September / October 2023
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Applied Radiology

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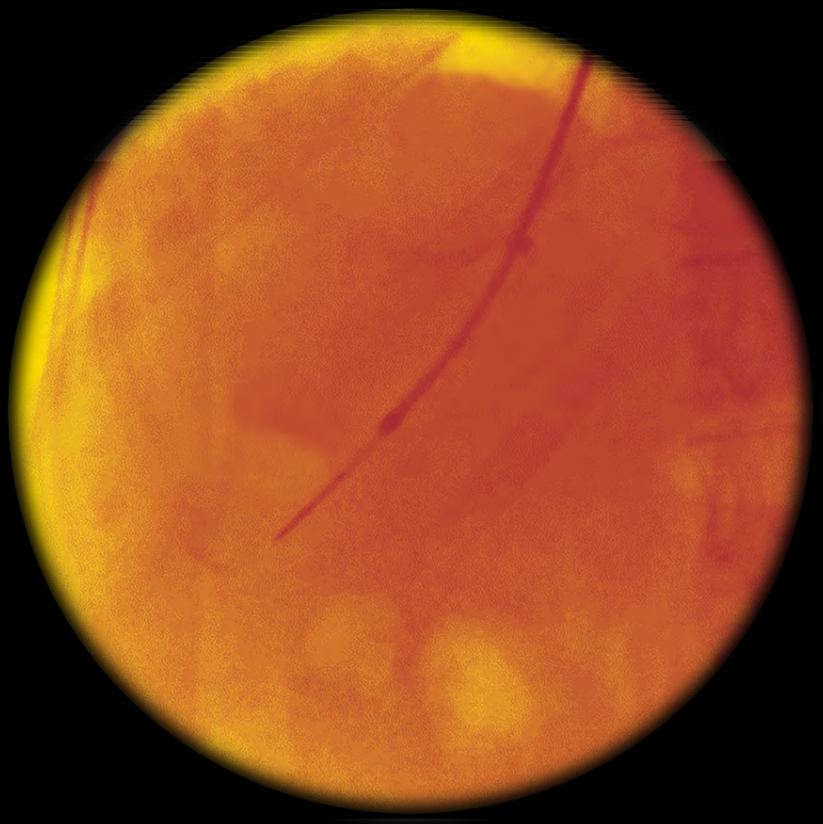
YEARS

The Journal of Practical Medical Imaging and Management

CME Percutaneous and Transvenous Liver Biopsy



Scope of Practice Legislation Across the US

Imaging and Treatment Opportunities in Alzheimer Disease

Subspecialty Teleradiology: Good or Bad for Medical Imaging?

Congenital Pulmonary Airway Malformation

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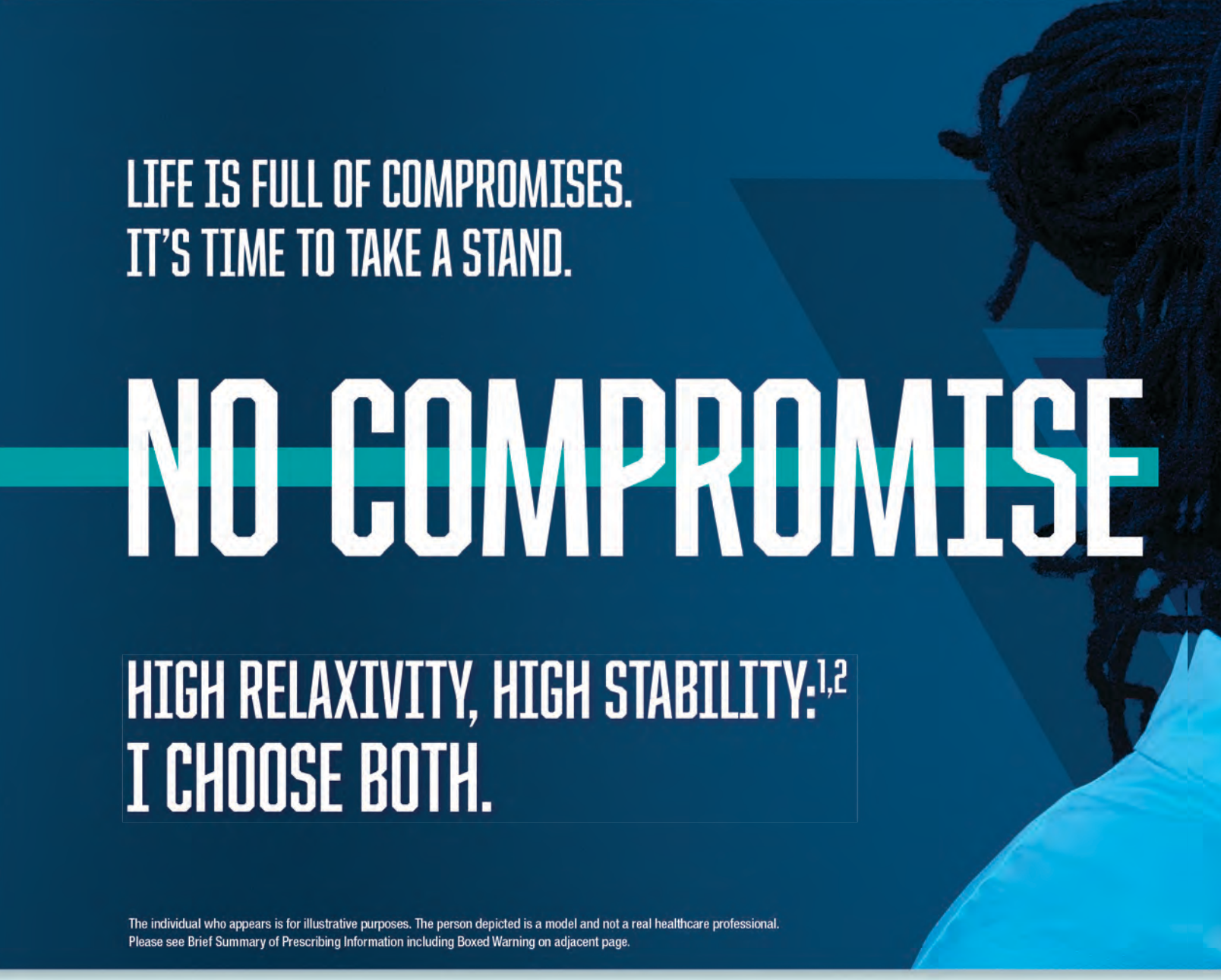

LIFE IS FULL OF COMPROMISES. IT'S TIME TO TAKE A STAND.

