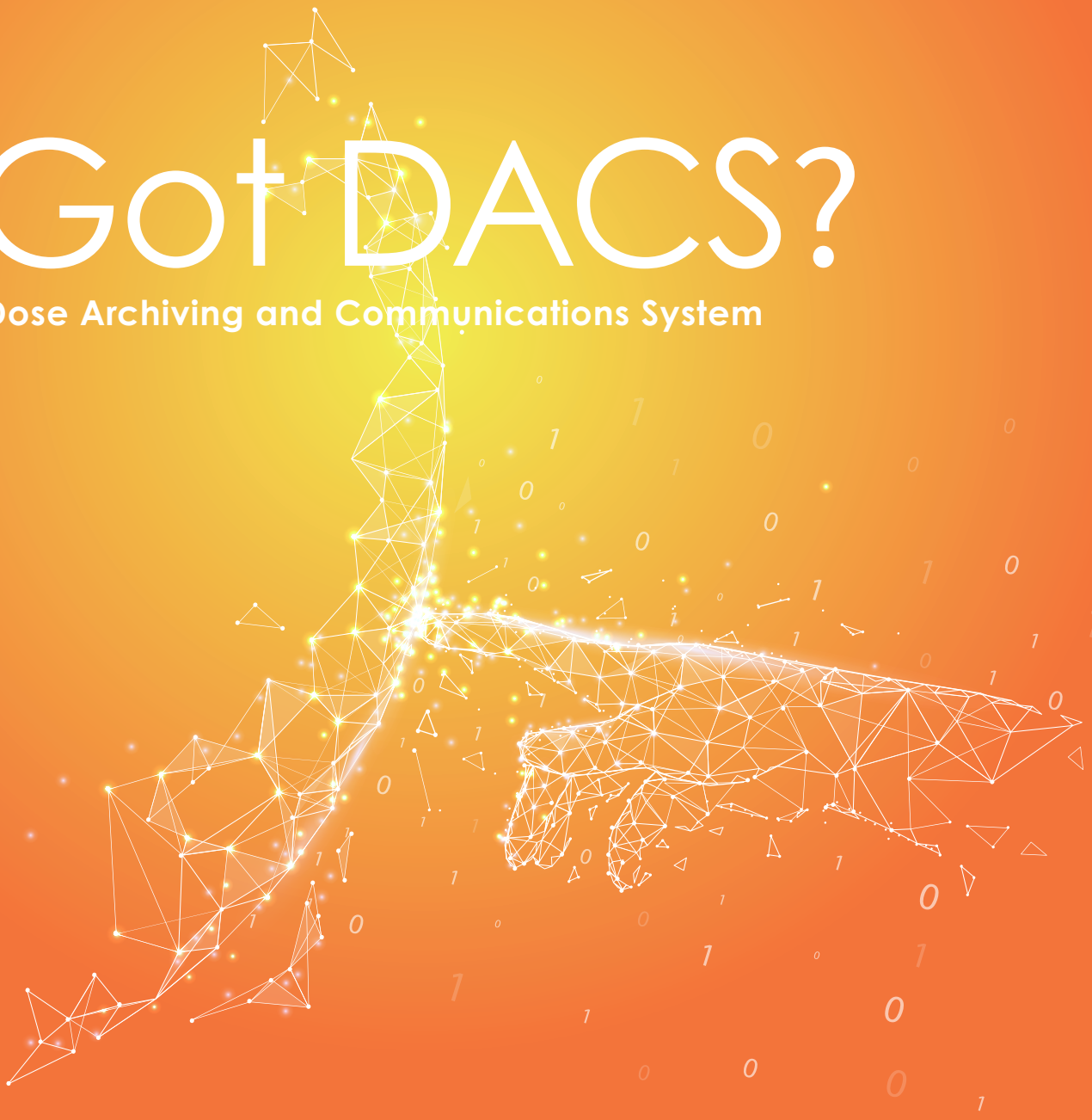
"When COVID came along, many radiology groups began developing and heavily implementing remote work within their own practices as opposed to hiring outside companies to do that work for them," he explains, referring to "nighthawk" imaging companies.

"My group has always tried to make sure we pay attention to work-life balance, and this [remote reading environment] has created a level of satisfaction among our radiologists," Dr Rubin says.

Guerbet
Digital Solutions

Got DACS?

Dose Archiving and Communications System



Dose&Care® is a state-of-the-art patient X-ray dose management solution to aid monitoring of patient radiation exposure. Contrast&Care® is an easy-to-use, injection data-management solution that integrates with existing medical platforms.

Both enable imaging centers to collect, archive and share information. Discover how Guerbet Digital Solutions can help you stay a step ahead.

Dose&Care® **Contrast**&Care®

GU03210026

While he personally prefers his dosimetrists to work on site, Dr Haffty acknowledges the popularity of work-from-home options has had an impact and has the potential to pull specialists such as physicists out of the field entirely or to different work environments.

Godby, who manages 500 to 700 exams daily at her trauma center, says the intensity of the hospital environment has become too demanding for some staff, who have begun weighing quality-of-life issues into their employment choices.

"We've got a lot of urgent care centers and free-standing emergency centers popping up, and these lower volume institutions are pulling some of our technologists away from the hospital," she explains. "People have taken a step back to ask themselves, 'Is this really what I want to continue to do?'"

She says the trend may impact her institution's ability to bring new talent into the profession and may even reduce the number of applicants to radiologic technology programs, "because people don't want to work in a hospital anymore."

In Dr Nazarian's view, many radiologists and technologists feel stuck in a situation of having too much work to do and not having enough people to do it.

"The pandemic has led to burnout levels as high as we've ever seen in medicine and in radiology," he says, adding that he has witnessed many staffers taking early retirement or choosing to work part-time or work in only some aspects of the field, such as teleradiology.

"For the people that remain, work multiplies on them," Dr Nazarian says. "On top of that, take the increased volumes of very sick people due to COVID itself."

Staffing Strategies and Support

Considering the regular waxing and waning of staffing, the current systemic problem of shortages presents a conundrum for organized radiology, Dr Nazarian points out. "If we train more people, it takes years to see the effects of that," he says. "In the past it's been cyclical—need, then glut. So, is this a permanent downcycle, or just a 'normal' cyclical phenomenon that's going to work its way out?"

As there is no certain answer to that question, industry associations continue to offer support in the form of survey analyses, career resources, and job banks. On the provider side, hiring managers are implementing tried-and-true and novel recruitment and retention strategies.

Godby's organization is connecting with student technologists before graduation with perks like sign-on bonuses; tuition support is also being considered. In light of the increasingly mobile workforce, Dr Rubin's practice is focusing on a flexible reading environment as well as on how artificial intelligence can be applied for more effective patient management. Dr Haffty stresses the need to offer competitive compensation and benefits—"the whole package,"—particularly when staff start to drift away for parallel-level jobs.

"It's always better to retain than recruit," Dr Haffty says.

Yet, even amid the shortages, experts agree that aside from an occasional longer-then-normal wait time, patient care has remained largely unaffected by staffing woes.

"The way we're trained is that when there's stress, we take it on ourselves and we work harder," Dr Nazarian says. "We don't pass it on to the patient or decrease the quality of care we provide."

References

1) Morse, S. Healthcare second largest sector hit by Great Resignation. *Healthcare Finance*. Jan. 5, 2022. Accessed June 1, 2022. *https://www.healthcarefinancenews.com/news/healthcare-second-largest-sector-hit-great-resignation*

2) Occupational Outlook Handbook: Radiologic and MRI Technologists. Last Modified April 18, 2022. Accessed June 1, 2022. *https://www.bls.gov/ooh/healthcare/radiologic-technologists.htm*

HARD DATA. HUMAN INSIGHTS.

A surface-level view of your patient isn't sufficient.

In today's healthcare world, you need to look deeper into the data – developing diagnosis based on the full picture.

With IBM Watson Imaging Patient Synopsis, our cloud-based solution – we're extracting all relevant EHR data into a single-view summary. So Radiologists can get the clinical context they need to make intelligently informed care decisions. All in a matter of seconds.

– Extract information from clinical reports
– Find the true "reason for exam" behind the imaging order
– Automatically load the patient summary in context
– Set up and receive automated reports

Guerbet Digital Solutions guerbet-us.com

GU12201247

AI: The Next Generation Radiology Extenders?

Amine Korchi, MD

Affiliation: Dr Korchi is a neuroradiologist at Onex Imaging Center, Groupe 3R, in Geneva, Switzerland, and Chief Medical Officer of Cerebriu. He is also a member of the Editorial Advisory Board of *Applied Radiology.*

As radiology has evolved from a back-office specialty, with radiologists isolated in dark rooms, to the central node of health care, information technology (IT) has evolved along with it. Today's IT devices provide us with immediate and remote access to images, improving our productivity and increasing our value to the healthcare enterprise.

But as the number of studies and images per study continue to grow, radiologist workloads have risen proportionately. Radiologists are fielding an ever-increasing number of questions, especially from non-imaging specialists; as a result, atop delivering a higher volume of reports, radiologists must now deal with the lower efficiency and higher risk of errors that accompany these interruptions.

The good news is that IT is helping us to meet the ever-increasing expectations of referring physicians. Software tools, some fueled by artificial intelligence (AI), already have the ability to serve as radiologist "extenders" that can automatically deliver imaging results to clinicians. This is especially useful where access to radiologists may be limited.

Indeed, AI can provide the powerful assistance radiologists need to satisfy the demands of the healthcare ecosystem for anywhere, anytime, access to imaging specialists. This can enable us to focus on more complex, specialized tasks, and help us avoid countless interruptions.

But for this to occur on a more widespread scale, AI must be adopted by the healthcare enterprise beyond radiology. Most AI tools currently available to radiologists have been developed primarily for radiologists and make only a minor impact on day-to-day practice. However, when they can be accessed by other specialists viewing a radiological exam when no radiologist is available, they can be immensely useful.

Take the emergency department, for example. Musculoskeletal radiographs may be reviewed first by emergency physicians to help them determine their treatment approach to a particular case. Only afterward will radiologists review the images; a formal report may not be returned until hours, days, or rarely even longer after the patient has been seen.

This has important ramifications for patient care. Emergency physicians are not experts in image analysis. They can miss fractures and/or lesions outside of their principal focus. Radiologist input is necessary even when delayed. But it goes without saying that this is not only an inefficient process, but one that may put patients at risk for being discharged with significant lesions.

Artificial intelligence and computer aided detection and diagnosis (CAD) technology can improve upon this process and minimize its risks by enhancing the diagnostic performance of non-expert readers in fracture detection[1] and empowering them to treat patients based on the additional information provided by the software.

The automation offered by AI is not intended to replace radiologists, but rather to augment the efficiency and value they provide to the healthcare system.

This has two beneficial outcomes. The first is that it gives the physician access to more accurate imaging information at the time of patient contact. Combined with the clinical examination and the physician's own judgment, this input can help render a more correct diagnosis and treatment approach the first time.

Second, AI-powered imaging technology may provide other medical professionals such as nurses or paramedics with the data they need to triage patients and deliver initial care more safely, effectively saving valuable time in the treatment pathway.

Moreover, by implementing radiology AI tools at enterprise level and getting them into everyone's hands, I believe we will be able to measure positive impacts on hard clinical outcomes and health economics, beyond mere radiological diagnostic performances.

There should be no fear that AI will put us radiologists out of work. Our tasks extend far beyond visual analysis of imaging studies.[2] In my view, diagnostic support does not compete with radiologists no matter where it comes from; on the contrary, AI support has the potential to improve the flow of care, reduce interruptions on our work, and increase our focus on complex, high-added-value tasks. The automation offered by AI is not intended to replace radiologists, but rather to augment their efficiency and value they provide to the healthcare system.

Given our expertise in medical imaging and health IT, radiologists are in the best position to identify and implement the appropriate AI software to support non-radiologists in any circumstance. Imaging specialists are also the best suited to monitor and maintain these tools for quality, performance, and safety.

By offering AI-based diagnostic support as a service, radiologists can boost their value to the healthcare enterprise and reduce the risk that incorrect clinical decisions will be made. This will improve efficiency and satisfaction among our referring physicians.

Indeed, by taking the lead in this transformation, we radiologists can strengthen our relevance and central position in health care in the era of artificial intelligence.

References

1) Guermazi A, et al. Improving radiographic fracture recognition performance and efficiency using artificial intelligence. *Radiology*. 2022;302(3):627-636.

2) Langlotz CP. Will artificial intelligence replace radiologists? *Radiology Artif Intell*. 2019;1(3):e190058.

The Dawn of Training Programs in Africa

Frank J Minja, MD; Mechris C Mango, MD, MMed; Fabian M Laage Gaupp, MD

A key driver of global radiology disparities is the lack of trained professionals and a lack of formal training programs, despite the increasing availability of previously cost-prohibitive radiology equipment.[1]

In Africa, limited access to radiology training programs is severe at both the diagnostic radiology (DR) residency and radiology subspecialty (RS) fellowship levels. Of 54 African sovereign countries (excluding disputed territories), only 18 have well-established DR residency programs, and only 8 report any subspecialty programs, with details readily available for only 5 of those 8 countries: Egypt, Ethiopia, Kenya, South Africa, and Tanzania.[2]

The earliest one-year RS programs, for interventional radiology (IR) and pediatric radiology, were established in South Africa in 2002 and 2009, respectively; both bestow postgraduate diplomas.[2] Interventional Radiology (IR) training in Egypt consists of institution-based clinical apprenticeships, with an optional subsequent pathway for certification by the Egyptian Board of Interventional Radiology following written and oral examinations.[3]

Affiliations: Emory University School of Medicine, Atlanta, GA. (Dr Minja); Muhimbili University of Health and Allied Sciences and Muhimbili Orthopaedic Institute, Dar es Salaam, Tanzania (Dr Mango); Yale School of Medicine, New Haven, CT (Dr Laage Gaupp).
Disclosures: None.

Four two-year radiology fellowship training programs in Ethiopia, Kenya, and Tanzania have been established within the past ten years. We will describe initiation of IR and Neuroradiology fellowship programs in Tanzania, with comparisons to Pediatric Radiology in Ethiopia (2015) and IR in Kenya (2020).[4,5] These four fellowship programs offer lessons on how to accelerate the development of RS training programs in Africa.

Tanzania

Interventional Radiology Fellowship

In 2017, an IR Readiness Assessment at Muhimbili National Hospital (MNH) in Dar es Salaam revealed a complete lack of trained IR personnel and disposable equipment as their two main obstacles to initiating IR service.[6,7]

Beginning in October 2018, through close collaboration among MNH, Muhimbili University of Health and Allied Sciences (MUHAS), and multiple US institutions including Yale and Emory Universities under the Road2IR consortium, rotating teams of IR faculty, nurses, and technologists were deployed to MNH for hands-on teaching.

A two-year Master of Science (MSc) Interventional Radiology curriculum was approved by MUHAS in 2019 and the first three IR trainees were enrolled.[7] To date, 48 faculty have traveled to Tanzania, most accompanied by nurses, technologists, medical students, and/or residents, once a month, on average.

The first three IR fellows graduated in 2021, with the next class of seven expected to graduate in August 2022. In addition, three Tanzanian IR nurses and three technologists have completed training, with additional nurses and technologists joining the program this year, helping to expand IR services to other hospitals in Tanzania.

MNH now offers nearly a full spectrum of IR procedures, ranging from core needle biopsies and abscess drainages to transarterial chemoembolization (TACE) and transjugular intrahepatic portosystemic shunts (TIPS).[8,9] Most of these procedures are provided year-round and are no longer limited by availability of visiting faculty, which confirms the feasibility and success of this training model utilizing rotating IR teaching teams (Figure).

Neuroradiology Fellowship

The success of the IR program created demand for additional subspecialty programs at MNH/MUHAS. The highest demand was for neuroradiology, given the complexity of cases seen at MNH, a tertiary referral center with a busy neurosurgery and neurology clinical services.

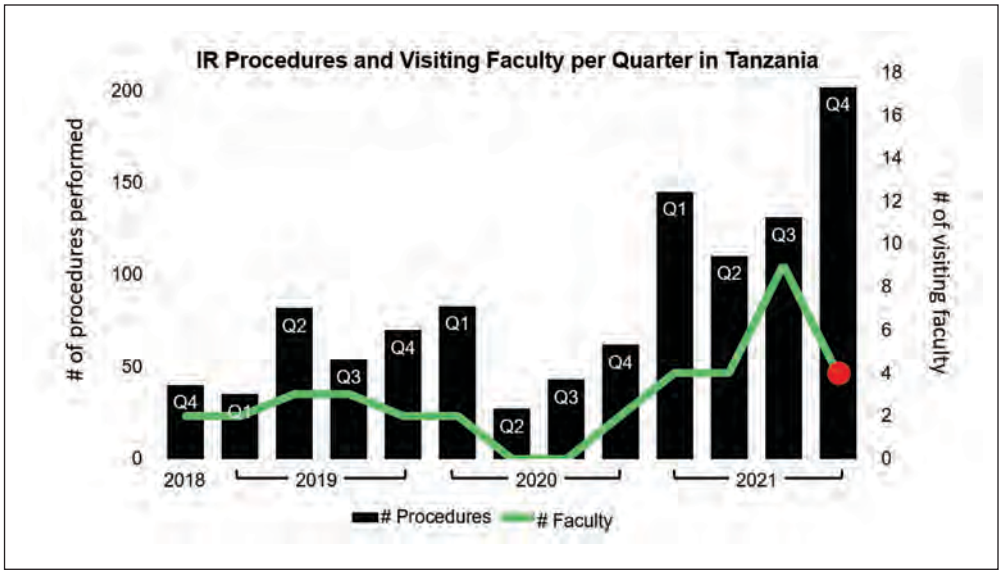


Figure. Number of procedures performed by Tanzanian IR trainees and number of international IR faculty in Tanzania from October 2018 to December 2021 by quarter. COVID-19 pandemic travel restrictions put a temporary hold on IR teaching trips in Q2 and Q3 2020. Following graduation of the first class in Q3 2021, the number of visiting faculty declined while the number of procedures increased.

The MUHAS approved a two-year MSc Neuroradiology curriculum supported by rotating visiting faculty, enrolling two inaugural fellows in 2020. During the first year, the fellows were mentored by two faculty from the Radiological Society of North America (RSNA) Global Learning Center (GLC) program. The MSc Neuroradiology training consists of daily clinical practice, virtual case review sessions, weekly didactic lecture sessions, and assessment examinations each semester.

In addition, the fellows are embedded in daily clinical practice at MNH and supervised by local attendings. During their first year, the fellows logged more than 1,000 clinical cases and participated in more than 50 virtual, one-hour case review sessions, which discussed more than 250 of their most challenging clinical cases. The fellows prepared weekly didactic lectures and presented at multi-disciplinary clinical meetings with neurosurgery, neurology, and pathology colleagues. On-site visits by the faculty mentors were limited by COVID-19 pandemic travel restrictions. This first class will graduate in late 2022.