NO COMPROMISE

HIGH RELAXIVITY, HIGH STABILITY:[1,2] I CHOOSE BOTH.

The individual who appears is for illustrative purposes. The person depicted is a model and not a real healthcare professional.
Please see Brief Summary of Prescribing Information including Boxed Warning on adjacent page.

VUEWAY™ (gadopiclenol) solution for injection

Indications
VUEWAY injection is indicated in adults and children aged 2 years and older for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in:

- the central nervous system (brain, spine and surrounding tissues),
- the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

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 for NSF appears highest among patients with:**
  - **Chronic, severe kidney disease (GFR <30 mL/min/1.73 m^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, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended VUEWAY dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.**

Contraindications
VUEWAY injection is contraindicated in patients with history of hypersensitivity reactions to VUEWAY.

Warnings
Risk of **nephrogenic systemic fibrosis** is increased in patients using GBCA agents that have impaired elimination of the drugs, with the highest risk in patients chronic, severe kidney disease as well as patients with acute kidney injury. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities.

Hypersensitivity reactions, including serious hypersensitivity reactions, could occur during use or shortly following VUEWAY administration. Assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders, administer VUEWAY only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, and observe patients for signs and symptoms of hypersensitivity reactions after administration.

INTRODUCING

Vueway™
(gadopiclenol) injection
485.1 mg/mL

HALF THE GADOLINIUM DOSE COMPARED TO OTHER MACROCYCLIC GBCAS IN APPROVED INDICATIONS.[1,3-6] FROM BRACCO, YOUR TRUSTED PARTNER IN MRI.

BRACCO
LIFE FROM INSIDE

Gadolinium retention can be for months or years in several organs after administration. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (brain, skin, kidney, liver and spleen). Minimize repetitive GBCA imaging studies, particularly closely spaced studies, when possible.

Acute kidney injury requiring dialysis has occurred with the use of GBCAs in patients with chronically reduced renal function. The risk of acute kidney injury may increase with increasing dose of the contrast agent.

Ensure catheter and venous patency before injecting as **extravasation** may occur, and cause tissue irritation.

VUEWAY may **impair the visualization of lesions** seen on non-contrast MRI. Therefore, caution should be exercised when Vueway MRI scans are interpreted without a companion non-contrast MRI scan.

The most common adverse reactions (incidence ≥ 0.5%) are injection site pain (0.7%), and headache (0.7%).

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.

Please see BRIEF SUMMARY of Prescribing Information for VUEWAY, including BOXED WARNING on Nephrogenic Systemic Fibrosis.

Manufactured for Bracco Diagnostics Inc. by Liebel-Flarsheim Company LLC - Raleigh, NC, USA 27616.

VUEWAY is a trademark of Bracco Imaging S.p.A.

References: 1. Vueway™ (gadopiclenol) Injection Full Prescribing Information. Monroe Twp., NJ: Bracco Diagnostics Inc.; September 2022. **2.** Robic C, Port M, Rousseaux O, et al. Physicochemical and Pharmacokinetic Profiles of Gadopiclenol: A New Macrocyclic Gadolinium Chelate With High T1 Relaxivity. *Invest Radiol.* 2019 Aug;54: 475–484. **3.** GADAVIST® (gadobutrol) Injection. Full Prescribing Information. Bayer HealthCare Pharmaceuticals Inc. Whippany, NJ; April 2022. **4.** DOTAREM® (gadoterate meglumine) Injection. Full Prescribing Information. Guerbet LLC. Princeton, NJ; April 2022. **5.** CLARISCAN™ (gadoterate meglumine) injection for intravenous use. Full Prescribing Information. GE Healthcare. Marlborough, MA; February 2020. **6.** ProHance® (Gadoteridol) Injection. Full Prescribing Information and Patient Medication Guide. Monroe Twp., NJ: Bracco Diagnostics Inc.; December 2020.

VISIT VUEWAY.COM FOR MORE INFORMATION

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Bracco Diagnostics Inc.

Vueway™

(gadopiclenol) injection, for intravenous use

BRIEF SUMMARY: Please see package insert of 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/1.73 m²), 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, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.**
- **For patients at highest risk for NSF, do not exceed the recommended Vueway 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) in the full Prescribing Information]*.**

INDICATIONS AND USAGE

Vueway™ (gadopiclenol) is a gadolinium-based contrast agent indicated in adult and pediatric patients aged 2 years and older for use with magnetic resonance imaging (MRI) to detect and visualize lesions with abnormal vascularity in:

- the central nervous system (brain, spine, and associated tissues),
- the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system).

CONTRAINDICATIONS

Vueway is contraindicated in patients with history of hypersensitivity reactions to gadopiclenol.

WARNINGS AND PRECAUTIONS

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/1.73 m²) as well as patients with acute kidney injury. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30-59 mL/min/1.73 m²) and little, if any, for patients with chronic, mild kidney disease (GFR 60-89 mL/min/1.73 m²). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle, and internal organs. Report any diagnosis of NSF following Vueway administration to Bracco Diagnostics Inc. (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 Vueway 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 *[see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3) in the full Prescribing Information]*. The usefulness of hemodialysis in the prevention of NSF is unknown.

Hypersensitivity Reactions With GBCAs, serious hypersensitivity reactions have occurred. In most cases, initial symptoms occurred within minutes of GBCA administration and resolved with prompt emergency treatment.

- Before Vueway 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 Vueway.
- Vueway is contraindicated in patients with history of hypersensitivity reactions to Vueway *[see Contraindications (4) in the full Prescribing Information]*.
- Administer Vueway only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.
- During and following Vueway administration, observe patients for signs and symptoms of hypersensitivity reactions.

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 gadodiamide causing greater retention than other linear agents such as gadoxetate disodium, and gadobenate dimeglumine. Retention is lowest and similar among the macrocyclic GBCAs such as gadoterate meglumine, gadobutrol, gadoteridol, and gadopiclenol.

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) in the full Prescribing Information]*. 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.

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.

Acute Kidney Injury In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent. Do not exceed the recommended dose.

Extravasation and Injection Site Reactions Injection site reactions such as injection site pain have been reported in the clinical studies with Vueway *[see Adverse Reactions (6.1) in the full Prescribing Information]*. Extravasation during Vueway administration may result in tissue irritation *[see Nonclinical Toxicology (13.2) in the full Prescribing Information]*. Ensure catheter and venous patency before the injection of Vueway.

Interference with Visualization of Lesions Visible with Non-Contrast MRI As with any GBCA, Vueway may impair the visualization of lesions seen on non-contrast MRI. Therefore, caution should be exercised when Vueway MRI scans are interpreted without a companion non-contrast MRI scan.

ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in labeling:

- Nephrogenic Systemic Fibrosis *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Hypersensitivity Reactions *[see Contraindications (4) and Warnings and Precautions (5.2) in the full Prescribing Information]*

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 safety of Vueway was evaluated in 1,047 patients who received Vueway at doses ranging from 0.025 mmol/kg (one half the recommended dose) to 0.3 mmol/kg (six times the recommended dose). A total of 708 patients received the recommended dose of 0.05 mmol/kg. Among patients who received the recommended dose, the average age was 51 years (range 2 years to 88 years) and 56% were female. The ethnic distribution was 79% White, 10% Asian, 7% American Indian or Alaska native, 2% Black, and 2% patients of other or unspecified ethnic groups.

Overall, approximately 4.7% of subjects receiving the labeled dose reported one or more adverse reactions.

Table 1 lists adverse reactions that occurred in >0.2% of patients who received 0.05 mmol/kg Vueway.

TABLE 1. ADVERSE REACTIONS REPORTED IN >0.2% OF PATIENTS RECEIVING VUEWAY IN CLINICAL TRIALS

Adverse Reaction	Vueway 0.05 mmol/kg (n=708) (%)
Injection site pain	0.7
Headache	0.7
Nausea	0.4
Injection site warmth	0.4
Injection site coldness	0.3
Dizziness	0.3
Local swelling	0.3

Adverse reactions that occurred with a frequency ≤ 0.2% in patients who received 0.05 mmol/kg Vueway included: maculopapular rash, vomiting, worsened renal impairment, feeling hot, pyrexia, oral paresthesia, dysgeusia, diarrhea, pruritus, allergic dermatitis, erythema, injection site paresthesia, Cystatin C increase, and blood creatinine increase.

Adverse Reactions in Pediatric Patients

One study with a single dose of Vueway (0.05 mmol/kg) was conducted in 80 pediatric patients aged 2 years to 17 years, including 60 patients who underwent a central nervous system (CNS) MRI and 20 patients who underwent a body MRI. One adverse reaction (maculopapular rash of moderate severity) in one patient (1.3%) was reported in the CNS cohort.

USE IN SPECIFIC POPULATIONS

Pregnancy Risk Summary There are no available data on Vueway use in pregnant women to evaluate for a drug-associated risk of major birth defects, miscarriage or other adverse maternal or fetal outcomes. GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. The available human data on GBCA exposure during pregnancy and adverse fetal outcomes are limited and inconclusive *(see Data)*. In animal reproduction studies, there were no adverse developmental effects observed in rats or rabbits with intravenous administration of Vueway during organogenesis *(see Data)*. Because of the potential risks of gadolinium to the fetus, use Vueway 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(s) are 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 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: Animal reproduction studies conducted with gadopiclenol showed some signs of maternal toxicity in rats at 10 mmol/kg and rabbits at 5 mmol/kg (corresponding to 52 times and 57 times the recommended human dose, respectively). This maternal toxicity was characterized in both species by swelling, decreased activity, and lower gestation weight gain and food consumption.

No effect on embryo-fetal development was observed in rats at 10 mmol/kg (corresponding to 52 times the recommended human dose). In rabbits, a lower mean fetal body weight was observed at 5 mmol/kg (corresponding to 57 times the recommended human dose) and this was attributed as a consequence of the lower gestation weight gain.

Lactation Risk Summary There are no data on the presence of gadopiclenol 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 excreted in breast milk. Additionally, there is limited GBCA gastrointestinal absorption in the breast-fed infant. Gadopiclenol is present in rat milk. When a drug is present in animal milk, it is likely that the drug will be present in human milk *(see Data)*. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Vueway and any potential adverse effects on the breastfed infant from Vueway or from the underlying maternal condition. Data In lactating rats receiving single intravenous injection of [^{153}Gd]-gadopiclenol, 0.3% and 0.2% of the total administered radioactivity was transferred to the pups via maternal milk at 6 hours and 24 hours after administration, respectively. Furthermore, in nursing rat pups, oral absorption of gadopiclenol was 3.6%.

Pediatric Use The safety and effectiveness of Vueway for use with MRI to detect and visualize lesions with abnormal vascularity in the CNS (brain, spine, and associated tissues), and the body (head and neck, thorax, abdomen, pelvis, and musculoskeletal system) have been established in pediatric patients aged 2 years and older.

Use of Vueway in this age group is supported by evidence from adequate and well-controlled studies in adults with additional pharmacokinetic and safety data from an open-label, uncontrolled, multicenter, single dose study of Vueway (0.05 mmol/kg) in 80 pediatric patients aged 2 to 17 years. The 80 patients consisted of 60 patients who underwent a CNS MRI and 20 patients who underwent a body MRI *[see Adverse Reactions (6.1) and Clinical Pharmacology (12.3) in the full Prescribing Information]*.

The safety and effectiveness of Vueway have not been established in pediatric patients younger than 2 years of age.

Geriatric Use Of the total number of Vueway-treated patients in clinical studies, 270 (26%) patients were 65 years of age and over, while 62 (6%) patients were 75 years of age and over. No overall differences in safety or efficacy were observed between these subjects and younger subjects.

This drug is known to be substantially excreted by the kidney, and the risk of adverse reactions to this drug may be greater in patients with impaired renal function. Because elderly patients are more likely to have decreased renal function, it may be useful to monitor renal function.

Renal Impairment In patients with renal impairment, the exposure of gadopiclenol is increased compared to patients with normal renal function. This may increase the risk of adverse reactions such as nephrogenic systemic fibrosis (NSF). Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. No dose adjustment of Vueway is recommended for patients with renal impairment. Vueway can be removed from the body by hemodialysis *[see Warnings and Precautions (5.1, 5.3, 5.4) and Clinical Pharmacology (12.3) in the full Prescribing Information]*.

OVERDOSAGE

Among subjects who received a single 0.3 mmol/kg intravenous dose of gadopiclenol (6 times the recommended dose of Vueway), headache and nausea were the most frequently reported adverse reactions. Gadopiclenol can be removed from the body by hemodialysis *[see Clinical Pharmacology (12.3) in the full Prescribing Information]*.

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

Nephrogenic Systemic Fibrosis Inform the patient that Vueway may increase the risk for NSF among patients with impaired elimination of the drugs and that NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs.