The second class of two neuroradiology fellows enrolled in 2021. The RSNA GLC program has expanded the volunteer faculty mentors from two to twelve, offering regular virtual case-review sessions three times per week. The neuroradiology fellowship provides both in-country subspecialty training and regular virtual consultation for challenging neuroradiology cases, to the immediate benefit of both MNH trainees and patients.

Ethiopia and Kenya

The pediatric fellowship program in Ethiopia was accredited in 2015 by Addis Ababa University in partnership with Children's Hospital of Philadelphia and other collaborating institutions. Two inaugural fellows graduated in 2017, and a second cohort began training in 2019.[4]

The Kenyan IR fellowship was accredited by the University of Nairobi in 2019 in partnership with University of North Carolina and RAD-AID International and enrolled its first two trainees in 2020.[5,10] This fellowship is supported by three in-country attendings and an established IR service, compared to the Tanzanian program, which had neither attendings nor IR service at its inception. RAD-AID International supplements the Kenyan attendings with volunteer faculty, nurses, and technologists who are deployed two to four times per year.[10]

Ingredients for Program Success

All four recently established fellowship programs in Ethiopia, Kenya, and Tanzania have demonstrated the feasibility of subspecialty programs, even without local subspecialists. The programs share three key characteristics that have contributed to their success:

Each program underwent a rigorous accreditation process by a local university;

The primary training site for each is located in the host country;

Each leveraged strong collaboration with an international institution or organization to help mobilize and coordinate volunteer faculty and staff.

The two-year fellowship programs provide ample time and structure for trainees to gain the necessary competencies in their subspecialties, compared to unstructured clinical apprenticeships or short-term observer-based models.[3,11]

Providing in-country training opportunities is a critical step toward addressing the severe radiology

Gadavist® (gadobutrol) injection Imaging Bulk Package (IBP)

Strong Signal. Strong Bond. Smart Workflow.

Gadavist is the **first and only** FDA-approved GBCA presentation for **multi-patient dosing*** in the MR suite.

* when used with the FDA-cleared Transfer Spike

Available in 30 mL and 65 mL bottles

Visit **Gadavist.com** to learn more

Indications

Gadavist® (gadobutrol) injection is a gadolinium-based contrast agent indicated for use with magnetic resonance imaging (MRI):

- To detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system in adult and pediatric patients including term neonates.
- To assess the presence and extent of malignant breast disease in adult patients.
- To assess myocardial perfusion (stress, rest) and late gadolinium enhancement in adult patients with known or suspected coronary artery disease (CAD).

Gadavist® is indicated for use in magnetic resonance angiography (MRA):

- To evaluate known or suspected supra-aortic or renal artery disease in adult and pediatric patients including term neonates.

Important Safety Information

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

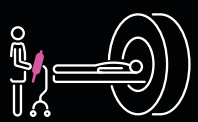
- The risk of NSF appears highest among patients with:
  - Chronic, severe kidney disease (GFR <30 mL/min/1.73m^2), or
  - Acute kidney injury
- Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (for example, age >60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.
- For patients at highest risk for NSF, do not exceed the recommended GADAVIST dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.

Contraindication and Important Information about Hypersensitivity Reactions: Gadavist® is contraindicated in patients with history of severe hypersensitivity reactions to Gadavist®. Anaphylactic and other hypersensitivity reactions with cardiovascular, respiratory, or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following Gadavist® administration. Before Gadavist® administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Gadavist®.

A Smart Choice for Your MR Department

Customized Patient Dosing

- The Gadavist Imaging Bulk Package is compliant with Joint Commission requirements for multi-patient dosing[1,2]
- Technologist and nurse staff can prepare and administer weight-based doses for patients directly in the scan room[2]



Streamlined Workflow

- One multi-dose set up in the MR scan room eliminates the need to reach for several single-use vials throughout the day
- Bottle label with space to specify discard date and time takes the guesswork out of proper bottle disposal

1 Bottle, 1 Spike, Multiple Patients

- Whether using a syringe for handheld or power injection, all you need is one bottle and one spike† when using the MEDRAD® Imaging Bulk Package Transfer Spike for multi-patient dosing[2]
- With 24-hour stand-time after initial spike, the same bottle can be used across multiple patient scans and staff shifts[2]
- Training videos for the Transfer Spike are available on radiologysolutions.bayer.com

† in addition to the typical disposable items needed for contrast administration

Reduced Waste

- The Imaging Bulk Package may enable more complete contrast usage compared to single-dose vials
- One bottle for multiple patients can mean use of fewer contrast bottles overall, and less departmental waste and associated costs compared to single-dose vials

Important Safety Information (continued)

Gadolinium Retention: Gadolinium is retained for months or years in several organs. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, retention varies among the linear agents. Retention is lowest and similar among the macrocyclic GBCAs. Consequences of gadolinium retention in the brain have not been established, but they have been established in the skin and other organs in patients with impaired renal function. While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent and minimize repetitive GBCA studies, when possible.

Acute Kidney Injury: In patients with chronic renal impairment, acute kidney injury sometimes requiring dialysis has been observed with the use of GBCAs. Do not exceed the recommended dose; the risk of acute kidney injury may increase with higher than recommended doses.

Extravasation and Injection Site Reactions: Ensure catheter and venous patency before the injection of Gadavist®. Extravasation into tissues during Gadavist® administration may result in moderate irritation.

Overestimation of Extent of Malignant Disease in MRI of the Breast: Gadavist® MRI of the breast overestimated the histologically confirmed extent of malignancy in the diseased breast in up to 50% of the patients.

Low Sensitivity for Significant Arterial Stenosis: The performance of Gadavist® MRA for detecting arterial segments with significant stenosis (>50% renal, >70% supra-aortic) has not been shown to exceed 55%. Therefore, a negative MRA study alone should not be used to rule out significant stenosis.

Adverse Reactions: The most frequent (≥0.5%) adverse reactions associated with Gadavist® in clinical studies were headache (1.7%), nausea (1.2%) and dizziness (0.5%).

Please see brief summary on adjacent pages.

References: 1. The Joint Commission. Sentinel Event Alert 52: Preventing infection from the misuse of vials. *Sentinel Event Alert*. 2014; 52. **2.** Gadavist [package insert]. Whippany, NJ: Bayer HealthCare Pharmaceuticals Inc; 2011.

Printed in the USA. PP-GADA-US-0633-1 April 2022

Gadavist®
(gadobutrol) injection
1 mmol/mL

GADAVIST (gadobutrol) injection, for intravenous use
Initial U.S. Approval: 2011

BRIEF SUMMARY OF PRESCRIBING INFORMATION
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)

Gadolinium-based contrast agents (GBCAs) increase the risk for NSF among patients with impaired elimination of the drugs. Avoid use of GBCAs in these patients unless the diagnostic information is essential and not available with non-contrasted MRI or other modalities. NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

- **The risk for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR < 30 mL/min/1.73m^2), or**
  - **Acute kidney injury.**
- **Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (for example, age > 60 years, hypertension or diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended Gadavist dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration *[see Warnings and Precautions (5.1)]*.**

1 INDICATIONS AND USAGE

1.1 Magnetic Resonance Imaging (MRI) of the Central Nervous System (CNS)

Gadavist is indicated for use with magnetic resonance imaging (MRI) in adult and pediatric patients, including term neonates, to detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system.

1.2 MRI of the Breast

Gadavist is indicated for use with MRI in adult patients to assess the presence and extent of malignant breast disease.

1.3 Magnetic Resonance Angiography (MRA)

Gadavist is indicated for use in magnetic resonance angiography (MRA) in adult and pediatric patients, including term neonates, to evaluate known or suspected supra-aortic or renal artery disease.

1.4 Cardiac MRI

Gadavist is indicated for use in cardiac MRI (CMRI) to assess myocardial perfusion (stress, rest) and late gadolinium enhancement in adult patients with known or suspected coronary artery disease (CAD).

4 CONTRAINDICATIONS

Gadavist is contraindicated in patients with history of severe hypersensitivity reactions to Gadavist.

5 WARNINGS AND PRECAUTIONS

5.1 Nephrogenic Systemic Fibrosis

Gadolinium-based contrast agents (GBCAs) increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR < 30 mL/min/1.73m^2) as well as patients with acute kidney injury. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30 to 59 mL/min/1.73m^2) and little, if any, for patients with chronic, mild kidney disease (GFR 60 to 89 mL/min/1.73m^2). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs. Report any diagnosis of NSF following Gadavist administration to Bayer Healthcare (1-888-842-2937) or FDA (1-800-FDA-1088 or www.fda.gov/medwatch).

Screen patients for acute kidney injury and other conditions that may reduce renal function. Features of acute kidney injury consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess renal function in the setting of acute kidney injury. For patients at risk for chronically reduced renal function (for example, age > 60 years, diabetes mellitus or chronic hypertension), estimate the GFR through laboratory testing.

Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA and degree of renal impairment at the time of exposure. Record the specific GBCA and the dose administered to a patient. For patients at highest risk for NSF, do not exceed the recommended Gadavist dose and allow a sufficient period of time for elimination of the drug prior to re-administration. For patients receiving hemodialysis, consider the prompt initiation of hemodialysis following the administration of a GBCA in order to enhance the contrast agent's elimination *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*. The usefulness of hemodialysis in the prevention of NSF is unknown *[see Clinical Pharmacology (12.3)]*.

5.2 Hypersensitivity Reactions

Anaphylactic and other hypersensitivity reactions with cardiovascular, respiratory or cutaneous manifestations, ranging from mild to severe, including death, have uncommonly occurred following Gadavist administration *[see Adverse Reactions (6)]*.

- Before Gadavist administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Gadavist.
- Administer Gadavist only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.

Most hypersensitivity reactions to Gadavist have occurred within half an hour after administration. Delayed reactions can occur up to several days after administration. Observe patients for signs and symptoms of hypersensitivity reactions during and following Gadavist administration.

5.3 Gadolinium Retention

Gadolinium is retained for months or years in several organs. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (for example, brain, skin, kidney, liver, and spleen). The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs. At equivalent doses, gadolinium retention varies among the linear agents with Omniscan (gadodiamide) and Optimark (gadoversetamide) causing greater retention than other linear agents [Eovist (gadoxetate disodium), Magnevist (gadopentetate dimeglumine), MultiHance (gadobenate dimeglumine)]. Retention is lowest and similar among the macrocyclic GBCAs [Dotarem (gadoterate meglumine), Gadavist (gadobutrol), ProHance (gadoteridol)].

Consequences of gadolinium retention in the brain have not been established. Pathologic and clinical consequences of GBCA administration and retention in skin and other organs have been established in patients with impaired renal function *[see Warnings and Precautions (5.1)]*. There are rare reports of pathologic skin changes in patients with normal renal function. Adverse events involving multiple organ systems have been reported in patients with normal renal function without an established causal link to gadolinium retention *[see Adverse Reactions (6.2)]*.

While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies particularly closely spaced studies, when possible.

5.4 Acute Kidney Injury

In patients with chronic renal impairment, acute kidney injury sometimes requiring dialysis has been observed with the use of some GBCAs. Do not exceed the recommended dose; the risk of acute kidney injury may increase with higher than recommended doses.

5.5 Extravasation and Injection Site Reactions

Ensure catheter and venous patency before the injection of Gadavist. Extravasation into tissues during Gadavist administration may result in moderate irritation *[see Nonclinical Toxicology (13.2)]*.

5.6 Overestimation of Extent of Malignant Disease in MRI of the Breast

Gadavist MRI of the breast overestimated the histologically confirmed extent of malignancy in the diseased breast in up to 50% of the patients *[see Clinical Studies (14.2)]*.

5.7 Low Sensitivity for Significant Arterial Stenosis

The performance of Gadavist MRA for detecting arterial segments with significant stenosis (>50% renal, >70% supra-aortic) has not been shown to exceed 55%. Therefore, a negative MRA study alone should not be used to rule out significant stenosis *[see Clinical Studies (14.3)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in labeling:

- Nephrogenic Systemic Fibrosis (NSF) *[see Boxed Warning and Warnings and Precautions (5.1)]*.
- Hypersensitivity reactions *[see Contraindications (4) and Warnings and Precautions (5.2)]*.

6.1 Clinical Trials Experience

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

The adverse reactions described in this section reflect Gadavist exposure in 7,713 subjects (including 184 pediatric patients, ages 0 to 17 years) with the majority receiving the recommended dose. Approximately 52% of the subjects were male and the ethnic distribution was 62% Caucasian, 28% Asian, 5%

Hispanic, 2.5% Black, and 2.5% patients of other ethnic groups. The average age was 56 years (range from 1 week to 93 years).

Overall, approximately 4% of subjects reported one or more adverse reactions during a follow-up period that ranged from 24 hours to 7 days after Gadavist administration.

Adverse reactions associated with the use of Gadavist were usually mild to moderate in severity and transient in nature.

Table 2 lists adverse reactions that occurred in ≥ 0.1% subjects who received Gadavist.

Table 2: Adverse Reactions

Reaction	Rate (%) n=7713
Headache	1.7
Nausea	1.2
Dizziness	0.5
Dysgeusia	0.4
Feeling Hot	0.4
Injection site reactions	0.4
Vomiting	0.4
Rash (includes generalized, macular, papular, pruritic)	0.3
Erythema	0.2
Paresthesia	0.2
Pruritus (includes generalized)	0.2
Dyspnea	0.1
Urticaria	0.1

Adverse reactions that occurred with a frequency of < 0.1% in subjects who received Gadavist include: hypersensitivity/anaphylactic reaction, loss of consciousness, convulsion, parosmia, tachycardia, palpitation, dry mouth, malaise and feeling cold.

6.2 Postmarketing Experience

The following additional adverse reactions have been reported during postmarketing use of Gadavist. Because these reactions are reported voluntarily from a population of uncertain size, it is not possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

- Cardiac arrest
- Nephrogenic Systemic Fibrosis (NSF)
- Hypersensitivity reactions (anaphylactic shock, circulatory collapse, respiratory arrest, pulmonary edema, bronchospasm, cyanosis, oropharyngeal swelling, laryngeal edema, blood pressure increased, chest pain, angioedema, conjunctivitis, hyperhidrosis, cough, sneezing, burning sensation, and pallor) *[see Warnings and Precautions (5.2)]*.
- General Disorders and Administration Site Conditions: Adverse events with variable onset and duration have been reported after GBCA administration *[see Warnings and Precautions (5.3)]*. These include fatigue, asthenia, pain syndromes, and heterogeneous clusters of symptoms in the neurological, cutaneous, and musculoskeletal systems.
- Skin: Gadolinium associated plaques

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

GBCAs cross the placenta and result in fetal exposure and gadolinium retention. The human data on the association between GBCAs and adverse fetal outcomes are limited and inconclusive *(see Data)*. In animal reproduction studies, although teratogenicity was not observed, embryolethality was observed in monkeys, rabbits and rats receiving intravenous gadobutrol during organogenesis at doses 8 times and above the recommended human dose. Retardation of embryonal development was observed in rabbits and rats receiving intravenous gadobutrol during organogenesis at doses 8 and 12 times, respectively, the recommended human dose *(see Data)*. Because of the potential risks of gadolinium to the fetus, use Gadavist only if imaging is essential during pregnancy and cannot be delayed.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and is 15 to 20%, respectively.

Data

Human Data.

Contrast enhancement is visualized in the placenta and fetal tissues after maternal GBCA administration.

Cohort studies and case reports on exposure to GBCAs during pregnancy have not reported a clear association between GBCAs and adverse effects in the exposed neonates. However, a retrospective cohort study, comparing pregnant women who had a GBCA MRI to pregnant women who did not have an MRI, reported a higher occurrence of stillbirths and neonatal deaths in the group receiving GBCA MRI. Limitations of this study include a lack of comparison with non-contrast MRI and lack of information about the maternal indication for MRI. Overall, these data preclude a reliable evaluation of the potential risk of adverse fetal outcomes with the use of GBCAs in pregnancy.

Animal Data

Gadolinium Retention

GBCAs administered to pregnant non-human primates (0.1 mmol/kg on gestational days 85 and 135) result in measurable gadolinium concentration in the offspring in bone, brain, skin, liver, kidney, and spleen for at least 7 months. GBCAs administered to pregnant mice (2 mmol/kg daily on gestational days 16 through 19) result in measurable gadolinium concentrations in the pups in bone, brain, kidney, liver, blood, muscle, and spleen at one month postnatal age.

Reproductive Toxicology

Embryolethality was observed when gadobutrol was administered intravenously to monkeys during organogenesis at doses 8 times the recommended single human dose (based on body surface area); gadobutrol was not maternally toxic or teratogenic at this dose. Embryolethality and retardation of embryonal development also occurred in pregnant rats receiving maternally toxic doses of gadobutrol (≥ 7.5 mmol/kg body weight; equivalent to 12 times the human dose based on body surface area) and in pregnant rabbits (≥ 2.5 mmol/kg body weight; equivalent to 8 times the recommended human dose based on body surface area). In rabbits, this finding occurred without evidence of pronounced maternal toxicity and with minimal placental transfer (0.01% of the administered dose detected in the fetuses).

Because pregnant animals received repeated daily doses of Gadavist, their overall exposure was significantly higher than that achieved with the standard single dose administered to humans.

8.2 Lactation

Risk Summary

There are no data on the presence of gadobutrol in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk and there is limited GBCA gastrointestinal absorption in the breast-fed infant. Gadobutrol is present in rat milk *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Gadavist and any potential adverse effects on the breastfed infant from Gadavist or from the underlying maternal condition.

Data

In lactating rats receiving 0.5 mmol/kg of intravenous [^{153}Gd]-gadobutrol, 0.01% of the total administered radioactivity was transferred to the pup via maternal milk within 3 hours after administration, and the gastrointestinal absorption is poor (approximately 5% of the dose orally administered was excreted in the urine).

8.4 Pediatric Use

The safety and effectiveness of Gadavist have been established in pediatric patients, including term neonates, for use with MRI to detect and visualize areas with disrupted blood brain barrier and/or abnormal vascularity of the central nervous system and for use in MRA to evaluate known or suspected supra-aortic or renal artery disease. Use of Gadavist in these indications is supported by adequate and well-controlled studies in adults and supportive imaging data in two studies in 135 patients 2 to less than 18 years of age and 44 patients less than 2 years of age with CNS and non-CNS lesions, and pharmacokinetic data in 130 patients 2 to less than 18 years of age and 43 patients less than 2 years of age, including term neonates *[see Clinical Pharmacology (12.3) and Clinical Studies (14.1)]*. The frequency, type, and severity of adverse reactions in pediatric patients were similar to adverse reactions in adults *[see Adverse Reactions (6.1)]*. No dose adjustment according to age is necessary in pediatric patients *[see Dosage and Administration (2.1), Clinical Pharmacology (12.3), and Clinical Studies (14.1)]*. The safety and effectiveness of Gadavist have not been established in preterm neonates for any indication or in pediatric patients of any age for use with MRI to assess the presence and extent of malignant breast disease, or for use in CMRI to assess myocardial perfusion (stress, rest) and late gadolinium enhancement in patients with known or suspected coronary artery disease (CAD).

NSF Risk

No case of NSF associated with Gadavist or any other GBCA has been identified in pediatric patients ages 6 years and younger. Pharmacokinetic studies suggest that clearance of Gadavist is similar in pediatric patients and adults, including pediatric patients age younger than 2 years. No increased risk factor for NSF has been identified in juvenile animal studies of gadobutrol. Normal estimated GFR (eGFR) is around 30 mL/min/1.73m^2 at birth and increases to mature levels around 1 year of age, reflecting growth in both glomerular function and relative body surface area. Clinical studies in pediatric patients younger than 1 year of age have been conducted in patients with the following

minimum eGFR: 31 mL/min/1.73m^2 (age 2 to 7 days), 38 mL/min/1.73m^2 (age 8 to 28 days), 62 mL/min/1.73m^2 (age 1 to 6 months), and 83 mL/min/1.73m^2 (age 6 to 12 months).

Juvenile Animal Data

Single and repeat-dose toxicity studies in neonatal and juvenile rats did not reveal findings suggestive of a specific risk for use in pediatric patients including term neonates and infants.

8.5 Geriatric Use

In clinical studies of Gadavist, 1,377 patients were 65 years of age and over, while 104 patients were 80 years of age and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients. In general, use of Gadavist in elderly patients should be cautious, reflecting the greater frequency of impaired renal function and concomitant disease or other drug therapy. No dose adjustment according to age is necessary in this population.

8.6 Renal Impairment

Prior to administration of Gadavist, screen all patients for renal dysfunction by obtaining a history and/or laboratory tests *[see Warnings and Precautions (5.1)]*. No dosage adjustment is recommended for patients with renal impairment.

Gadavist can be removed from the body by hemodialysis *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

10 OVERDOSAGE

The maximum dose of Gadavist tested in healthy volunteers, 1.5 mL/kg body weight (1.5 mmol/kg; 15 times the recommended dose), was tolerated in a manner similar to lower doses. Gadavist can be removed by hemodialysis *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]*.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity studies of gadobutrol have been conducted.

Gadobutrol was not mutagenic in *in vitro* reverse mutation tests in bacteria, in the HGPRT (hypoxanthine-guanine phosphoribosyl transferase) test using cultured Chinese hamster V79 cells, or in chromosome aberration tests in human peripheral blood lymphocytes, and was negative in an *in vivo* micronucleus test in mice after intravenous injection of 0.5 mmol/kg.

Gadobutrol had no effect on fertility and general reproductive performance of male and female rats when given in doses 12.2 times the human equivalent dose (based on body surface area).

13.2 Animal Toxicology and/or Pharmacology

Local intolerance reactions, including moderate irritation associated with infiltration of inflammatory cells was observed after paravenous administration to rabbits, suggesting the possibility of occurrence of local irritation if the contrast medium leaks around veins in a clinical setting *[see Warnings and Precautions (5.5)]*.

17 PATIENT COUNSELING INFORMATION

- Advise the patient to read the FDA-approved patient labeling (Medication Guide).

Nephrogenic Systemic Fibrosis

Instruct patients to inform their physician if they:

- Have a history of kidney disease and/or liver disease, or
- Have recently received a GBCA

GBCAs increase the risk of NSF among patients with impaired elimination of drugs. To counsel patients at risk of NSF:

- Describe the clinical manifestation of NSF
- Describe procedures to screen for the detection of renal impairment

Instruct the patients to contact their physician if they develop signs or symptoms of NSF following Gadavist administration, such as burning, itching, swelling, scaling, hardening and tightening of the skin; red or dark patches on the skin; stiffness in joints with trouble moving, bending or straightening the arms, hands, legs or feet; pain in the hip bones or ribs; or muscle weakness.

Common Adverse Reactions

Inform patients that they may experience:

- Reactions along the venous injection site, such as mild and transient burning or pain or feeling of warmth or coldness at the injection site
- Side effects of headache, nausea, abnormal taste and feeling hot

General Precautions

Gadolinium Retention

- Advise patients that gadolinium is retained for months or years in brain, bone, skin, and other organs in patients with normal renal function. The clinical consequences of retention are unknown. Retention depends on multiple factors and is greater following administration of linear GBCAs than following administration of macrocyclic GBCAs. *[see Warnings and Precautions (5.3)]*.

Instruct patients receiving Gadavist to inform their physician if they:

- Are pregnant or breastfeeding
- Have a history of allergic reaction to contrast media, bronchial asthma or allergic respiratory disorder

Manufactured for:

Bayer HealthCare

Bayer HealthCare Pharmaceuticals Inc.
Whippany, NJ 07981
Manufactured in Germany

6905905BS

disparities in Africa. Adapted to local conditions, these three key ingredients of the programs could help to accelerate subspecialty programs in Africa.

References

1) Mollura DJ, Lungren MP, eds. Radiology in Global Health: Strategies, Implementation, and Applications. New York, NY: Springer, 2014. http://link.springer.com/10.1007/978-1-4614-0604-4. Accessed May 23, 2022.

2) Iyawe EP, Idowu BM, Omoleye OJ. Radiology subspecialisation in Africa: A review of the current status. *S Afr J Rad*. 2021;25(1):2168.

3) El Tawab KA, Wahab SM. The status of interventional radiology training: The Egyptian experience. *Arab J Intervent Radiol.* 2020;4:3.

4) Zember J, Reid J, Gorfu Y, Solomon DZ, Darge K. Pediatric radiology fellowship creation as an international education outreach effort in Ethiopia. *J Grad Med Educ.* 2020 Feb;12(1):98-103.

5) Brown B, Culp M, Olabu BO, et al. Meeting the need for IR training in Kenya. *J Vasc Interv Radiol.* 2020;31(11):1929–1932.e1.

6) Kline AD, Dixon RG, Brown MK, et al. Interventional radiology readiness assessment tool for global health. *J Global Radiol.* 2017; 3.

7) Laage Gaupp FM, Solomon N, Rukundo I, et al. Tanzania IR initiative: training the first generation of interventional radiologists. *J Vasc Interv Radiol.* 2019;30(12):2036–2040.

8) Mbuguje EM, Alswang JM, Rukundo I, et al. Safety and effectiveness of transthoracic core needle biopsy in a newly established interventional radiology rpogram in Tanzania. *Arab J Intervent Radiol* 2021;5:82-87.

9) Rukundo I, Mbuguje E, Naif A, et al. Establishment of a percutaneous nephrostomy service to treat obstructive uropathy secondary to cervical cancer in Tanzania. *Arab J Intervent Radiol* 2022; DOI: 10.1055/s-0042-1744507

10) McKenney AS, Garg T, Kim E, Kesselman A. Addressing global radiology disparities: increasing access to interventional radiology education. *Radiographics.* 2021 Sep-Oct;41(5):E142-E144.

11) Sharma S, Ganga K. Establishing IR in emerging countries: a skill development initiative. *J Vasc Interv Radiol* 2019;30(6):956–960.

Pneumatosis Cystoides Intestinalis

Ana Margarida C Alves, MD; Diogo Sá, MD; Raquel M Maia, MD

Case Summary

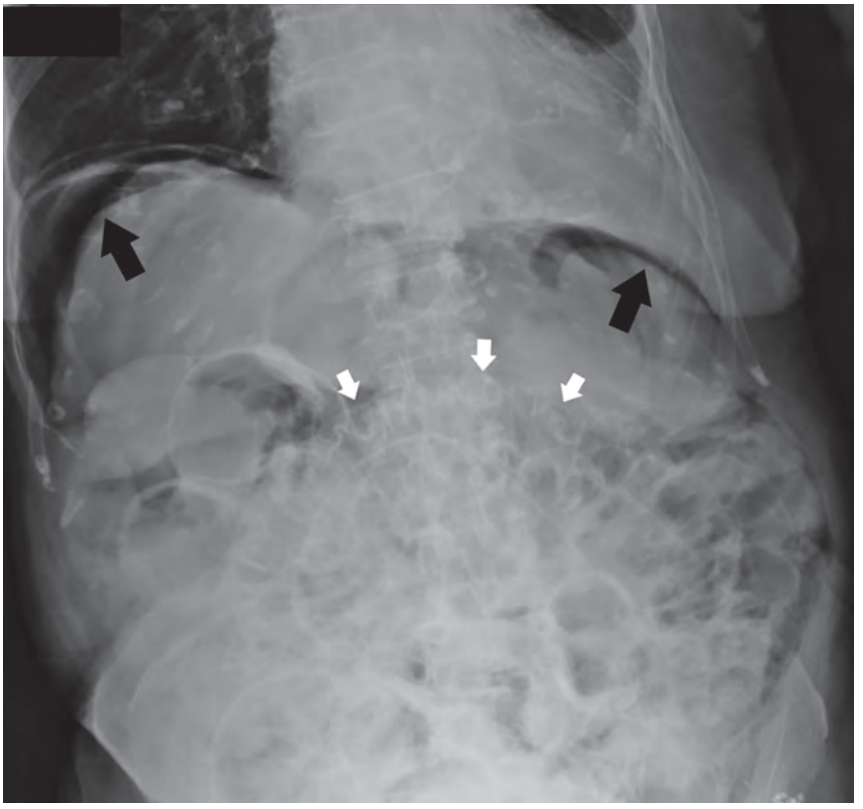
An elderly patient presented to the emergency department with a 48-hour history of diffuse abdominal pain and abdominal distension accompanied by an episode of vomiting. The patient had been chronically constipated but had no nausea, anorexia, diarrhea, or fever.

Previous medical history included congestive heart failure and atrial fibrillation, and no prior surgeries. Physical examination revealed mild diffuse abdominal pain with guarding. Laboratory tests were unremarkable, with normal white blood cell count, c-reactive protein and serum lactate.

Imaging Findings

Abdominal radiography revealed a large-volume pneumoperitoneum, with mild distension of small bowel loops but no gas-fluid levels (Figure 1). A subsequent contrast-enhanced computed tomography (CT) scan demonstrated a large amount of free air and multiple cystic spaces within the wall of a segment of the jejunum and duodenum. There were also cystic spaces within the omentum and parietal peritoneal fascia, as well as several diverticula in the jejunum (Figure 2). There were no signs of bowel obstruction.

Figure 1. Seated abdominal radiograph. Large pneumoperitoneum (black arrows) with the Rigler double wall sign. Segmental pneumatosis intestinalis can be seen as roundish air streaks in the wall of a small-bowel loop (white arrows). There is mild small-bowel distension.

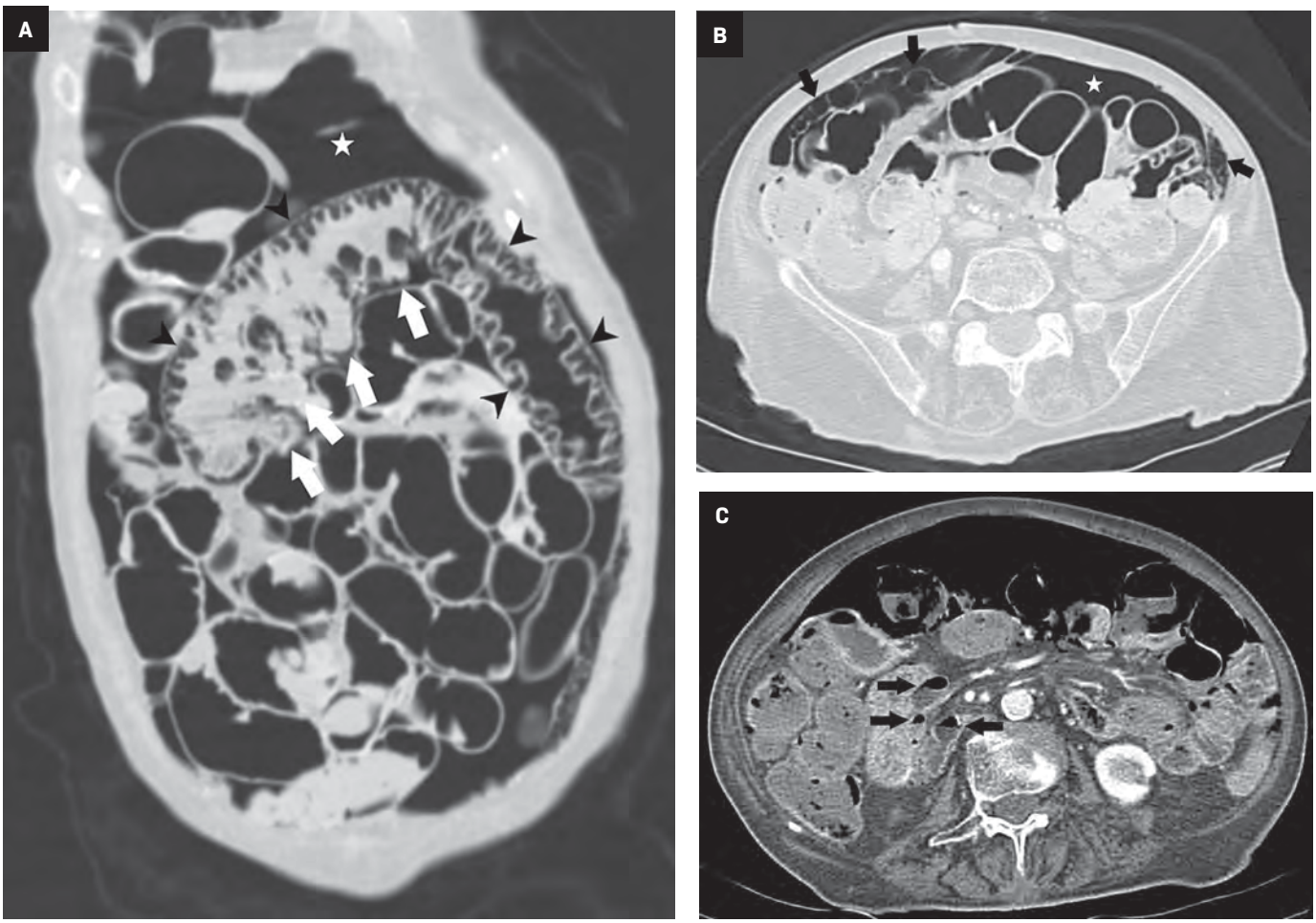


An emergency laparotomy revealed thickening of a jejunal segment with some diverticula associated with mesentery gas infiltration. No vascular compromise was found. Owing to suspicion of diverticular perforation, a segmental bowel resection was performed.

Pathology revealed multiple empty cysts expanding the submucosa, as well as in the subserosal layer with a sponge-like appearance, and some jejunal diverticula without

Affiliation: Centro Hospitalar Universitário do Porto, Porto, Portugal.

Figure 2. Contrast-enhanced abdomen and pelvis CT (A) Coronal image in lung window setting. Multiple cystic spaces in the wall of jejunum (arrowheads) and several diverticula in the same jejunal segment (arrows). Large pneumoperitoneum is also shown (star). (B) Axial image in lung window setting. Large pneumoperitoneum (star). Multiple cystic spaces are seen within the omentum and parietal peritoneal fascia (arrows). (C) Axial shows several small bowel diverticula (arrows) without signs of inflammation.



signs of complication. Histological examination demonstrated several empty cysts predominantly in the submucosa but also in the mucosa, muscularis propria, and subserosa, which were lined by multinucleated giant cells (Figure 3).

Diagnosis

Pneumatosis cystoides intestinalis

Discussion

Pneumatosis intestinalis is a radiographic or physical finding characterized by the presence of gas within the wall of the intestine. Mesenteric ischemia and bowel obstruction represent the most life-threatening causes of pneumatosis intestinalis.[1]

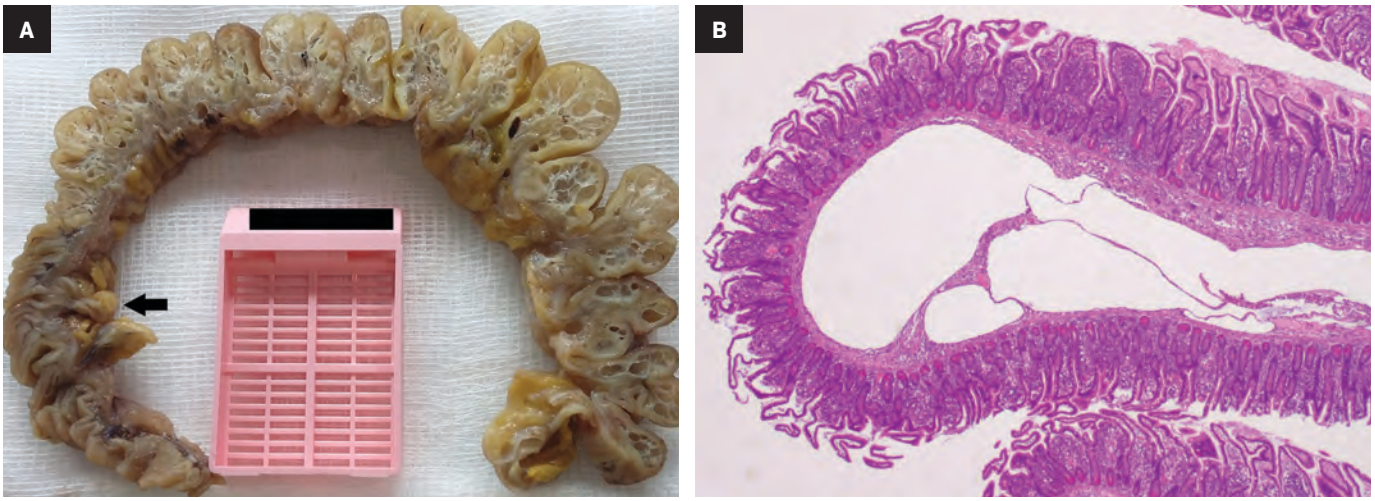
A rare and benign subtype of intestinal pneumatosis, pneumatosis cystoides intestinalis (PCI) is characterized by multilocular, gas-filled cysts localized in the intestinal submucosa and subserosa. The condition can occur anywhere along the gastrointestinal tract, but the colon is the most common localization.[2] Pneumatosis has been also found in unusual regions such as the mesentery, omentum, and hepatogastric ligament.[3]

Pneumatosis cystoides intestinalis can be divided into primary and secondary types. Causes of secondary PCI include pulmonary disease, inflammatory bowel disease, connective tissue disorders, iatrogenic procedures, certain medications, and organ transplantation.[4] There are only a few case reports of pneumatosis intestinalis associated with jejunal diverticulosis.[5,6] Zakhour and Clark suggested that the association of pneumatosis and diverticulosis could be related to mechanical and bacterial factors.[6]

Patients may be asymptomatic or they may demonstrate a broad spectrum of nonspecific gastrointestinal symptoms such as abdominal pain, distention and/or obstruction, as well as diarrhea, nausea, and vomiting.[7]

The imaging modalities most frequently used to diagnose pneumatosis intestinalis are radiography

Figure 3. (A) Gross specimen of the resected segment of the jejunum (opened). Multiple empty cysts expand the submucosa, presenting a sponge-like appearance. There are some cysts in subserosal layer, as well as a diverticulum (arrow) along the mesenteric border. (B) Histological image of jejunum wall (H&E stain, original magnification, 20x) demonstrates multiple cysts in submucosal layer.



and CT, the latter of which is the most sensitive and specific for the condition. On radiography, PCI is characterized by radiolucency within the wall of the GI tract.[4] Abdominal radiographic findings are detected in approximately two-thirds of patients.[7] On CT, PCI appears as segmental or diffuse cystic spaces along the wall of the intestine; it can also appear in the mesentery and omentum. Visualization of CT images in lung windows helps to detect PCI.[4]

Two patterns of pneumatosis intestinalis have been described: a bubble-like or cystoid pattern characterized by separate bubbles of gas with a cystic appearance, and a linear pattern in which the gas has a curvilinear and a circumferential form in the bowel wall.[1]

The presence of linear pneumatosis and additional findings such as bowel-wall thickening, absent or intense mucosal enhancement, distended bowel, arterial or venous occlusion, ascites, large volume pneumoperitoneum, and portal or mesenteric venous gas increases the possibility of pneumatosis intestinal due to a life-threatening cause.[7] Importantly, spontaneous small pneumoperitoneum can be associated with PCI, due to the rupture of subserosal cysts in the bowel wall.[4]

Histopathologic diagnosis of PCI is made in the presence of submucosal or subserosal empty spaces lined by multinucleated giant cells and macrophages.[5]

Pneumatosis cystoides intestinalis is often benign and only requires conservative treatment with antibiotics (especially metronidazole) and/or normobaric or hyperbaric oxygen therapy with follow-up. Surgical treatment should be considered for patients who remain symptomatic despite medical therapy or who develop PCI-related complications such as bowel obstruction, perforation, peritonitis, and necrosis.[7]

In our case, bowel resection was performed owing to the presence of a large amount of free peritoneal air and jejunal diverticula that raised the suspicion of perforation.