Instruct the patients to contact their physician if they develop signs or symptoms of NSF following Vueway 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 *[see Warnings and Precautions (5.1) in the full Prescribing Information]*.

Gadolinium Retention Advise patients that gadolinium is retained for months or years in brain, bone, skin, and other organs following Vueway administration even 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) in the full Prescribing Information]*.

Injection Site Reactions Inform the patient that Vueway may cause reactions along the venous injection site, such as mild and transient burning or pain or feeling of warmth or coldness at the injection site *[see Warnings and Precautions (5.5) in the full Prescribing Information]*.

Pregnancy Advise pregnant women of the potential risk of fetal exposure to Vueway *[see Use in Specific Populations (8.1) in the full Prescribing Information]*.

Rx only

US Patent No. 10,973,934

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EDITORIAL

Please Welcome the Next Generation

Erin Simon Schwartz, MD

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. Dr Schwartz can be reached at erin@appliedradiology.com.

In my January/February 2023 editorial, I put out a "Call for Service," asking for your help in supporting the Early Career Radiologist section, our new editorial board division being spearheaded by Associate Editor Yasha Parikh Gupta, MD.

To say we received an enthusiastic response to the call is nothing short of an understatement. Dr Gupta and I are extremely gratified that so many of you stepped up to volunteer your efforts. Through this department, we envision addressing the needs and concerns of a vitally important segment of the *Applied Radiology* readership.

So without further ado, please join us in congratulating the new members of our editorial advisory board:

Joshua H. Baker, DO/PhD Candidate
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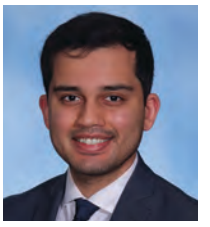
East Lansing, Michigan



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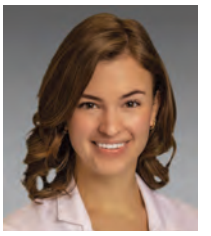

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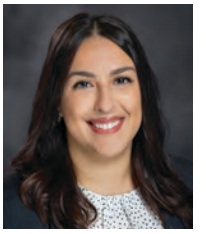

Kaitlin Zaki-Metias, MD
Chief Radiology Resident, Trinity Health Oakland Hospital/Wayne State University School of Medicine, Pontiac, Michigan

Dr Gupta and I look forward to working with all of these professionals and sharing the unique perspectives they will bring to you, our readers. After this group settles in, we will consider giving more of you the opportunity to join the team.

Once again, a heartfelt thank you to the many early career physicians and students who answered our call for service. We are grateful for your support.

Percutaneous and Transvenous Liver Biopsy

Description

Liver biopsy is an invaluable adjunct to laboratory findings in diagnosing and treating varioius liver diseases. However, the various methods of obtaining liver samples, their indications and contraindications, as well as the nuances and rationale behind choosing one method over another are not all well understood by interventional radiologists.

This activity is designed to explain different ways of performing liver biopsy and some other ancillary interventions to obtain liver tissue samples. We aim to explain the indications, contraindications, efficacy, patient selection, and potential complications associated with these procedures.

Learning Objectives

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

- Explain indications and contraindications of percutaneous liver biopsy.
- Explain indications and contraindications of transvenous liver biopsy.
- Describe the safety and efficacy of each approach.
- Describe potential complications associated with each approach and how to reduce them.

Target Audience

- Radiologists
- Related Imaging Professionals

Authors

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Affiliations: Anne Burnett Marion School of Medicine at TCU, Fort Worth, Texas (Mr Sterabadi); Division of Vascular and Interventional Radiology; Department of Radiology; University of Michigan Medical Center, Ann Arbor, Michigan (Drs Anbari, Khaja, Kapoor).

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Disclosures

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CME DETAILS ON PAGE 7

Percutaneous and Transvenous Liver Biopsy

Amir Hossein Mostafavi Sterabadi, BS; Hassan Anbari, MBChB; Minhaj S. Khaja, MD, MBA; Baljendra S. Kapoor, MD

Interventional radiology plays a key role in diagnosing, managing, and determining the prognosis of patients with liver pathology. Together with clinical and laboratory findings (aspartate or alanine aminotransferase, alkaline phosphatase), pathological evaluation following image-guided liver biopsy allows for histological characterization of disease.[1]

Indications for Liver Biopsy

Image-guided biopsy is useful in a number of ways with respect to diagnosing, treating, and managing patients with liver conditions. These include:

- Differentiating drug-related hepatotoxicity from autoimmune hepatitis in the absence of previous hepatotoxicity warnings.[2]
- Assisting in the diagnosis of hereditary conditions such as Wilson disease, A1-antitrypsin-1 deficiency, and hereditary hemochromatosis. In Wilson disease, a hepatic copper content > 250 µg/g has been reported as the best biochemical evidence for diagnosis;[3] hereditary hemochromatosis can be diagnosed based on iron distribution within the tissue.[4]
- Identifying drug-induced fibrosis secondary to treatment with methotrexate; pre- and post-treatment biopsies, as well as follow-up biopsies, are recommended for patients after each accumulated dose of 1.5 grams.[2]
- Grading and staging of non-alcoholic fatty liver disease (NAFLD), alcoholic liver disease, chronic hepatitis, and many other associated illnesses.[2] In chronic hepatitis C (or persistent hepatitis B) patients, biopsy results help to determine the need for antiviral therapy. It is also recommended that biopsies be acquired every two to three years for assessment of disease progression.[2] Based on recommendations by the American Association for the Study of Liver Disease (AASLD), the diagnostic and prognostic ability of liver biopsy for advanced fibrosis in patients with chronic hepatitis C infection cannot be achieved by noninvasive testing alone.[2]
- Staging for prognostic values and offering insight into physiological response to drug treatment and management regimens.[2]
- Assessing the acuity and degree of rejection In the setting of liver transplantation.[2,5]
- Identifying unexplained abnormalities of liver testing or hepatomegaly, hepatic neoplasms and lesions, infections, unexplained cholestasis, metabolic and genetic disorders, and fever of unknown origin.[2]

Percutaneous Liver Biopsy

Percutaneous liver biopsy (PLB) has been used to identify hepatic pathology since the first core biopsy was performed in 1880 by Paul Ehrlich in Germany and was adapted as a staple in histological liver diagnostics in 1957 by Menghini.[6,7] The technical aspects of PLB differ from that of transvenous liver biopsy (TVLB). In the setting of non-image-guided PLB, the area of maximum dullness can be identified by percussion over the right hemithorax between the sixth and ninth intercostal space.[8]