Conclusion

Owing to its rarity and nonspecific symptoms, PCI can be easily misdiagnosed. Correlating clinical history, imaging findings, and laboratory results is fundamental to differentiating benign from urgent cases and preventing misdiagnosis and inadequate treatment.

References

1) Khalil PN, Huber-Wagner S, Ladurner R, Kleespies A, Siebeck M, Mutschler W, et al. Natural history, clinical pattern, and surgical considerations of pneumatosis intestinalis. *Eur J Med Res*. 2009;14:231-239. doi:10.1186/2047-783x-14-6-231.

2) Wu LL, Yang YS, Dou Y, Liu QS. A systematic analysis of pneumatosis cystoids intestinalis. *World J Gastroenterol.* 2013;19(30):4973-4978. doi:10.3748/wjg.v19.i30.4973.

3) Wang Y, Wang Y, Zheng Y, Jiang H, Zhang J. Pneumatosis cystoides intestinalis: six case reports and a review of the literature. *BMC Gastroenterology*. 2018;18:100. doi:10.1186/s12876-018-0794-y.

4) Ho LM, Paulson EK, Thompson WM. Pneumatosis intestinalis in the adult: benign to life-threatening causes. *AJR Am J Roentgenol*. 2007;188(6):1604-1613. doi:10.2214/AJR.06.1309.

5) Sammon AM, Malcolm AJ. Pneumatosis cystoides intestinalis secondary to chronic jejunal diverticulitis. *Postgrad Med J*. 1979;55(649):820-821. doi:10.1136/pgmj.55.649.820.

6) Zakhour HD, Clark RG. Intramural gas cysts in a case of diverticular disease of the jejunum. *Histopathology*. 1982;6(3):363-369. doi:10.1111/j.1365-559.1982.tb02730.x.

7) Sugihara Y, Harada K, Ogawa H, Otsuka F, Okada H. Pneumatosis cystoides intestinalis. *J Lung Health Dis.* 2018;2:24-7. doi:10.29245/2689-999X/2017/1.1121.

Plasmablastic Lymphoma

Xiao Bi, MD; Rajeev Varma, MD

Case Summary

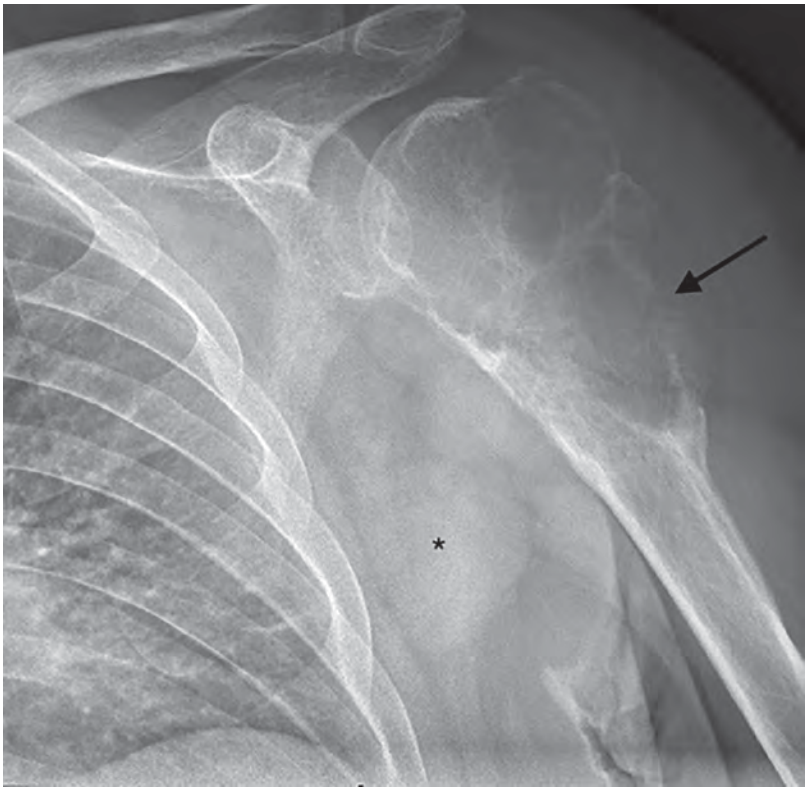
An adult presented with left shoulder pain and difficulty raising their arm after a fall three days previously. The medical history was notable for type II diabetes mellitus, hypertension, and hyperlipidemia. A physical examination showed weakness in abduction and external rotation of the left shoulder, with no evidence of neurovascular deficit. Complete blood count and chemistry panel were unremarkable. Laboratory tests were positive for Epstein-Barr virus (EBV) and negative for human immunodeficiency virus (HIV).

Imaging Findings

Radiography of the left shoulder revealed a lytic, expansile, eccentrically located lesion with a narrow zone of transition within the humoral head and extending to the subchondral bone without sclerotic margins (Figure 1). There was loss of cortex on the lateral aspect of the lesion, concerning for pathologic fracture. Based on the clinical history and appearance of the lesion, it was first thought to be a giant cell tumor (GCT).

The differential diagnosis included aneurysmal bone cyst, which was considered less likely given the patient's age and subchondral extension of the lesion. The concern for a soft-tissue component or other aggressive process led to further imaging and biopsy.

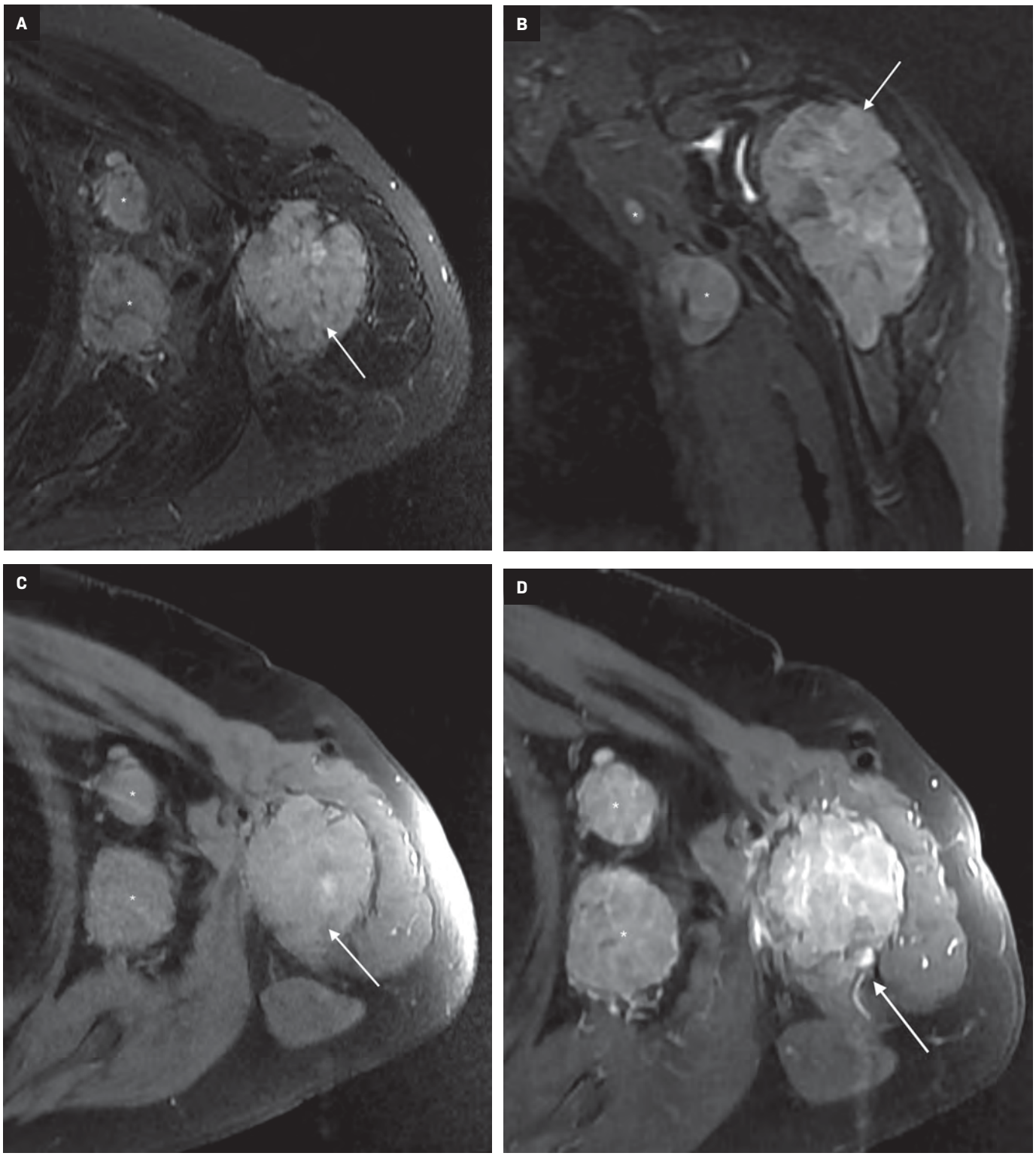
Figure 1. Radiograph shows an expansile, eccentric, lytic lesion of the humeral head with a narrow zone of transition. There is loss of cortex concerning for pathologic fracture on the lateral aspect of the lesion (arrow). There is also a soft-tissue density in the axillary region corresponding to an enlarged lymph node (*).



Subsequent pre- and post-Gadolinium contrast magnetic resonance imaging showed the lesion to be 5.6 cm x 5.5 cm x 9.8 cm with low signal on T1 sequences, heterogeneous hyperintensity with areas of low signal intensity on fluid sensitive sequences, including short tau inversion recovery (STIR), and mild post-contrast enhancement (Figure 2).

Affiliation: Harbor-UCLA Medical Center, Torrance, California.

Figure 2. Axial STIR (A), coronal STIR (B), and pre- and postcontrast T1 images with fat saturation (C,D) MR images of the humoral head mass (arrows) show it to be mildly enhancing with hypo-to-isointensity with regard to muscle signal and heterogeneous STIR hyperintensity. There is cortical erosion with extension of the mass into the surrounding soft tissues. There are also two enlarged axillary lymph nodes (*).



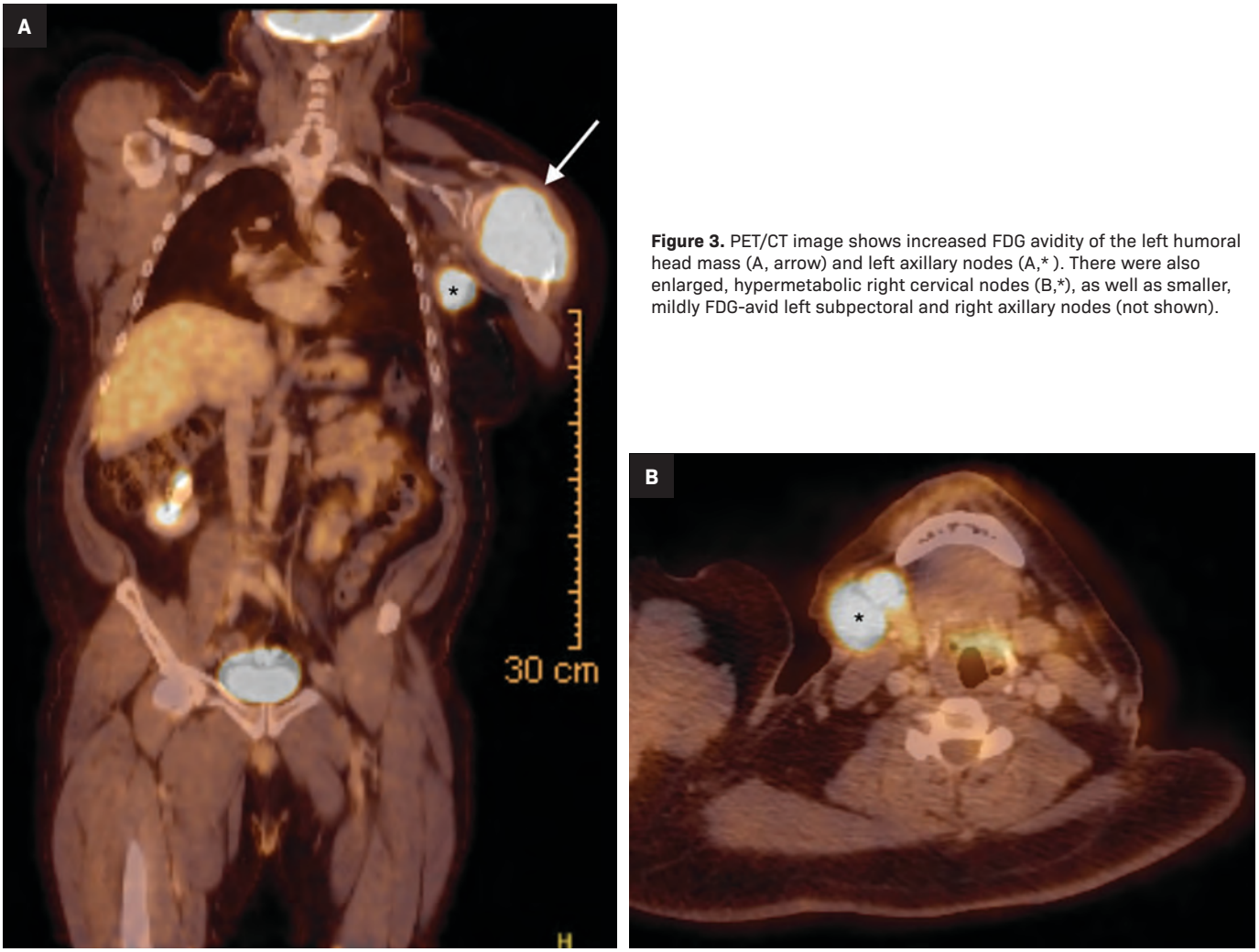


Figure 3. PET/CT image shows increased FDG avidity of the left humoral head mass (A, arrow) and left axillary nodes (A,*). There were also enlarged, hypermetabolic right cervical nodes (B,*), as well as smaller, mildly FDG-avid left subpectoral and right axillary nodes (not shown).

There was cortical erosion with extension of the lesion into the surrounding soft tissues. Additionally, there were two pathologically enlarged axillary lymph nodes (2.4 and 3.3 cm in short axes). A review of the initial radiograph showed these lymph nodes to be present in retrospect (Figure 1).

Staging (18)F-fluorodeoxyglucose (FDG) positron emission tomography/computed tomography (PET/CT) showed hypermetabolism of the humoral lesion with a maximum standardized uptake value (SUV) of 11.7 and of the axillary lymph nodes with maximum SUV of 11.6 (Figure 3). There were also hypermetabolic right cervical (maximum SUV 14.3), left subpectoral (maximum SUV 3.7), and right axillary lymph nodes (max SUV 4.4) concerning for additional sites of disease.

Diagnosis

Plasmablastic lymphoma

Discussion

Plasmablastic lymphoma (PBL) is a rare, highly aggressive, diffuse large B-cell lymphoma variant characterized by proliferation of CD20-neoplastic cells with immunophenotype resembling plasmablasts, a plasma cell precursor. Initially described as an oral cavity lesion in HIV-positive patients,[1] PBL is now known to occur in other anatomic locations, including the gastrointestinal tract, skin, and, less commonly, the bones,[2-4] as well as in non-HIV-associated immunosuppressed and even immunocompetent patients.[4]

Extra-oral involvement appears to be more common in HIV-negative patients, while oral involvement remains the predominant manifestation in HIV-positive patients.[2] Additionally, Epstein-Barr virus infection is present in a high percentage of cases.[3]

Osseous PBL has varied and nonspecific imaging findings, with case reports showing overlap with osteosarcoma and plasmacytoma, resulting in a significant risk of misdiagnosis.[4,5] Differentiation occurs on the basis of histopathology and immunohistochemistry.[4]

Our case showed imaging findings mimicking those of giant cell tumor[6] and, to a lesser extent, aneurysmal bone cyst,[7] on initial plain films. Subsequent cross-sectional imaging findings of lymphadenopathy pointed toward a more malignant etiology, which was confirmed by tissue biopsy.

Owing to the rarity of this disease, there are currently no consensus treatment guidelines.[5] A number of chemotherapy regimens have been tried, with mixed results.[5] The median overall survival is 6-19 months.[5] Given PBL's poor prognosis, it is important to differentiate this disease from benign entities.

Conclusion

Plasmablastic lymphoma has imaging features overlapping with other benign and malignant entities, including giant cell tumors and aneurysmal bone cysts. In a patient with a presumed benign lytic lesion such as giant cell tumor, findings of regional lymphadenopathy should prompt suspicion for an alternative malignant etiology, including plasmablastic lymphoma.

References

1) Delecluse HJ, Anagnostopoulos I, Dallenbach F, et al. Plasmablastic lymphomas of the oral cavity: a new entity associated with the human immunodeficiency virus infection. *Blood*. 1997;89(4):1413-20.

2) Hansra D, Montague N, Stefanovic A, et al. Oral and extraoral plasmablastic lymphoma: similarities and differences in clinicopathologic characteristics. *Am J Clin Pathol*. 2010;134:710–719.

3) Lopez A, Abrisqueta P. Plasmablastic lymphoma: current perspectives. *Blood Lymphat Cancer*. 2018;8:63-70.

4) Sarker AK, Im HJ, Paeng JC, et al. Plasmablastic lymphoma exclusively involving bones mimicking osteosarcoma in an immunocompetent patient: A case report. *Medicine (Baltimore)*. 2016;95(28):e4241.

5) Diaz R, Amalaseelan J, Imlay-gillespie L. Plasmablastic lymphoma masquerading solitary plasmacytoma in an immunocompetent patient. *BMJ Case Rep*. 2018;2018:1-4.

6) Chakarun CJ, Forrester DM, Gottsegen CJ, Patel DB, White EA, Matcuk GR. Giant cell tumor of bone: review, mimics, and new developments in treatment. *Radiographics*. 2013;33(1):197-211.

7) Kransdorf MJ, Sweet DE. Aneurysmal bone cyst: concept, controversy, clinical presentation, and imaging. *AJR Am J Roentgenol*. 1995;164(3):573-80.

FUJIFILM
Value from Innovation

Built to perform.

BASED ON INSIGHTS THAT IMPACT PATIENT CARE

We all know that screening is the best way to detect breast cancer earlier and digital breast tomosynthesis (DBT) improves image quality for better detection. But now it's time to get smarter about it.

ASPIRE Cristalle with DBT is built with insight into image quality, operational excellence, and a better patient experience.

SUPERIOR DIAGNOSTIC ACCURACY — superior (lower) recall rates for non-cancer cases

LESS STRESSFUL EXAM — patented Comfort Paddle gently adapts to the breast's curves for noticeably improved comfort

LOW DOSE — achieve exceptional images with gentle dose for every breast type.

ASPIRE Cristalle
with Digital Breast Tomosynthesis

SEE MORE OF THE INSIGHTS that helped create one of the world's most precise and comfortable mammography systems at **cristalle.fujimed.com**

All claims made in comparison to Fujifilm FFDM alone.

Hereditary Angioedema

Luke M Lammers; Richard B Towbin, MD; Carrie M Schaefer, MD; Alexander J Towbin, MD

Case Summary

A teenager with a known personal and family history of hereditary angioedema (HAE) presented to the emergency department with generalized abdominal pain, constipation, and nonbilious, non-bloody emesis for several days without signs of obstruction. On physical examination there was generalized abdominal pain without peritoneal signs. Laboratory studies demonstrated mild leukocytosis (14×10^9/L) but were otherwise within normal limits.

Imaging Findings

Computed tomography (CT) of the abdomen and pelvis with contrast (Figure 1) showed wall thickening involving the distal duodenum and proximal jejunum. There was contrast enhancement of the mucosa and submucosal edema. The enhancing bowel loops were mildly distended with fluid and there was a small volume of ascites.

Diagnosis

Hereditary angioedema

The differential diagnosis for focal small-bowel wall thickening in an adolescent includes enteritis, Crohn disease, ischemic bowel, and lymphoma.[1] In this patient, the diagnosis of HAE was known, making the other entities less likely.

Leukocytosis with neutrophilia is often present during episodes of acute HAE.[2] It is important to differentiate bradykinin-mediated angioedema from histamine-mediated angioedema, as the latter has features of urticaria and pruritis and usually involves triggers such as drugs, foods, and viruses.

Discussion

Hereditary angioedema is an autosomal dominant disorder typically resulting from the lack (HAE type 1) or dysfunction (HAE type 2) of C1-inhibitor protein.[3] C1-inhibitor protein primarily acts to control the creation of kinin proteins such as bradykinin and to limit the activation of the intrinsic complement cascade.[4] Bradykinin is a protein that acts as a potent vasodilator and is known to be the principal mediator of angioedema.

Local trauma or stress may trigger these cascades, resulting in significant angioedema. The classic trigger for HAE is angiotensin-converting enzyme (ACE) inhibitor use because ACE breaks down bradykinin. When patients with genetically impaired C1-inhibitor function use ACE inhibitors, bradykinin levels can markedly increase, leading to angioedema.[4] Though ACE-inhibitors are primarily used for hypertension management in adults, they play a role in heart failure management in the pediatric population.[5]

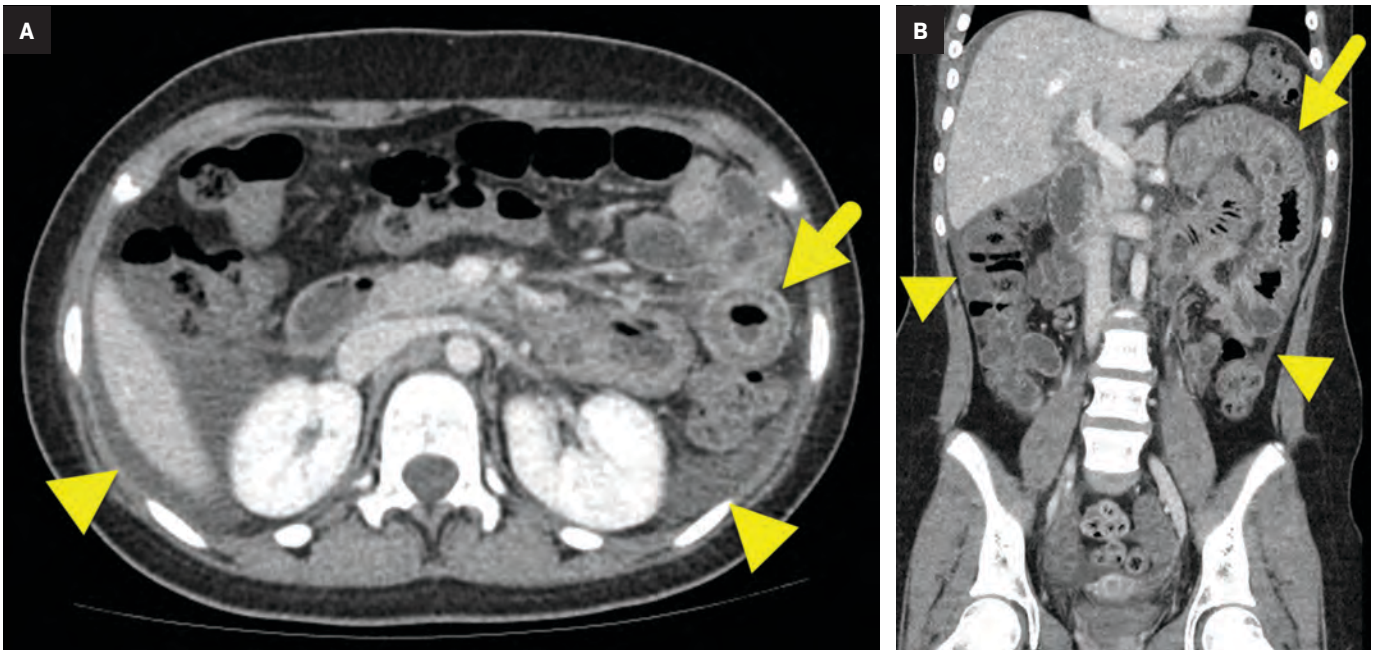
The estimated prevalence of HAE is 1 in 50,000; it typically presents within the first two decades of life. There tends to be a strong family history of HAE, although spontaneous HAE occurs in up to 25% of patients.[6]

Typically, symptoms of HAE involve the upper airway, skin, and gastrointestinal (GI) tract. Symptoms include skin swelling that is deforming and painful but not pruritic, upper airway swelling, which can result in dyspnea and even asphyxiation; and GI symptoms including obstruction and pain.[4] Attacks of HAE last 2 to 5 days and usually resolve without therapy. Prodromal symptoms, including an erythema marginatum rash, are possible.[4]

In HAE with GI involvement, contrast-enhanced abdominal CT typically shows bowel wall thickening, often with mural stratification or the "halo" sign, a result of a thickened, low-density submucosal layer secondary to edema with mucosal and subserosal enhancement.[6] It is possible for wall thickening to be asymmetric as opposed to circumferential.[6] There is often adjacent free fluid.[6] Imaging findings are typically nonspecific given the

Affiliations: University of Arizona College of Medicine-Phoenix (Mr Lammers); Phoenix Children's Hospital (Drs R Towbin, Schaefer); Cincinnati Children's Hospital, University of Cincinnati College of Medicine (Dr A Towbin)

Figure 1. (A) Axial and (B) coronal contrast-enhanced CT shows regional wall thickening and mural stratification (arrow) of the distal duodenum and proximal jejunum. A small volume of ascites (arrowheads) is also present.



number of other causes of intestinal wall edema.[1] The edema is usually segmental, with the duodenum and jejunum most commonly affected during an acute episode of HAE involving the bowel;[7] the ileum, colon, and stomach are much less frequently involved.[7]

Sonography is often utilized in the pediatric population with findings of HAE and may show free intraperitoneal fluid and bowel wall edema.[8] Magnetic resonance imaging may be used to confirm bowel wall thickening but is more likely to be used for brain imaging when there is concern for associated cerebral edema in the setting of HAE with GI involvement.[10]

HAE is confirmed through serum assays, including measurement of C4 complement, concentration of C1-INH, and functional C1-INH.[9] The C4 level, a highly sensitive measure, is typically less than 30% of mean normal levels.[9] Additional laboratory findings may include a leukocytosis with neutrophilic predominance and varying levels of c-reactive protein from normal to elevated, including elevations at baseline.[11]

The greatest morbidity from HAE comes from laryngeal edema; thus, management of acute attacks should focus on ensuring airway patency.[4,5] Additionally a concentrate of C1-INH may be helpful during acute attacks and as prophylaxis, but its cost and availability limit its use.[2,4] In a patient with recurrent episodes of unexplained abdominal pain with no identifiable trigger and CT findings reflecting bowel wall edema, HAE should be considered as a diagnosis.

References

1) De Backer AI, De Schepper AM, Vandevenne JE, et al.. CT angioedema of the small bowel. Am J Roentgenol. 2001; 176(3):649-652.

2) Ohsawa, I., Nagamachi, S., Suzuki, H. et al. Leukocytosis and high hematocrit levels during abdominal attacks of hereditary angioedema. *BMC Gastroenterol.* 2013, 123. https://doi.org/10.1186/1471-230X-13-123

3) Ciaccia D, Brazer S, Baker M. Acquired C1 esterase inhibitor deficiency causing intestinal angioedema: CT appearance. *Am J Roentgenol.* 1993;151:1215-1216.

4) Caccia S, Suffritti C, Cicardi M. Pathophysiology of hereditary angioedema. *Pediatr Allergy Immunol Pulmonol.* 2014;27(4):159-163.

5) Momma K. ACE inhibitors in pediatric patients with heart failure. *Paediatr Drugs.* 2006; 8(1):55-69.

6) Banday AZ, Kaur A, Jindal AK, Rawat A, Singh S. An update on the genetics and pathogenesis of hereditary angioedema. *Genes Dis.* 2019;7(1):75-83.

7) Ishigami K, Averill SL, Pollard JH, McDonald JM, Sato Y. Radiologic manifestations of angioedema. *Insights Imaging.* 2014; 5(3):365-374.

8) Henao MP, Kraschnewski JL, Kelbel T, Craig TJ. Diagnosis and screening of patients with hereditary angioedema in primary care. *Ther Clin Risk Manag.* 2016; 12:701-711.

9) Farkas H, Harmat G, Kaposi PN, Karádi I, Fekete B, Füst G, Fáy K, Vass A, Varga L. Ultrasonography in the diagnosis and monitoring of ascites in acute abdominal attacks of hereditary angioneurotic oedema. *Eur J Gastroenterol Hepatol.* 2001; 13(10):1225-1230.

10) Ali MA, Borum ML. Hereditary angioedema: what the gastroenterologist needs to know. *Clin Exp Gastroenterol.* 2014; 7:435-445.

11) Hofman ZL, Relan A, Hack CE. C-reactive protein levels in hereditary angioedema. *Clin Exp Immunol.* 2014 Jul; 177(1):280-286.

Sellar Atypical Teratoid Rhabdoid Tumor

Raza Mushtaq, MD; Jeremy Hughes, MD

Case Summary

A young adult woman with no significant medical history presented with diplopia, right mydriasis, and right ophthalmalgia. The patient also endorsed a history of extreme migraine headache and right facial paresthesias. Symptoms were progressive over a 2-year period. Laboratory evaluation was unremarkable.

Imaging workup revealed a large, parasellar mass. The patient subsequently underwent staged surgical resection. Following the second staged procedure, the patient underwent repeat imaging, which demonstrated extensive areas of cerebral vasospasm. Two-month follow-up imaging demonstrated tumor progression.

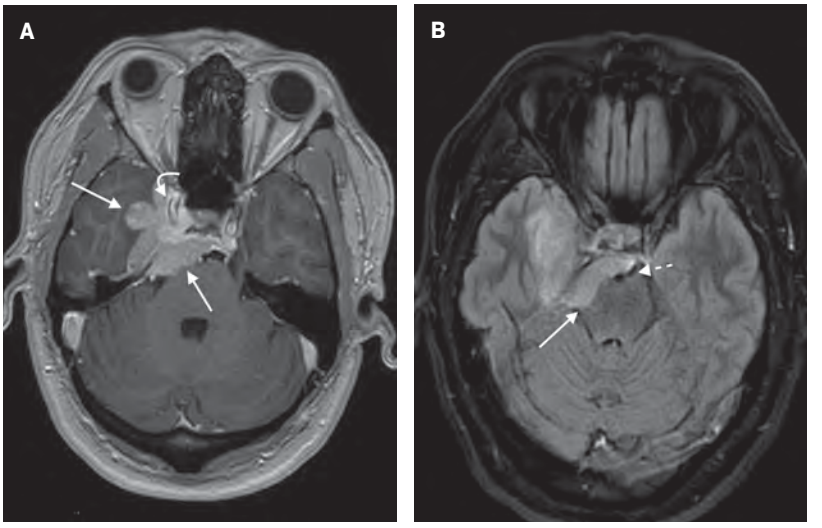
Imaging Findings

Preoperative MRI (Figure 1) demonstrated a large, contrast-enhancing, T2/FLAIR hyperintense, dural-based mass in the right parasellar region. The mass encased and narrowed the right internal carotid artery and abutted the basilar artery.

Postoperative digital subtraction angiography (DSA, Figure 2) demonstrated cerebral vasospasm most prominent in the right anterior circulation. Diffusion-weighted imaging (DWI) demonstrated multifocal, right cerebral hemisphere infarcts.

Two months after surgery, axial FLAIR MRI imaging (Figure 3) revealed progression of disease with new tumor extending caudally into the pre-pontine cistern.

Figure 1. Preoperative contrast-enhanced axial T1 MRI (A) and axial fat-suppressed fluid-attenuated inversion recovery (FLAIR) imaging (B) demonstrate a large, contrast-enhancing FLAIR hyperintense, extra-axial, dural-based mass (solid white arrows) in the right parasellar region. The mass encases and narrows the cavernous segment of the right internal carotid artery (A, curved arrow) and abuts the basilar artery (B, dashed white arrow).



Diagnosis

Sellar-subtype atypical teratoid rhabdoid tumor (ATRT), WHO grade IV

Discussion

There is a broad differential diagnosis for sellar/parasellar masses, including benign and malignant neoplasms, as well as numerous nonneoplastic etiologies.[1] Primary differential consideration is meningioma. As the most common extra-axial central nervous system (CNS) tumor, meningiomas may occur anywhere dura is present, including in the sellar/parasellar region. A broad, "dural tail" is one characteristic imaging feature of a meningioma.

Affiliation: Barrow Neurological Institute, Phoenix, Arizona

Typical meningiomas are of low grade and grow slowly. However, some high-grade and atypical meningiomas can be locally aggressive and show rapid growth.[2]

Atypical teratoid rhabdoid tumor (ATRT) is a rare malignant tumor of childhood, constituting approximately 1% of all pediatric brain tumors, but 10-20% of those occurring in children under three years. They are typically seen as intra-axial masses in young children.[3,4] These are highly aggressive tumors with substantial potential to metastasize within and beyond the CNS.[5] ATRT demonstrates variable imaging features but typically presents as a large, heterogeneously enhancing, intra-axial mass with mixed solid and cystic components related to varying degrees of necrosis, hemorrhage, and/or calcifications.[5] The solid components typically show restricted diffusion on diffusion imaging.

Histologically, ATRTs are composed of rhabdoid cells with vacuolated cytoplasm and mesenchymal spindle-shaped tumor cells.[4,5] Varying degrees of primitive neuroectodermal tumor (PNET) cells can create a diagnostic dilemma in differentiating ATRTs from PNET.[5] More recently, immunohistochemical analysis has been used to differentiate and characterize ATRT. The new WHO classification defines ATRT as loss of either integrase-interactor 1 (INI-1), tumor suppression gene, or loss of Brahma-related gene 1 (BRG1) protein. Tumors that share histological resemblance but do not harbor genetic alterations are characterized as CNS embryonal tumors with rhabdoid features.[6]

The sellar subtype of ATRT is an extremely rare variant found almost exclusively in young adult women and, in contrast to the more common pediatric ATRT, is extra-axial and occurs characteristically in a sellar location. Approximately 50 case reports have been published in English literature.[3,4,7] On imaging,

Figure 2. Postoperative (A) demonstrates cerebral vasospasm most prominent in the right anterior circulation. Diffusion-weighted imaging (B) demonstrates a right posterior middle cerebral artery territory infarct owing to the vasospasm.