Image-guided PLB has largely replaced the non-image-guided PLB and is usually performed under ultrasound guidance. However, CT and other modalities are also implemented. Image-guided PLB helps to evaluate for the presence of overlying organs and vascular lesions at risk for bleeding, such as hepatic hemangioma (Figure 1).[8]

The potential complications associated with PLB range from pain and transient hypotension to intraperitoneal or intrahepatic hemorrhage,

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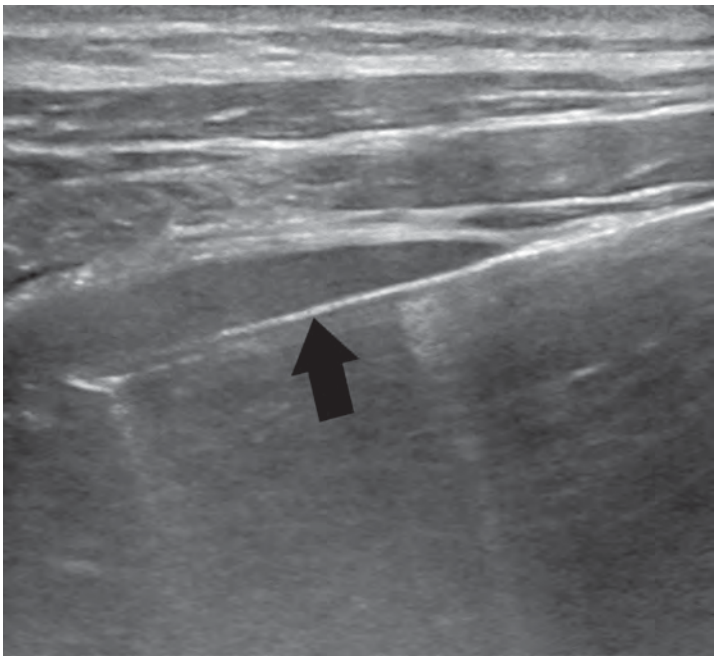

Figure 1. Ultrasound-guided PLB. Liver biopsy needle (black arrow) in liver parenchyma using a subcapsular approach to avoid large hepatic venous structures.

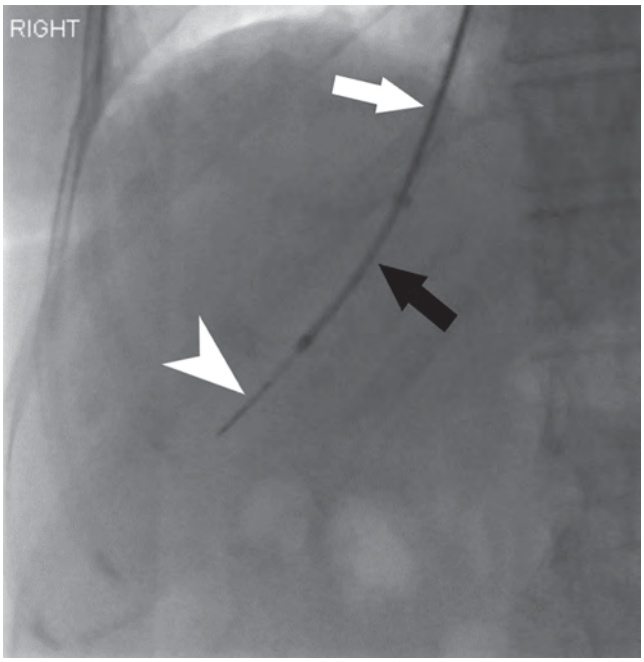

Figure 2. Fluoroscopic guidance for TJLB. Advancement of guiding sheath (white arrow) into the hepatic vein centrally. Cannula (black arrow) advanced peripherally within liver parenchyma contains biopsy needle (white arrowhead) for sampling.

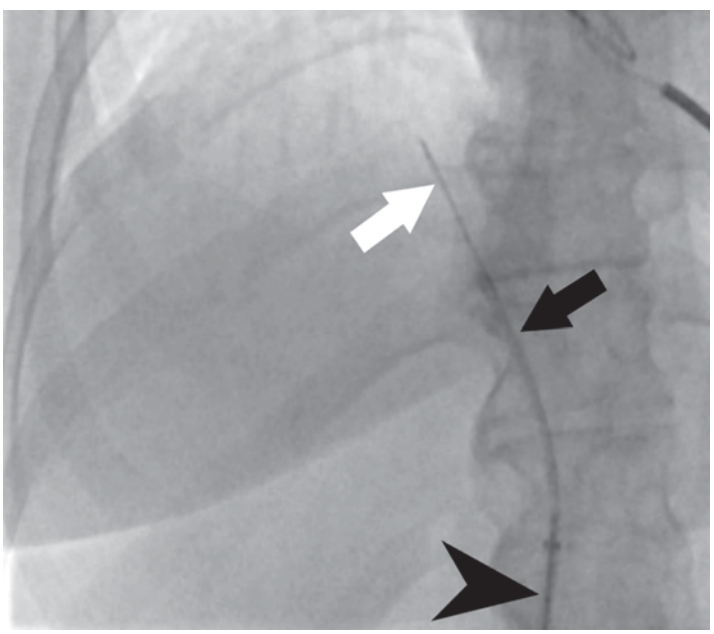

Figure 3. Fluoroscopic guidance for transvascular liver biopsy. Femoral access was utilized in this patient. Note the cranial trajectory of the 18G needle (white arrow) within the liver parenchyma, as advanced through the cannula system sitting at the hepatocaval confluence (black arrow), and guiding sheath situated within the inferior vena cava (black arrowhead).