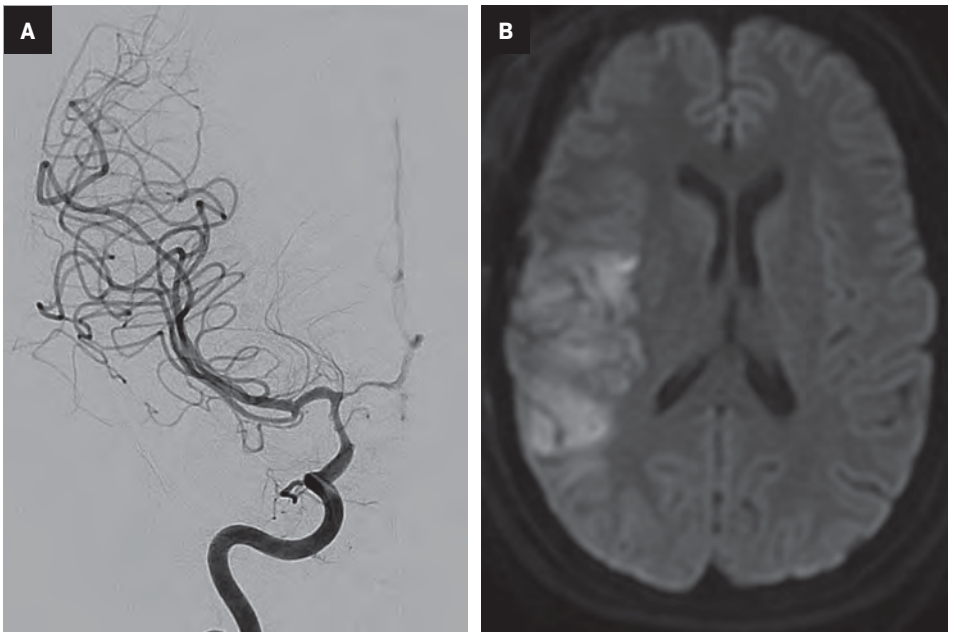
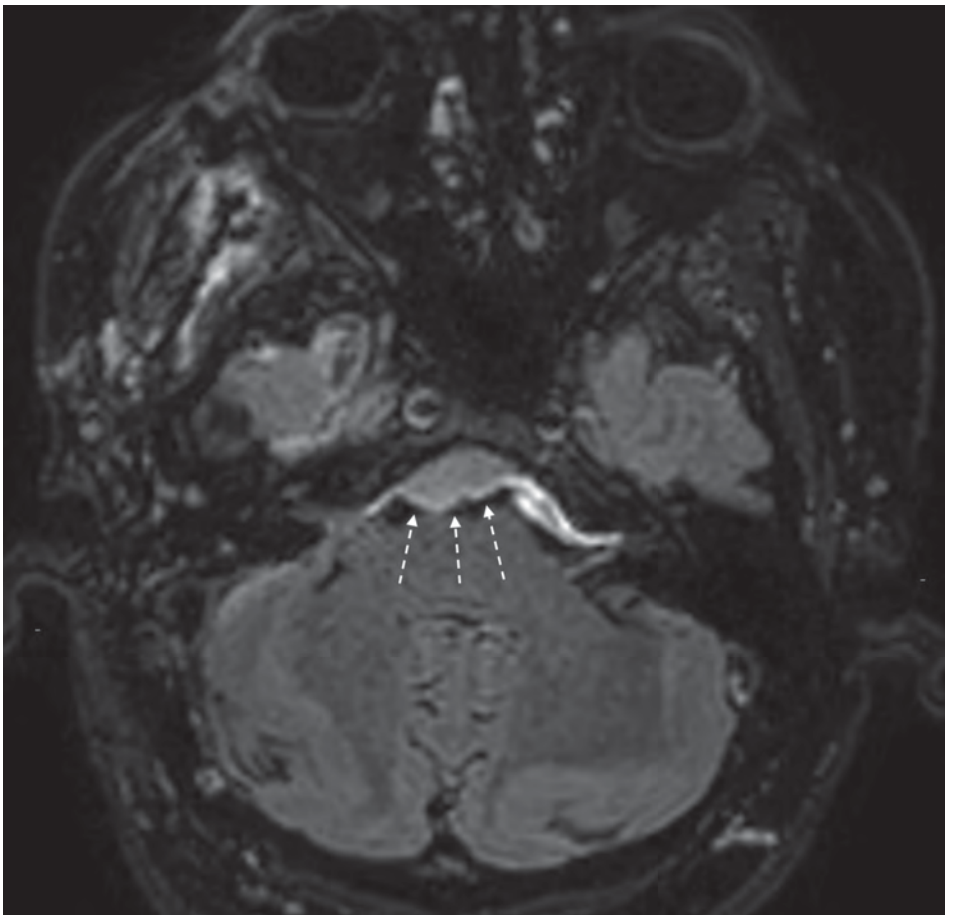


Figure 3. Follow-up axial fat-suppressed FLAIR reveals progression of disease, with tumor extending caudally into the prepontine cistern (thin dashed arrows).



the tumors have been described as enhancing extra-axial lesions located within the parasellar region. Peripherally located cysts may be present.[7] These tumors are aggressive, with mean survival of 23 months. The most common presenting clinical symptoms relate to local mass effect, which includes blurry vision and hypopituitarism features.[7] Most tumors recur following resection.

Nakata, et al, described sellar ATRT as a distinct clinicopathological entity occurring exclusively in adult women in the sellar region. They also found different INI-1 alterations compared to classic pediatric ATRT. A characteristic histologic vascular pattern of hemangiopericytoma-like, stag-horn vasculature is thought to distinguish sellar ATRT.[4]

Pathology in our case showed loss of INI-1, confirming the diagnosis of ATRT. The patient developed vasospasm postoperatively. While vasospasm may be related to recent surgery, vasospasm related to the underlying tumor is also a possibility. Siddiqui, et al, reported a pathological confirmed case of sellar ATRT in a 55-year-old woman presenting with 1 week of headache and blurred vision. The patient was found to have a suprasellar mass with subarachnoid hemorrhage and cerebral vasospasm preoperatively.[7]

Conclusion

Sellar subtype atypical teratoid rhabdoid tumors (ATRT) are rare, aggressive, WHO grade IV tumors. Sellar ATRT likely represents a distinct clinicopathological entity occurring almost exclusively in young adult women with somewhat differing imaging features and histologic and mutation patterns from typical ATRT.

References

1) Freda PU, Post KD. Differential diagnosis of sellar masses. *Endocrinol Metab Clin North Am*. 1999;28(1):81-117.

2) Kane AJ, Sughrue ME, Rutkowski MJ, et al. Anatomic location is a risk factor for atypical and malignant meningiomas. *Cancer*. 2011;117(6):1272-1278.

3) Shitara S, Akiyama Y. Atypical teratoid/rhabdoid tumor in sellar turcica in an adult: A case report and review of the literature. *Surgical Neurology International*. 2014;5.

4) Nakata S, Nobusawa S, Hirose T, et al. Sellar atypical teratoid/rhabdoid tumor (ATRT). *Am J Surg Pathol*. 2017;41(7):932-940.

5) Meyers SP, Khademian ZP, Biegel JA, Chuang SH, Korones DN, Zimmerman RA. Primary intracranial atypical teratoid/rhabdoid tumors of infancy and childhood: MRI features and patient outcomes. *Am J Neuroradiol*. 2006;27(5):962-971.

6) Louis DN, Perry A, Reifenberger G, et al. The 2016 world health organization classification of tumors of the central nervous system: A summary. *Acta Neuropathol*. 2016;131(6):803-820.

7) Siddiqui M, Thoms D, Samples D, et al. Atypical teratoid/rhabdoid tumor presenting with subarachnoid and intraventricular hemorrhage. *Surgical Neurology International*. 2019;10. doi: 10.25259/SNI-59-2019.

Osteoid Osteoma Treatment: Image-guided Resection Vs Image-guided Ablation

Alexxa Wirth; Richard B Towbin, MD; Carrie M Schaefer, MD; Alexander J Towbin, MD

Case Summary

A child who plays catcher in baseball had a 2-month history of left hip pain, more severe at night, that improved with ibuprofen. Physical examination demonstrated decreased left hip range of motion and guarding when rotating the hip.

Imaging Features

Magnetic resonance imaging (MRI) showed a focal area of marrow edema (Figure 1) seen along the medial central aspect of the junction of the left femoral neck and proximal shaft. Anteriorly a small focal nidus involved the cortex. Sagittal STIR images showed mild edema overlying the osseous, cortically-based nidus with mild local periosteal reaction. All findings were consistent with a diagnosis of osteoid osteoma (OO).

After treatment planning (Figure 2) the osteoid osteoma was treated percutaneously using a combination of percutaneous resection and radiofrequency ablation (Figure 3).

Affiliations: University of Arizona College of Medicine-Phoenix (Ms Wirth), Phoenix Children's Hospital, Phoenix, Arizona (Drs Schaefer, R Towbin); Children's Hospital Medical Center, and University of Cincinnati, Cincinnati, Ohio (Dr A Towbin).

Discussion

Osteoid osteoma is a benign, bone-forming neoplasm that accounts for 12% of all skeletal neoplasms .[1] Osteoid osteomas are highly vascularized tumors consisting of osteoid and woven bone that typically do not exceed 1.5 cm in diameter.[1,2] While OOs can occur anywhere in the skeleton, they are most commonly found in the cortex of long bones, with a higher predominance in the lower extremities.[1, 2, 3] These lesions are commonly seen in patients between 10 and 30 years old; they occur more often in males at about a 2:1 ratio.[4] Patients with OOs present with pain, classically occurring at night and relieved with nonsteroidal anti-inflammatory drugs (NSAIDs).[5] Their nonspecific symptoms and poorly localized pain may delay diagnosis and treatment.

Osteoid osteomas appear as round to oval, radiolucent lesions with a central nidus surrounded by a well-circumscribed sclerotic rim on radiographs. Intramedullary and intra-articular lesions usually lack the sclerotic margin as well as periosteal reaction.[4] If radiographs are inconclusive, computed tomography (CT) is valuable for diagnostic confirmation and treatment planning. [1,3,5]

The use of MRI to diagnose OOs is controversial, as the nidus cannot be clearly detected in up to 35% of cases.[2] On MRI the nidus can best be visualized on T1 contrast-enhanced images as low-to-intermediate signal intensity that enhances with gadolinium-based contrast.[2] Additionally, T2 fat-suppressed images may be used to identify the nidus.

Dynamic contrast-enhanced MRI (DCE-MRI) is more sensitive than traditional MRI in detecting OO. In DCE-MRI, OOs are visualized as a peak in signal enhancement during the arterial phase.[2] This technique is utilized to distinguish OO from Brodie abscess, where Brodie abscess has a central, nonenhanced area and OO has diffuse enhancement.[2]

Treatment Approaches

Observation with pain control may be considered in patients with OOs, as they may heal without intervention.[6] Unfortunately, symptom resolution

Figure 1. Coronal STIR (A) shows focal area of marrow edema in the medial central aspect of the junction of the left femoral neck and proximal shaft. Axial T1 (B) shows a nidus (arrow) involving the anterior cortex intertrochanteric region and marrow edema. Sagittal STIR (C) reveals mild edema overlying the osseous, cortically-based nidus (circle) with some local periosteal reaction and marrow edema.

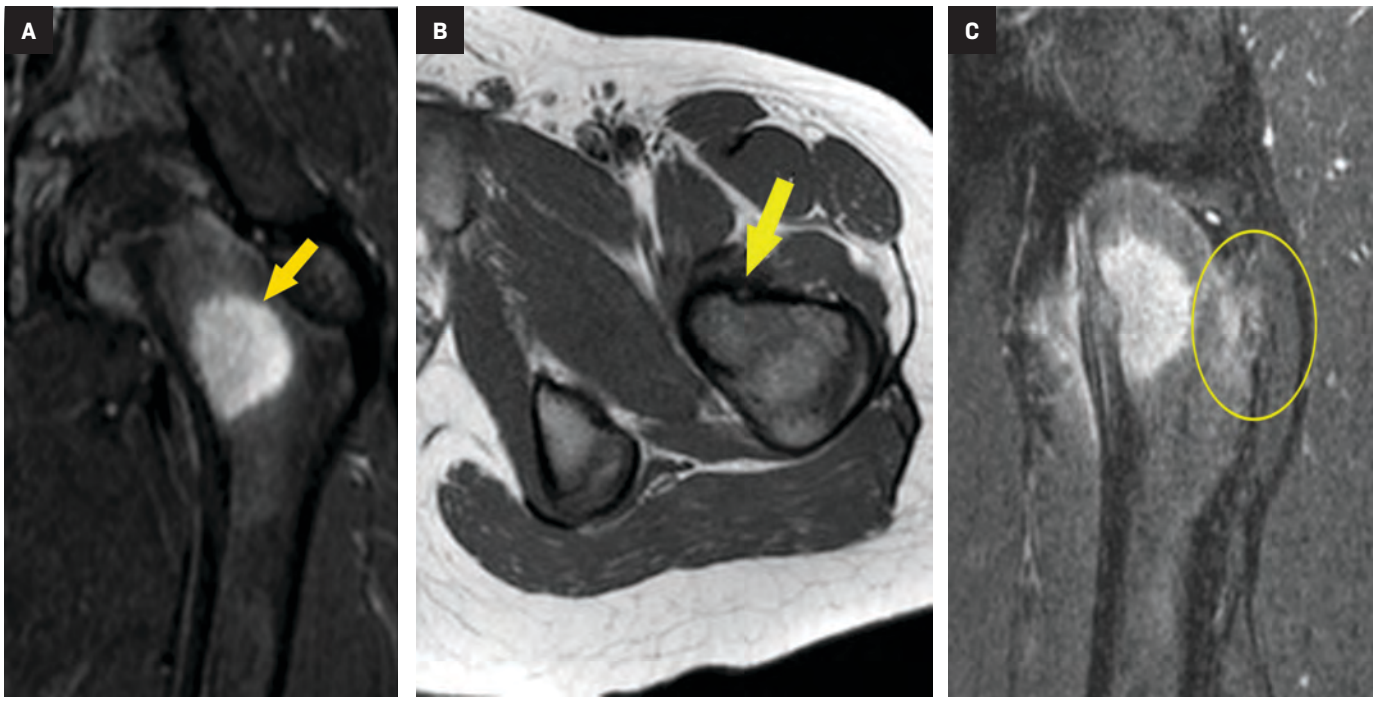
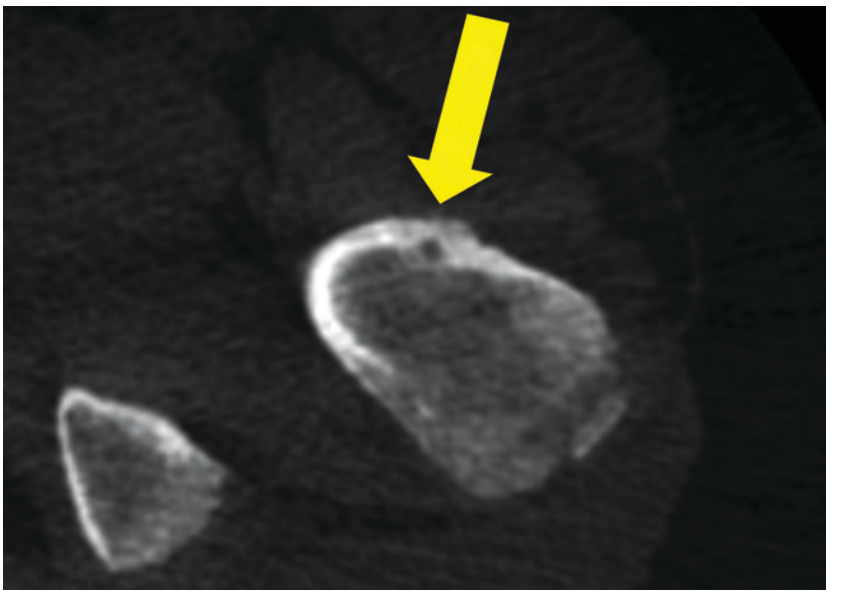


Figure 2. A lucent nidus in the anterior cortex of the left proximal femur (yellow arrow).



may take 2-3 years or longer, making this a rarely chosen and impractical approach.[6] Treatment should be considered in patients who do not respond to NSAIDs, who are at risk for renal and gastrointestinal complications of long-term NSAID use, and in skeletally immature patients due to risk of growth disturbance.[6,7] The goal of intervention is excising or destroying the entire nidus to cure the lesion and provide symptomatic relief.

Historically, open *en bloc* excision with cortical shaving and curettage of the nidus cavity was standard of treatment.[6,7] However, this approach comes with challenges in localizing the tumor, which may lead to incomplete removal and an increased risk of recurrence.[6,7] Additionally, resecting weight-bearing bone often necessitates instrumentation with fixation devices, casting, and longer periods of restriction on weight bearing and return to activities.[6,7]

Despite intraoperative CT guidance and/or nuclear imaging with

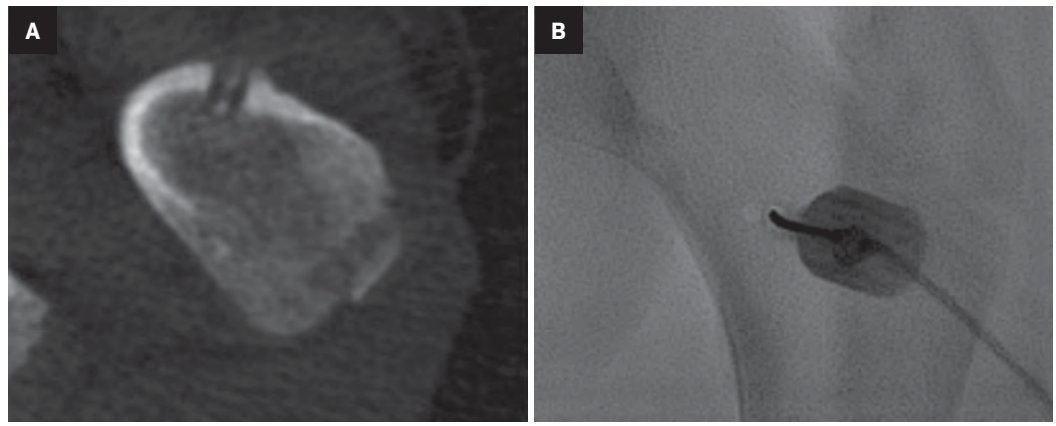


Figure 3. A precisely positioned cortical defect was created with image-guidance of a trephine (A) followed by a radiofrequency probe with a 7 mm active tip into and through the nidus (B). Radiofrequency ablation was performed for 6.5 minutes at 70°C. The OO was successfully treated.

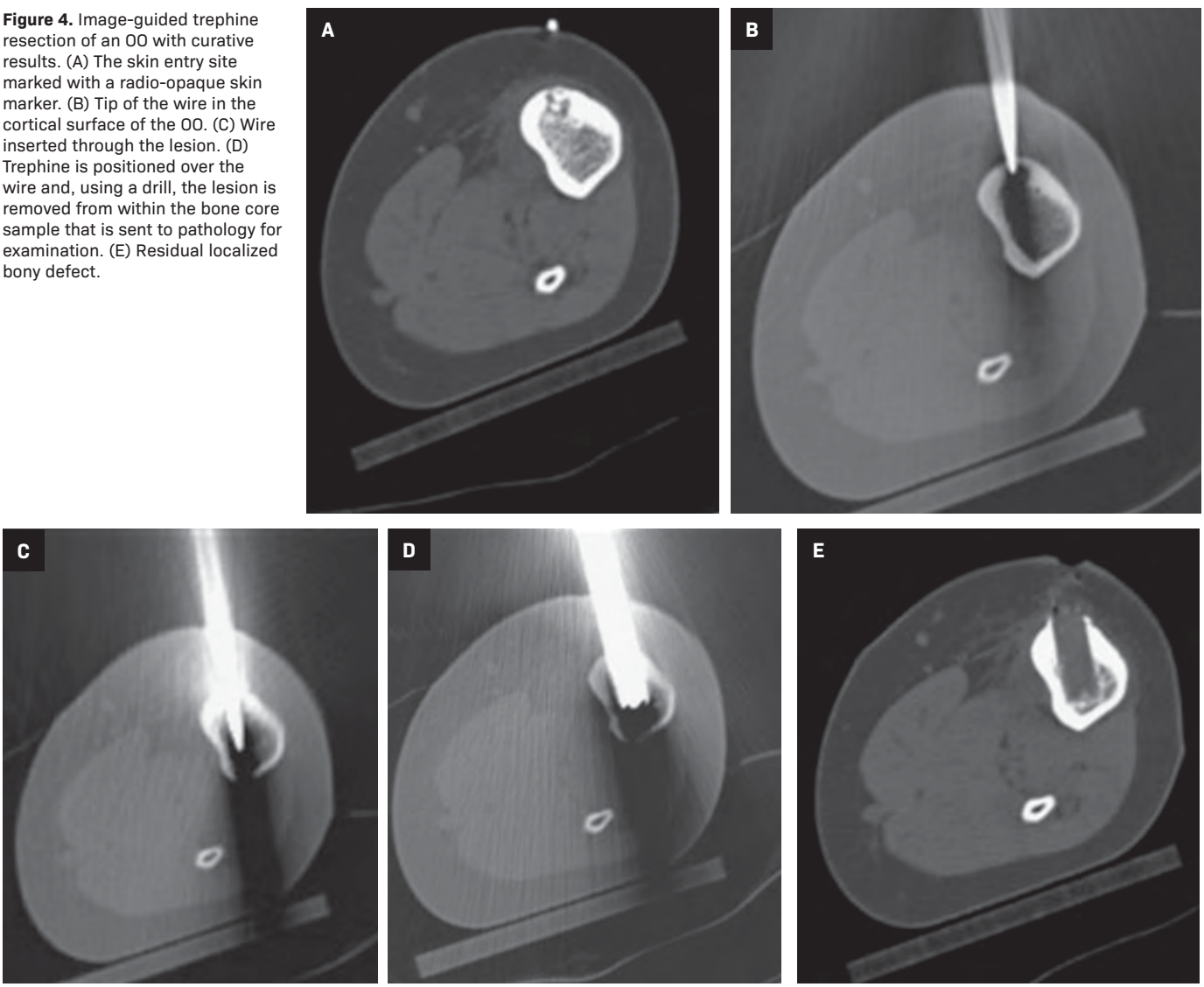


Figure 4. Image-guided trephine resection of an OO with curative results. (A) The skin entry site marked with a radio-opaque skin marker. (B) Tip of the wire in the cortical surface of the OO. (C) Wire inserted through the lesion. (D) Trephine is positioned over the wire and, using a drill, the lesion is removed from within the bone core sample that is sent to pathology for examination. (E) Residual localized bony defect.

radiotracers to guide open *en bloc* excision, minimally invasive procedures have become the mainstay of treatment. The image-guided approaches are more precise and have lower complication rates and recovery times. They are also less costly and usually can be performed on an outpatient basis.