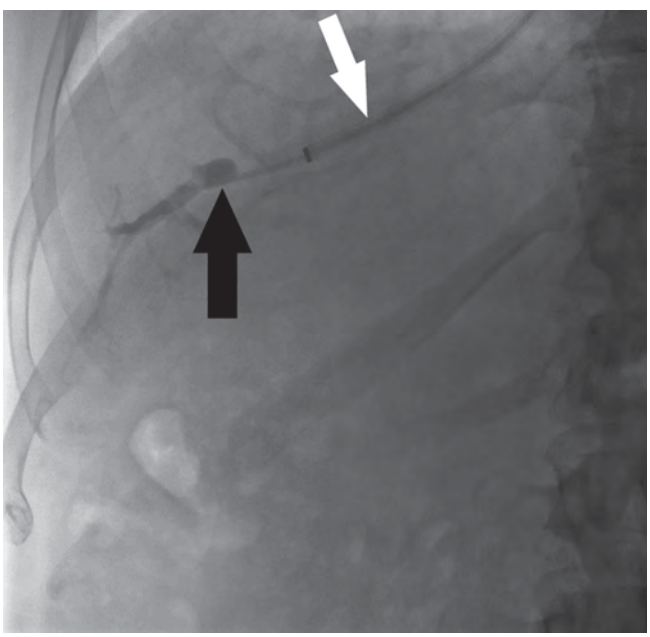

Figure 4. Fluoroscopic guidance for TJLB. Occlusion balloon (black arrow) insufflated within hepatic vein for wedged hepatic pressure measurement. Simultaneous measurement of free hepatic pressure can be performed with guiding sheath (white arrow).

hemothorax, colon or gallbladder perforation, and pneumothorax. Nevertheless, PLB remains the standard procedure for obtaining hepatic tissue specimens.[9]

Contraindications to Percutaneous Liver Biopsy

Contraindications to PLB include severe congenital and acquired coagulopathy, patient inability to cooperate with positioning and breath-holding, extrahepatic biliary obstruction, and local infection.[10] With respect to severe coagulopathy, multiple parameters must be considered when performing a PLB such as international normalized ratio (INR), prothrombin time (PT), platelet count, and nonsteroidal anti-inflammatory drug (NSAID) use. In the United States, standard PLB is often withheld in patients with a PT-INR above 1.8, according to Society of Interventional Radiology (SIR) guidelines, but current data reveals uncertainty with regard to the risk of bleeding in such situations. The AASLD position paper on liver biopsy concluded that there is "no specific PT-INR and/or platelet count cutoff at or above which potentially adverse bleeding can be reliably predicted".[10] Hence, the decision to perform liver biopsy in the setting of severe coagulopathy should be made cautiously and weighted according to the risks and benefits of the procedure.[10]

In addition, patients undergoing PLB must be able to hold their breath to avoid laceration of the liver or liver capsule and subsequent intrahepatic and/or intraperitoneal hemorrhage.[9] Extrahepatic biliary obstruction is a relative contraindication, owing to the risk of inadvertent bile leakage; previous studies have shown instances of biliary peritonitis, septicemia, and even patient death.[2,11] Use of NSAIDS within 3-5 days of PLB is considered a contraindication, owing to increased risk of bleeding.[2] PLB is also contraindicated in the setting of local infection within the pleural space, peritoneal cavity, or right lung, owing to the risk of seeding the liver, resulting in infectious hepatitis or hepatic abscess.[10]

Relative contraindications to PLB also include morbid obesity, ascites, amyloidosis, and hydatid cysts. Morbid obesity may result in acquisition of an ineffective biopsy specimen owing to the need for deeper needle navigation through subcutaneous fat and tissue to engage the liver. Massive ascites is an absolute contraindication in the utilization of PLB. There is uncertainty as to the increased risk of bleeding with ascites, but the absolute contraindication may stem from risk of inadequate sampling secondary to traversing the ascitic fluid to engage the liver for specimen acquisition.

Biopsies should be performed with caution in vascular tumors or hemangiomas based on the increased risk of bleeding with these tumors. This can be reduced by ensuring there is a healthy liver parenchymal tract towards the targeted lesion.[2]

Transvenous Liver Biopsy

Transvenous liver biopsy (TVLB) is an alternative to PLB and can be effective in patients with contraindications to PLB. Initially described by Dotter in 1964 and clinically performed for the first time by Hanafee in 1967, TVLB is often performed under ultrasound guidance through the right internal jugular vein (IJ), though left IJ and femoral vein access have also been described and practiced safely.[12] Following venous access, the right hepatic vein is typically targeted under fluoroscopic guidance.[12] Breath-holding can provide additional assistance in selecting the hepatic vein in IJ access, as it will increase the angle between the inferior vena cava and right hepatic vein to above 90°.[12] A sampling system such as TLAB (Argon Medical Devices, Plano, Texas), is then advanced over a wire within a guiding sheath to the desired location, ideally the central right hepatic vein, slightly peripheral to the expected location of liver hilum with the needle directed anteriorly (Figure 2). Peripheral puncture should be avoided, particularly in the small, cirrhotic liver, to prevent injuring the liver capsule. Rotational fluoroscopy will confirm the position within the hepatic vein. Middle hepatic vein access is an acceptable alternative, and the sampling direction is typically in a more neutral position in these cases. Operators should also note the differing trajectories, caudal versus cranial, when IJ or femoral access is used, respectively (Figure 3).

Indications for Transvenous Liver Biopsy

Many indications for TVLB result from contraindications to PLB; these include low PT levels, platelet counts below 50,000/mL, large volume ascites, and use of anticoagulants or antiplatelets that cannot be withheld.[12,13] Other indications for TVLB stem from the risk of bleeding associated with conditions such as amyloidosis, chronic renal insufficiency, and hereditary hemorrhagic telangiectasia, among others.[12-14] Another advantage to the transvenous approach is its ability to obtain other diagnostic values for assessing suspected portal hypertension. The intravascular catheter position allows for measuring hepatic vein, right atrium, inferior vena cava, and indirect portal pressures (wedge or precapillary pressure) as well as calculating the portosystemic gradient (Figure 4).[12]

Efficacy and Safety Parameters: Transjugular versus Percutaneous Liver Biopsy

Recently, a retrospective multicenter database review of adult patients undergoing PLB or TJLB sought to identify complication and readmission rates based on demographic and hepatic comorbidity matching.[15] The study found that

TJLB had a statistically significant lower rate of hematomas compared to that of PLB (0.20% versus 1.20% p= 0.049).[15] The same study also identified a higher rate of cardiac complications with the transjugular approach than with the percutaneous approach (0.40% vs. 0.00% p=0.045).[15]

A modification to standard PLB is the plugged liver biopsy. Plugged liver biopsy involves filling the biopsy needle track with fresh frozen plasma, fibrin sealant, cyanoacrylate glue, or gelatine sponge following removal of the initial coaxial introducer needle.[16] A 2010 comparative study of the effectiveness and safety of TJLB versus plugged-PLB (using Gelfoam pledgets) performed in patients with severe liver disease associated with ascites, impaired coagulation, or both found that technical success rates were 97.4% and 99.1% for TJLB and plugged-PLB, respectively.[17] TJLB was also shown to have a lower average length of core specimens (1.29 vs 1.43 cm) and lower average number of specimens obtained (2.44 vs 2.8) when compared to those of PLB. However, both methods yielded adequate and sufficient samples for disease diagnosis in that study.[17]

A 2017 study compared the efficacy of fibrosis staging using TJLB with that of PLB based on a prospective review of patients undergoing 18G TJLB or 16G PLB.[18] The subjective interpretation of sample adequacy found a statistically significant difference in the proportion of core fragmentation between TJLB and PLB (35.89% vs 21.67% p = 0.0462), but it also found that a four-core TJLB provided enough tissue volume to meet fibrosis-staging guidelines and approach the efficacy results of a 16G PLB.[18]

Conclusion

Transvenous and percutaneous approaches for liver biopsy are important procedures within the interventional radiologist's armamentarium. Transjugular liver biopsy provides adequate sampling as compared to that of PLB, with the latter often being considered the primary method for sampling liver tissue. In situations where contraindications exist for PLB, the transjugular approach provides an efficacious route for specimen acquisition in patients with advanced liver disease and hemostatic disorders.[15] Transvenous liver biopsy also offers utility in manometric evaluation of patients with suspected portal hypertension and for preoperative risk stratification. Interventional radiologists should be familiar with the technical aspects, risks, and benefits of these options.

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REVIEW

Scope of Practice Legislation Across the US: Current Trends in Evidence, Advocacy, and Action

Joshua H. Baker, MS; David Youmans, MD; Kurt Schoppe, MD; Andrew Moriarty, MD

Scope of practice (SoP) for nonphysician providers (NPPs) has long been the subject of controversy in the medical community. This includes radiology, as evidenced by the attention focused on the topic at the 2023 Centennial Meeting of the American College of Radiology (ACR).

An understanding of the issues and legislative challenges surrounding SoP is relevant to practicing radiologists and radiologists-in-training. This article aims to provide a foundational review of legislative challenges, relevant research, and other important considerations pertinent to SoP as it relates to radiology.

COVID-19 Puts a Spotlight on Scope of Practice

The severity and breadth of the COVID-19 pandemic created a sustained requirement for more care than could be achieved by the existing physician workforce. The responsibilities of many physicians moved beyond their areas of specialization to help address the needs of the most severely ill patients.

These extraordinary circumstances left many physician duties uncovered or put on pause; as a result, many NPPs assumed some of these responsibilities, in effect expanding their scope of practice, albeit temporarily.

But as the pandemic receded and most physicians returned to their "normal" practice, debate around permanent practice independence for advanced practice registered nurses (APRNs), physician assistants (PAs), and other NPPs gained momentum. For NPPs, the temporary adaptations to the global pandemic added fuel to their drive for greater practice autonomy, and legislative proposals for full practice authority increased.

According to the US Department of Health and Human Services, "nurse practitioners (NPs), clinical nurse specialists, and PAs are health care providers who practice either in collaboration with or under the supervision of a physician" and designates them as NPPs.[1]

The Balanced Budget Act of 1997 expanded reimbursement for NPP services from rural areas to all geographic and healthcare settings. As a result, nurse practitioners and clinical nurse specialists are allowed to bill Medicare directly, while PAs must continue to be billed by an employer.

With respect to education, PAs train in an accelerated format based on the traditional medical school curriculum. In contrast, APRNs receive a bachelor of science in nursing and a master's or doctorate degree in nursing practice in addition to specific clinical licensure in an area of practice such as anesthesia (eg, certified registered nurse anesthetist). These curricula focus on care delivery and patient-centered management as opposed to the basic and clinical science coursework covered in the medical school model.

The ACR defines non-physician radiology providers (NPRPs), which includes NPPs, and registered radiology assistants (RAs), and develops policies and guidelines regarding their scope of practice.[2] Radiology assistants are critical to many imaging practices and, by definition, work under the supervision of radiologists.[3] The two professions have historically worked hand-in-hand; it's worth noting that RAs are not seeking scope expansion.[4]

In the first half of 2023, the ACR identified 41 bills in 21 states related to increasing scope or full practice authority for PAs and 40 bills in 18 states for APRNs. Bills expanding SoP for PAs have been passed in four states: Arkansas, Arizona,

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Colorado, and Montana. To date, 26 states and the District of Columbia have assigned full practice authority rights to APRNs.

Legislative proposals addressing radiology, meanwhile, range from allowing NPRPs to order radiologic examinations to certifying PAs in fluoroscopy with 40 hours each of didactic and clinical training.

In addition, some state legislative proposals go beyond SoP issues to focus on shifting their entire oversight structure of radiology. In Tennessee, for example, SB 1191 and HB 1388 would eliminate the state Radiologic Imaging and Radiation Therapy Board of Examiners. In its place, the Tennessee Department of Health Division of Health-Related Boards would license all persons performing radiologic imaging, radiography, or radiation therapy procedures in any healthcare setting.

The original language of California's assembly bill 890 would have allowed NPPs to order, perform, and interpret diagnostic imaging scans. Fortunately, the ACR and the California Radiological Society joined forces to successfully get imaging interpretation excluded from the final bill. This effort highlights the power of advocacy to prevent SoP proposals harmful to radiology from getting passed into law. It also points up the vital importance for radiology practices to stay abreast of SoP legislation in their own state.

SoP Research is Mixed

Proponents of expanding NPP scope of practice argue that NPPs can improve access to healthcare in rural and underserved areas, while also saving the healthcare system in dollars and cents.

However, many medical organizations have raised concerns regarding the limited experience of NPPs, educational oversight, and potential unforeseen cost escalation of expanding NPP scope of practice. The ACR, for example, signed onto an American Medical Association letter opposing HR 2713, known as the "Improving Care and Access to Nurses Act."[5] This law would continue the trend of reducing or eliminating physician supervision of NPPs.

Allowing NPPs to practice to the top of their license arguably also does not universally achieve desired results; eg, expanding access to and improving the quality of healthcare in rural and underserved areas. A study of rural and nonrural primary care practices examining the utilization of NPs from 2008 to 2016 demonstrated only a modest difference between the two, with NPs constituting 25.2% and 23.0% of providers in rural and nonrural practices, respectively.[6]

At least two other studies, Barnes et al and Hughes et al, have shown that NPPs order more imaging than physicians following office-based evaluation and management (E&M) visits and in emergency department (ED) settings.[7,8] The authors of the Hughes study suggest that giving NPPs greater autonomy in radiology "may have ramifications on care and overall costs at the population level."