Currently, the preferred minimally invasive approaches to treatment consist of CT-guided percutaneous excision, CT-guided radiofrequency ablation, and CT-guided cryoablation.

CT-guided Percutaneous Excision

In this method, a trephine or cannulated drill and a wire are used to excise the lesion under CT guidance.[7–9] This approach is highly precise and is correlated with a high clinical success rate and minimal complications (Figure 4).[7–9] This approach offers the benefit of a surgical specimen to confirm complete lesion removal. On rare occasions, a self-limiting nerve injury or infection may be associated with this approach. Fenichel, et al,[9] noted mild femoral neuropraxia in one patient after removal of a lesion from the acetabular roof. Towbin, et al,[8] noted sensory loss over the proximal thigh after removal of a lesion of the femoral neck.

In both instances, symptoms were self-limiting and resolved in less than 2 months.[8,9] This complication was also noted with CT-guided radiofrequency ablation.[10] Another consideration for this approach is the concern that excision of the nidus and surrounding cortex may predispose the patient to a pathological fracture. Fortunately, this occurs in less than 1% of cases.

CT-guided Radiofrequency Ablation

Computed tomography-guided radiofrequency ablation is the most commonly used technique to treat OO. In this procedure, a bone-cutting needle creates a defect in the adjacent cortex. A radiofrequency probe is then introduced into the lesion through a guide needle. The tip of the probe is heated to 70–90°C for 5-6 minutes.[7] This technique is associated with excellent pain relief, reduced operative morbidity, and low recurrence rates.[4] While tissue sampling can be performed with this technique, histologic diagnosis is less successful, occurring in less than 50% of cases, when compared to CT percutaneous excision, which removes the entire nidus.[7]

CT-guided Cryoablation

Computed tomography-guided cryoablation utilizes multiple freeze and thaw cycles at -40°C to induce tissue necrosis.[10] Lindquester, et al,[10] found the technique to have a success rate statistically similar to CT-guided radiofrequency ablation, with the added benefit of significantly less pain, a decreased need for post-operative analgesia, and faster patient discharge. As a newer technique, CT-guided cryoablation has a smaller body of evidence than CT-guided radiofrequency ablation.

Conclusion

Osteoid osteoma is a benign tumor that most commonly presents in the long bones of adolescent males. Diagnosis is based on clinical symptoms of night pain relieved by NSAIDs and the presence of round or oval radiolucent nidus on skeletal radiographs and/or CT. Treatment includes NSAIDs and removal of the lesion.

CT-guided ablation and CT-guided percutaneous excision have replaced open *en block* excision as treatments of choice owing to their superior precision, reduced complication rates, and shorter recovery time. Emerging research into CT-guided cryoablation shows the procedure has similar success rates as CT-guided radiofrequency ablation with decreased pain and faster recovery, factors that in time may lead it to be preferred over radiofrequency ablation.

References

1) Hakim DN, Pelly T, Kulendran M, Caris JA. Benign tumours of the bone: A review. *J Bone Oncol*. 2015;4(2):37-41. Published 2015 Mar 2. doi:10.1016/j.jbo.2015.02.001

2) Malghem J, Lecouvet F, Kirchgesner T, Acid S, Vande Berg B. Osteoid osteoma of the hip: imaging features. *Skeletal Radiol*. 2020;49(11):1709-1718.

3) Healey JH, Ghelman B. Osteoid osteoma and osteoblastoma. Current concepts and recent advances. *Clin Orthop Relat Res*. 1986 Mar;(204):76-85. PMID: 3956019.

4) Goldblum JR, Lamps LW, McKenney JK, Myers JL. *Rosai and Ackerman's Surgical Pathology E-Book*. 11th ed. Elsevier; 2017.

5) May CJ, Bixby SD, Anderson ME, et al. Osteoid osteoma about the hip in children and adolescents. *J Bone Joint Surg Am*. 2019;101(6):486-493. doi:10.2106/JBJS.18.00888

6) Noordin S, Allana S, Hilal K, et al. Osteoid osteoma: contemporary management. *Orthop Rev (Pavia)*. 2018;10(3):7496. Published 2018 Sep 25. doi:10.4081/or.2018.7496

7) Atesok KI, Alman BA, Schemitsch EH, Peyser A, Mankin H. Osteoid osteoma and osteoblastoma. *J Am Acad Orthop Surg*. 2011;19(11):678-689. doi:10.5435/00124635-201111000-00004

8) Towbin R, Kaye R, Meza MP, Pollock AN, Yaw K, Moreland M. Osteoid osteoma: percutaneous excision using a CT-guided coaxial technique. *AJR Am J Roentgenol*. 1995;164(4):945-949. doi:10.2214/ajr.164.4.7726054

9) Fenichel I, Garniack A, Morag B, Palti R, Salai M. Percutaneous CT-guided curettage of osteoid osteoma with histological confirmation: a retrospective study and review of the literature. *Int Orthop*. 2006;30(2):139-142. doi:10.1007/s00264-005-0051-1

10) Lindquester WS, Crowley J, Hawkins CM. Percutaneous thermal ablation for treatment of osteoid osteoma: a systematic review and analysis. *Skeletal Radiol*. 2020;49(9):1403-1411. doi:10.1007/s00256-020-03435-7

Sacrococcygeal Teratoma

JoAnn J Nam; Richard B Towbin, MD; Carrie M Schaefer, MD; Alexander J Towbin, MD

Case Summary

An infant with a prior history of urinary tract infections and negative renal ultrasound and voiding cystourethrogram presented for evaluation of sacral swelling.

Imaging Findings

Ultrasonography over the sacrum (Figure 1) revealed a cystic/solid presacral soft tissue mass. Lumbosacral spine radiograph demonstrated soft tissue density projecting over the sacrum and rectum with ill-defined, irregular cortices of the distal sacrum and coccyx (Figure 2). Pelvic contrast-enhanced magnetic resonance imaging (MRI) confirmed a 7 cm mass with a sacrococcygeal teratoma. It also showed spinal canal, sacral and lumbar vertebral-body involvement including L3 vertebral body height loss, (Figure 3).

Affiliations: University of Arizona College of Medicine-Phoenix (Ms Nam); Phoenix Children's Hospital (Drs R Towbin, Schaefer); Cincinnati Children's Hospital; Children's Hospital Medical Center, University of Cincinnati College of Medicine (Dr A Towbin).

Diagnosis

Sacrococcygeal teratoma (SCT).

The differential diagnosis includes SCT and congenital neural tube defects, such as an anterior sacral meningocele. In addition, one should consider benign lesions and malignant tumors. Benign lesions that could involve the pre-sacral region would include lymphatic malformations, dermoid cysts, and enteric cysts. Neoplastic pathologies including sacral chordomas, sacral schwannoma, neurofibroma, neuroblastomas, and rhabdomyosarcomas are considerations.

Discussion

A sacrococcygeal teratoma (SCT) is a germ cell tumor that is located close to the sacrum and coccyx. SCT arises from aberrant migration of primordial germ cells from the yolk sac to the gonads and accounts for approximately 3% of cancers in children <15 years of age.[1] SCTs are the most common extragonadal germ cell tumor (GCT) in young children. SCT is more common in girls than boys [4:1]. Most SCTs are benign but they may grow to a large size. If rapid tumor growth occurs in utero the associated high blood flow can result in heart failure and hydrops. Although the differential diagnosis for a sacral mass can include a neural tube defect, such as a myelocystocele or a myelomeningocele, SCTs are more likely to be presacral rather than dorsal to the sacrum, leading to mass effect such as bladder outlet obstruction, hydronephrosis, and rectal stenosis or atresia.[2]

GCTs can be divided into three main subtypes: mature, immature, and malignant. Malignant teratomas can be challenging to accurately diagnose as malignant components may be missed on histologic examination. Therefore, screening with beta-human chorionic gonadotropin or alpha-fetoprotein is important to assess for malignant components.[2] Specifically, SCTs are often described using the Altman Classification, which morphologically categorizes according to the extent to which SCT is external or internal, with Type 1 being primarily external and Type 4 being primarily internal. Type 1 and Type 2 SCTs are often detected with prenatal ultrasound, as the external component is more easily observed; Type 4 SCTs typically do not present

Figure 1. (A) Pelvic ultrasound shows a presacral soft tissue mass containing both solid and cystic components. (B) Doppler imaging shows increased blood flow to the mass

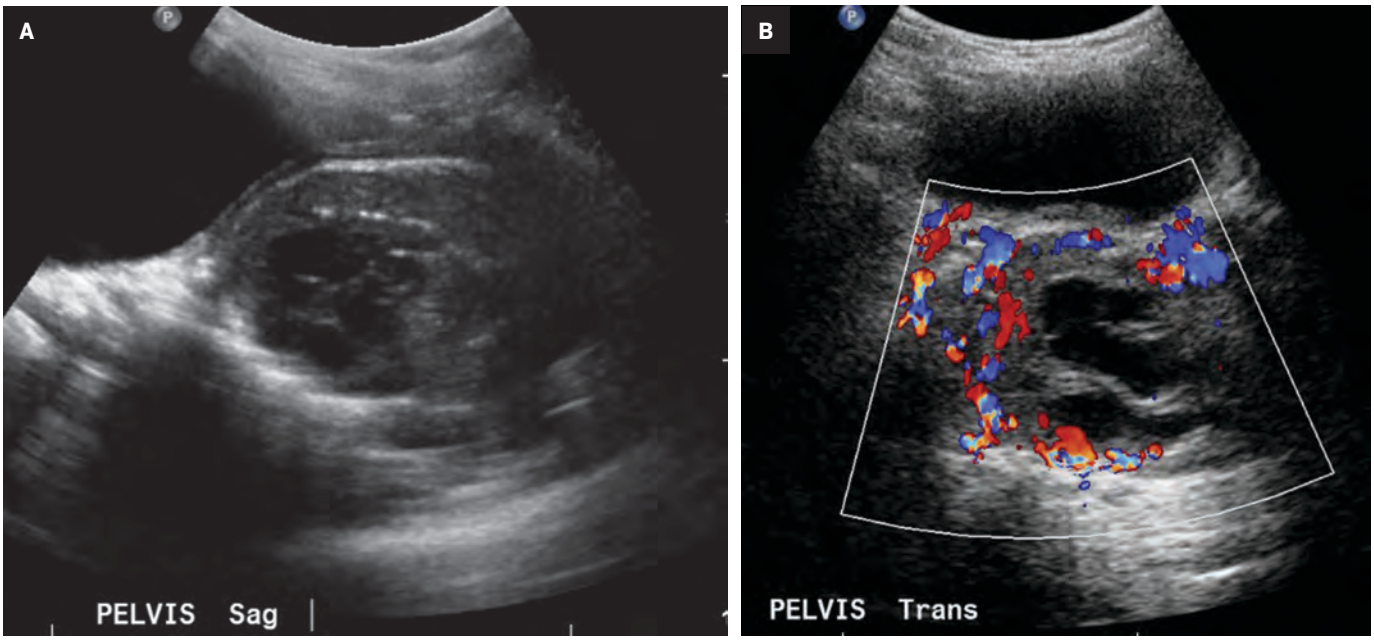
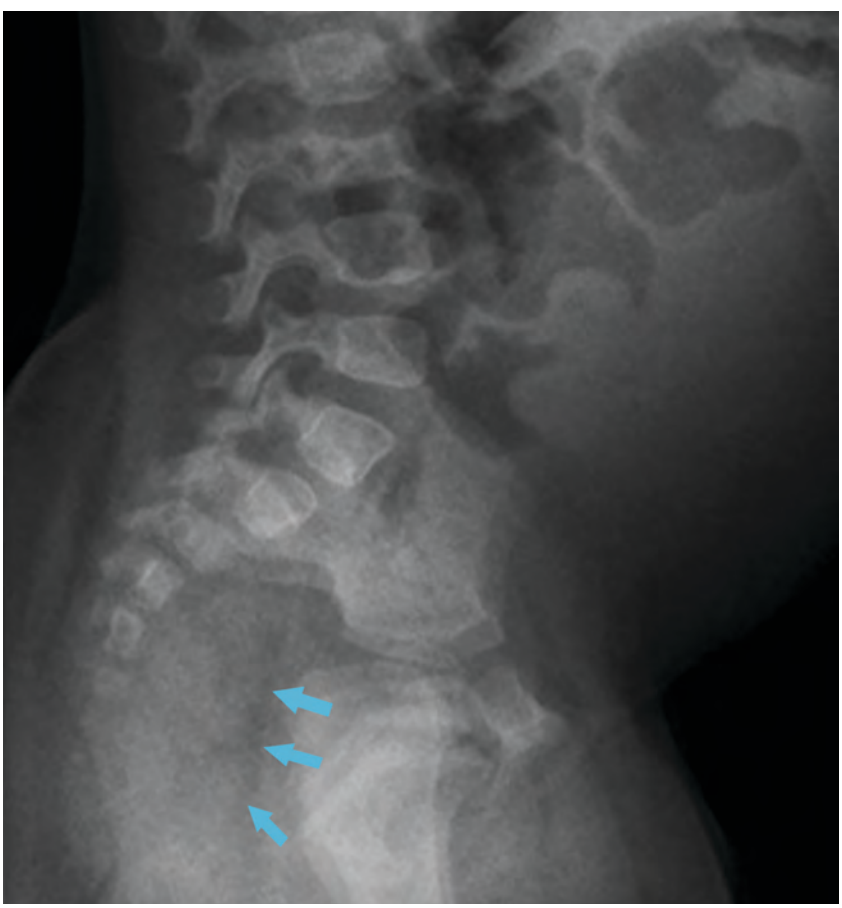


Figure 2. Lumbosacral spine computed radiography demonstrates soft tissue density projecting over the sacrum and rectum (blue arrows) with ill-defined, irregular cortices of the distal sacrum and coccyx.

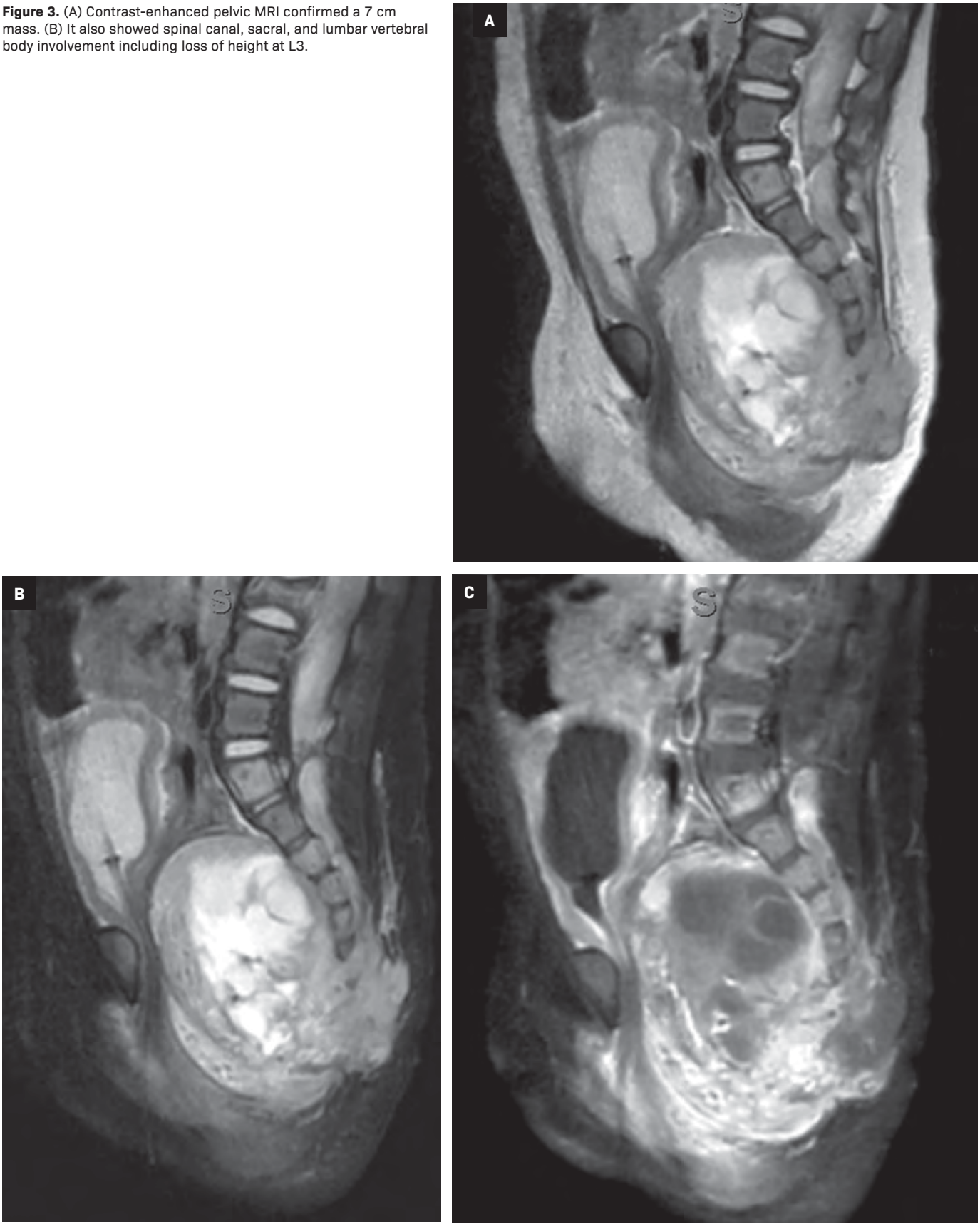


until infancy and early childhood. Type 4 SCTs are more commonly associated with malignant components.[3]

Sacrococcygeal teratomas frequently present in utero or early infancy and may be asymptomatic or can present with weakness, pain, paralysis, and/or symptoms related to bladder or rectal obstruction.[4] Approximately 32% of SCTs are diagnosed postnatally during the initial newborn assessment that occurs within the first 24 hours following birth.[5] However, SCTs are often diagnosed in utero by obstetrical ultrasound or fetal MRI.[5] Once identified, serial ultrasounds are performed with the primary goals of (1) identifying fetuses with a high risk of hydrops and (2) intervening as necessary.

Ultrasonography of mature SCTs can show anechoic regions, indicating cystic components of the tumor.[6] Ultrasonography, including color Doppler, of these tumors can also assess for tumor size, high-output cardiac states, and vascular steals, which are associated with increased risk for the progression to hydrops.[7] Prenatal monitoring also allows for the identification of positive prognostic factors, such as cystic tumor type and minimal or no abnormal vascularity, and poor prognostic factors, including

Figure 3. (A) Contrast-enhanced pelvic MRI confirmed a 7 cm mass. (B) It also showed spinal canal, sacral, and lumbar vertebral body involvement including loss of height at L3.



hydrops, large size, solid tumor with hypervascularity, and immaturity.[5, 8]

The treatment of SCTs diagnosed in utero often focuses on managing the tumor's effect on the cardiovascular system to decrease the risk of the development of hydrops and allow the fetus to mature appropriately. Fetal surgery, via laser or radiofrequency ablation, and minimally invasive surgery, may be indicated in certain high-risk cases of SCTs with poor prognostic factors for survival such as high-output cardiac failure and intra-lesional hemorrhage.[9, 10]

Postnatally, SCTs are evaluated with MRIs, the diagnostic procedure of choice. Radiography may demonstrate a calcified mass from the lower pelvic region and the impact of the mass effect and compression of adjacent structure such as colonic displacement, ureteric displacement, and dilatation, intraspinal extension, and metastasis.[6] MRI can show the full extent of the tumor and complications resulting from it, including colonic displacement, ureteric dilatation, intraspinal extension, and metastases.[5] Treatment often includes surgical resection. Complete removal of SCTs must include removal of the entire coccyx, but it may be difficult to achieve complete resection of SCTs because they lack capsular or pseudo-capsular components.

Treatment after delivery of a neonate with SCT is surgical resection. In some cases, multiple procedures may also be necessary to ensure complete resection of the tumor, especially in cases where malignant components of the tumor are detected.[11]

Following surgery, benign SCTs are often managed with observation. In contrast, malignant and/or metastatic SCTs often require adjuvant or neoadjuvant chemotherapy. Recurrence of SCTs can occur either locally or at distant sites, and management includes additional surgeries or chemotherapy depending on the pathology of the tumor. Survival rates of SCTs also differ based on histopathology. Mature, benign SCTs have a survival rate of approximately 98% compared to a 60% survival rate for immature, malignant SCTs.[5]

Conclusion

Sacrococcygeal teratomas are commonly diagnosed in utero using prenatal ultrasonography. High-risk lesions may be monitored with serial ultrasound so that surgical intervention can be performed in fetuses at high risk for hydrops and fetal demise. In neonates, SCTs often present with symptoms of weakness, pain, paralysis, and urologic and/or anorectal dysfunction. Treatment of SCTs typically involves postnatal surgical resection and chemotherapy in those with malignant changes.

References

1) Yadav DK, Acharya SK, Bagga D, Jain V, Dhua A, Goel P. Sacrococcygeal teratoma: clinical characteristics, management, and long-term outcomes in a prospective study from a tertiary care center. *J Indian Assoc Padiatr Surg*. 2020; 25:15-21

2) Yu JA, Sohaey R, Kennedy AM, Selden NR. Terminal myelocystocele and sacrococcygeal teratoma: a comparison of fetal ultrasound presentation and perinatal risk. *AJNR Am J Neuroradiol.* 2007; 28(6):1058-1060. https://doi.org/10.3174/ajnr.A0502.

3) Altman RP, Randolph JG, Lilly JR. Sacrococcygeal teratoma: American Academy of Pediatrics Surgical Section Survey-1973. *J Pediatr Surg.* 1974; 9(3):389-398. doi: 10.1016/s0022-3468(74)80297-6.

4) Mahour GH. Sacrococcygeal teratomas. *CA Cancer J Clin.* 1988; 38(6):362-367. https://doi.org/10.3322/canjclin.38.6.362.

5) Ayed A, Tonks AM, Lander A, Kilby MD. A review of pregnancies complicated by congenital sacrococcygeal teratoma in the West Midlands region over an 18-year period: population-based, cohort study. *Prenat Diagn.* 2015; 35(11):1037-1047. doi: 10.1002/pd.4641.

6) Smith D, Weerakkody Y. Sacrococcygeal teratoma. *Radiopaedia.* https://radiopaedia.org/articles/sacrococcygeal-teratoma?lang=us. Accessed May 15, 2020.

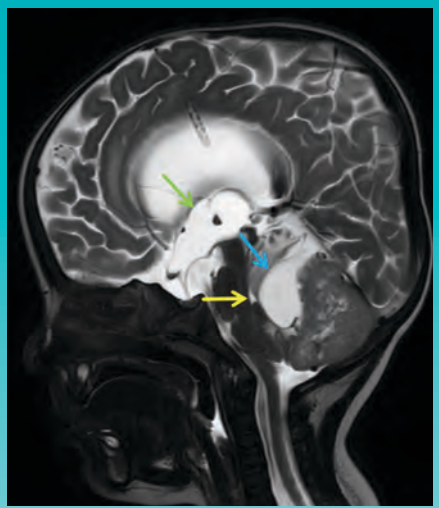
7) Flake AW. Fetal sacrococcygeal teratoma. *Semin Pediatr Surg.* 1993; 2(2):113-120. https://pubmed.ncbi.nlm.nih.gov/8062028/. Accessed May 3, 2020.

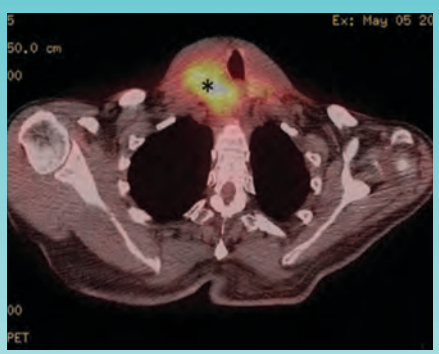
8) Benachi A, Durin L, Vasseur Maurer S, et al. Prenatally diagnosed sacrococcygeal teratoma: a prognostic classification. *J Pediatr Surg*. 2006; 41(9):1517-1521. doi: 10.1016/j.jpedsurg.2006.05.009.

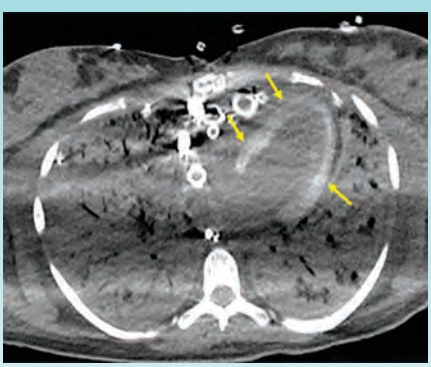
9) Lee MY, Won HS, Hyun MK, et al. Perinatal outcome of sacrococcygeal teratoma. *Prenat Diagn*. 2011; 31(13):1217-1221. doi: 10.1002/pd.2865.

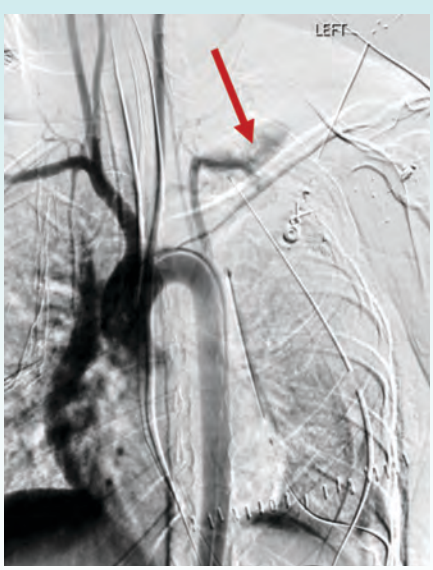
10) Van Mieghem T, Al-Ibrahim A, Deprest J, et al. Minimally invasive therapy for fetal sacrococcygeal teratoma: case series and systematic review of the literature. *Ultrasound Obstet Gynecol.* 2014; 43(6):611-609. doi: 10.1002/uog.13315.

11) Calaminus G, Schneider DT, Bökkerink JP, et al. Prognostic value of tumor size, metastases, extension into bone, and increased tumor marker in children with malignant sacrococcygeal germ cell tumors: a prospective evaluation of 71 patients treated in the German cooperative protocols Maligne Keimzelltumoren (MAKEI) 83/86 and MAKEI 89. *J Clin Oncol.* 2003; 21(5):781-786. doi: 10.1200/JCO.2003.03.125.









AppliedRadiology®

The Journal of Practical Medical Imaging and Management

Call for Cases

If you have an interesting case we want to know about it!

Sharing your case is a fantastic opportunity to gain recognition for your work and receive feedback from peers all over the world!

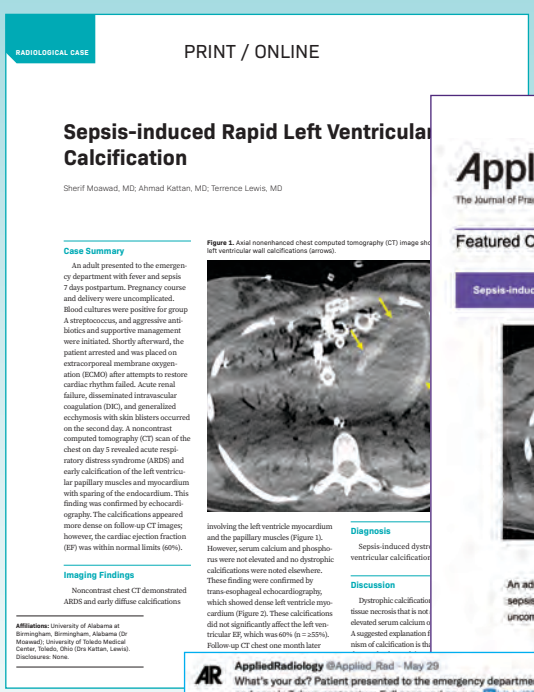
Author Guidelines* can be found at

https://appliedradiology.com/author-guidelines

- Abdominal
- Thoracic
- Genitourinary
- GI
- Emergency
- Interventional
- Vascular
- Peds
- Breast
- Neuro
- MSK
- Oncologic
- Cardiac
- Molecular Imaging
- Nuclear Medicine

* Cases undergo peer review before being accepted for publication.

PRINT / ONLINE


RADIOLOGICAL CASE

Sepsis-induced Rapid Left Ventricular Calcification

Sherif Moawad, MD; Ahmad Kattan, MD; Terrence Lewis, MD

Case Summary

An adult presented to the emergency department with fever and sepsis 7 days postpartum. Pregnancy course and delivery were uncomplicated. Blood cultures were positive for group A streptococcus, and aggressive antibiotics and supportive management were initiated. Shortly afterward, the patient arrested and was placed on extracorporeal membrane oxygenation (ECMO) after attempts to restore cardiac rhythm failed. Acute renal failure, disseminated intravascular coagulation (DIC), and generalized ecchymosis with skin blisters occurred on the second day. A noncontrast computed tomography (CT) scan of the chest on day 5 revealed acute respiratory distress syndrome (ARDS) and early calcification of the left ventricular papillary muscles and myocardium with sparing of the endocardium. This finding was confirmed by echocardiography. The calcifications appeared more dense on follow-up CT images; however, the cardiac ejection fraction (EF) was within normal limits (60%).

Imaging Findings

Noncontrast chest CT demonstrated ARDS and early diffuse calcifications involving the left ventricle myocardium and the papillary muscles (Figure 1). However, serum calcium and phosphorus were not elevated and no dystrophic calcifications were noted elsewhere. These finding were confirmed by trans-esophageal echocardiography, which showed dense left ventricle myocardium (Figure 2). These calcifications did not significantly affect the left ventricular EF, which was 60% (n = ≥55%). Follow-up CT chest one month later

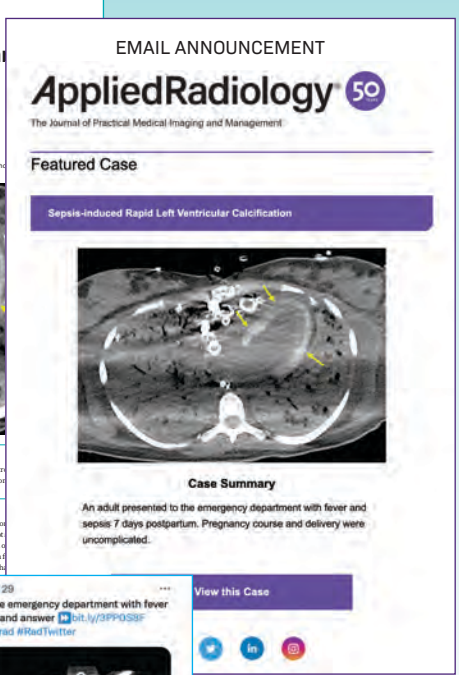
Figure 1. Axial nonenhanced chest computed tomography (CT) image sho left ventricular wall calcifications (arrows).

Diagnosis

Discussion

Affiliations: University of Alabama at Birmingham, Birmingham, Alabama (Dr Moawad); University of Toledo Medical Center, Toledo, Ohio (Drs Kattan, Lewis).
Disclosures: None.

EMAIL ANNOUNCEMENT


AppliedRadiology 50

The Journal of Practical Medical Imaging and Management

Featured Case

Sepsis-induced Rapid Left Ventricular Calcification

Case Summary

An adult presented to the emergency department with fever and sepsis 7 days postpartum. Pregnancy course and delivery were uncomplicated.

View this Case

SOCIAL MEDIA


AppliedRadiology @Applied_Rad · May 29

What's your dx? Patient presented to the emergency department with fever and sepsis 7 days postpartum Full case and answer bit.ly/3PP0S3F #radiology #RadRes #FOAMed #FOAMrad #RadTwitter

Think left and think right and think low and think high.
Oh, the thinks you can think of if only you try!
—Dr Seuss

I Am on the Right Side

C Douglas Phillips, MD, FACR

The whole idea of humans having two sides is a problem for radiologists.

From the outset, we look at everything backwards. Remember the mind-bending idea the first time you wrapped your cortex around that fact? It takes the first half of a radiology residency to figure out that right is left and left is right (except for 3D VR images, which are NOT. Figure that out.).

This leads to an eternal issue for radiologists: it is a miracle we can drive correctly on the right, and direct people to our house ("Take a left at the big tree---uh, no, that's a right at the big tree. Well, anyway, you'll know."). Those socks with R or L on them are just plain evil.

Consequently, we field hundreds of calls to fix the sides in a dictation. Most times, I just do it myself. I pull up the report and I find that I indeed was dictating the right side but called it left repeatedly. My bad.

Other times, I only pull the side error in the impression. Got it right everywhere else, but in the home stretch with the finish line in view, I threw a shoe. Reversed it. We have software built into the dictation system that's supposed to fix this potential cause of extended work hours, or at least call it to your attention. The software, unfortunately, is nearly worthless.

OK, though. When was the last time you disagreed with the referrer about the side of the pathology and **you** were right? You know what I mean. Request says one thing, findings say another. So, you do the obvious, natural thing (well, at least most of us do). You open the EMR and find out what the office note says. And, voila, the office note is wrong. Phone call inevitably results.

Them: *"Hi. Calling you about the findings on Billy Bob. You said it's left. That's incorrect. Symptoms and my notes say it was right. Could you addend that? I'm seeing them this afternoon."*

Me: *"Well, it is on the left on the study, and I did pull up your office notes. Indeed, you said right, so I pulled up the tech and nurse's notes from the imaging center. Both talked to the patient and said left."*

Them: *"No, that's wrong. It's the right. Like my office note. I'm looking at it now."*

Me: *"Well, it's **still** on the left on the study and I also pulled up the patient comment notes from their visit. They said they had a problem on the left. In fact, it's right here, 'My problem is my left ear.'*

Them: *"Impossible. Let me look at my office note again."*

Me: *"I also checked their audiogram. It was abnormal on the left."*

Them: *"(long pause) Let me get back to you. Click."*

I take that as a victory. They are few, but we cherish them. I know that for the next month, I will always be wrong, but I did pull this one out.

Keep doing that good work. Mahalo.

Dr Phillips is a Professor of Radiology, Director of Head and Neck Imaging, at Weill Cornell Medical College, NewYork-Presbyterian Hospital, New York, NY. He is a member of the *Applied Radiology* Editorial Advisory Board.

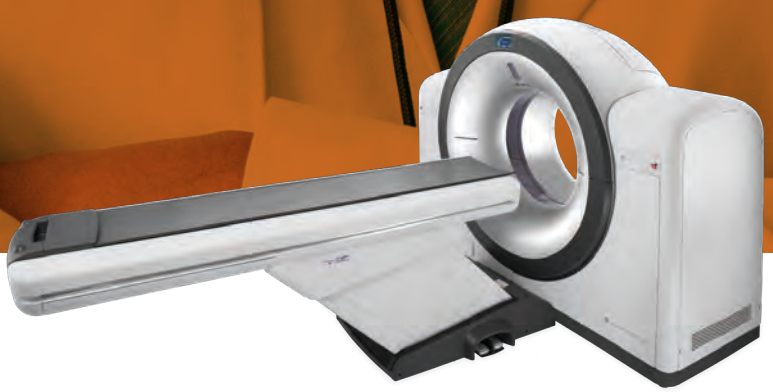
FUJIFILM
Value from Innovation

Visionary Performance.

For the Radiologist, a quick, confident diagnosis means everything to your patient.

Persona CT delivers fast, sharp images to facilitate confident decision-making.

Be visionary.



#VisionaryCT

Persona CT

In the business of Radiology, what does it take to thrive?

Find out at AHRA 2022
Bayer Booth 917

Bayer wants to help you thrive in the business of radiology. See how maximizing technology can help you do more in a challenging, ever-changing environment.

Refresh and refuel at the Bayer Booth 917:

- **Meet your VIP guide.**
- **Assess the needs of your organization.**
- **Fuel up with energizing snacks and solutions.**

And plan to attend the **Breast Magnetic Resonance Imaging (MRI) Current Practice** symposium with Christopher Comstock, MD*.

Start thriving with Bayer!

*This is a Bayer sponsored event. Dr. Comstock is a paid Bayer consultant and is compensated for this event.