These cost control concerns are seemingly confirmed in a study comparing NP and physician productivity and outcomes in EDs in the Veterans Health Administration (VHA) system. The counterfactual analysis by the National Bureau of Economic Research comparing the current VHA environment of approximately 25% of patients being seen by NPs to the counterfactual of physician-only staffing found that VHA spending increased by an estimated $160 million due to higher resource utilization and adverse outcomes among patients.[9]

These trends are also reflected in other medical specialties where increasing NPP-led care has been

associated with increased opioid[10] and antibiotic[11] prescribing, lower-quality referrals,[12] and overutilization of biopsies.[13]

However, other studies comparing NPP care with physician-led care report improved outcomes with no difference in safety and costs.[14-16] These conflicting lines of evidence represent a scientific controversy and significant issue for radiology, especially considering that most state-level policymakers do not have a healthcare background, nor do they have the expertise to assess either the rigor of published literature or the impact of any given proposal on the healthcare system. This potential cognitive gap underscores the need for radiologists to educate and engage themselves on issues related to SoP legislation in their own state and beyond.

NPP utilization is increasing within radiology, as demonstrated by an increase of 16.3% in radiologist-employed NPP claims between 2017 and 2019. Most radiologist-employed NPPs are limited to performing interventional procedures, clinical E&M, and non-invasive imaging; only 3.6% perform imaging interpretation.[17] Despite this small percentage, a recent study demonstrated an association between less restrictive SoP regulations and higher levels of image interpretation by NPPs.[18] This shows that SoP legislation can have unintended consequences for radiology and our patients; professional advocacy is needed to shape legislation that brings about useful change without placing patients at risk.

Indeed, practices may realize significant cost savings by delegating common procedures, such as central venous access, thoracentesis, paracentesis, and percutaneous liver and kidney biopsies, to NPRPs so that interventional radiologists can handle more complex cases.[19] In addition, streamlining reimbursement for these procedures when performed by NPRPs would be one helpful direction for a legislative change instead of seeking a broader relaxation of SoP restrictions on NPRPs.

Exploring all avenues to increase patient access to and maintain the highest quality of care in radiology is essential. Recent research presents potential alternative solutions to the challenges of providing rural and other populations with greater access to healthcare and medical imaging. For example, a comparison of osteopathic and allopathic radiologist practice settings showed that osteopathic radiologists are more likely to practice in rural and disadvantaged communities compared to their allopathic colleagues.[20] Therefore, recruiting more osteopathic graduates to radiology may represent a viable strategy to improve access in areas of critical need, particularly given that DOs are a rapidly growing proportion of medical school graduates in the US.[21]

Technologies such as artificial intelligence are also streamlining radiology workflow and should continue to improve productivity and accuracy.[22] Bottom line: many options aside from expanding scope of access for NPPs are available to address costs, volume, access, and other current and future challenges.

Get Involved

The scope-of-practice legislative landscape is constantly changing. Individual radiologists and practices, national organizations like the ACR Radiology Advocacy Network, and state societies are all vital to making the profession's voice heard at the state and federal levels. The ACR has established a scope-of-practice fund that can supply state societies with financial support to lobby for (or against) scope-of-practice legislation.[23] The ACR also publishes a monthly e-newsletter, Advocacy in Action, that regularly updates on scope-of-practice legislation.[24]

Ultimately, safety is and should be the top priority for everyone in radiology. We owe it to ourselves and to our patients to be our own best advocates.

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Alzheimer Disease Imaging in the Era of Anti-Amyloid Treatment

Suzie Bash, MD, and Lawrence N. Tanenbaum, MD

The landscape of diagnostic evaluation and treatment of Alzheimer disease (AD) is rapidly changing. While there is still no cure for AD, recent developments are bringing increased hope to the millions of Americans suffering from this progressively debilitating condition. Here we offer an overview of recent regulatory, treatment, and imaging developments that promise to significantly impact AD patients, their families, their physicians, and neuroimaging specialists.

An estimated 6.7 million Americans suffer from AD, which doubles in prevalence every five years after the age of 65.[1,2] One in three seniors will die of dementia.[1] Since 2000, death from heart disease has decreased by 7%, but death from AD has increased by 145%.[1]

Conventional and quantitative brain MRI, as well as fluorodeoxyglucose (FDG), amyloid, and tau PET are utilized in the evaluation and clinical care pathway for dementia patients (Figures 1-4). With the recent emergence of disease-modifying therapies (DMT) for AD, neuroradiologists will play a critical role in the detection and characterization of treatment-related complications.

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Disclosures: Drs Bash and Tanenbaum are consultants to Icometrix and members of the Editorial Advisory Board of *Applied Radiology.*

New Regulatory Developments

In July 2023, the US Food and Drug Administration (FDA) approved Leqembi® (lecanemab), a monoclonal antibody (MAB) co-manufactured by Eisai and Biogen, for treatment of early-stage AD. This decision was the catalyst for the Centers for Medicare & Medicaid Services (CMS) to immediately affirm that the agency would cover the medication broadly. Even before this, the Veteran's Health Administration — the largest health system in the US — was already covering the drug.

This represents a pivotal step in the pathway to drug access for millions of Americans. While the current suggested retail price of lecanemab is high ($26,500 annually per patient), AD currently costs our nation upwards of $355 billion per year and this number is expected to increase to $1 trillion by 2050.[1,3] Medicare patients will only have to pay the standard 20% coinsurance of the drug cost once they meet their Part B deductible. Referrers must enter patients in a registry that requires completion of a short, easy-to-use data submission form. Other DMTs will soon follow, but at the present time, lecanemab is the only one granted traditional FDA approval. A predecessor drug, Aduhelm® (aducanumab), Biogen's predecessor drug, received accelerated FDA approval but is not covered by CMS outside of clinical trials.

Confirmation of beta-amyloid (Aβ) plaque is required prior to initiation of therapy. Amyloid PET is of paramount importance as an alternative to the more invasive lumbar puncture cerebrospinal fluid analysis for evidence of the protein. In July, CMS proposed rescinding the national non-coverage determination (NCD) restricting amyloid PET coverage, permitting individual Medicare administrative contractors to make coverage determinations. When and at what rate CMS will start reliably reimbursing for amyloid PET is unclear as of this writing.

It is important to note that lecanemab is approved only for patients with early-stage cognitive impairment, including mild cognitive impairment (MCI) due to AD or mild AD. Estimates are that approximately 1.5 million Americans will be candidates for on-label therapy.[1]

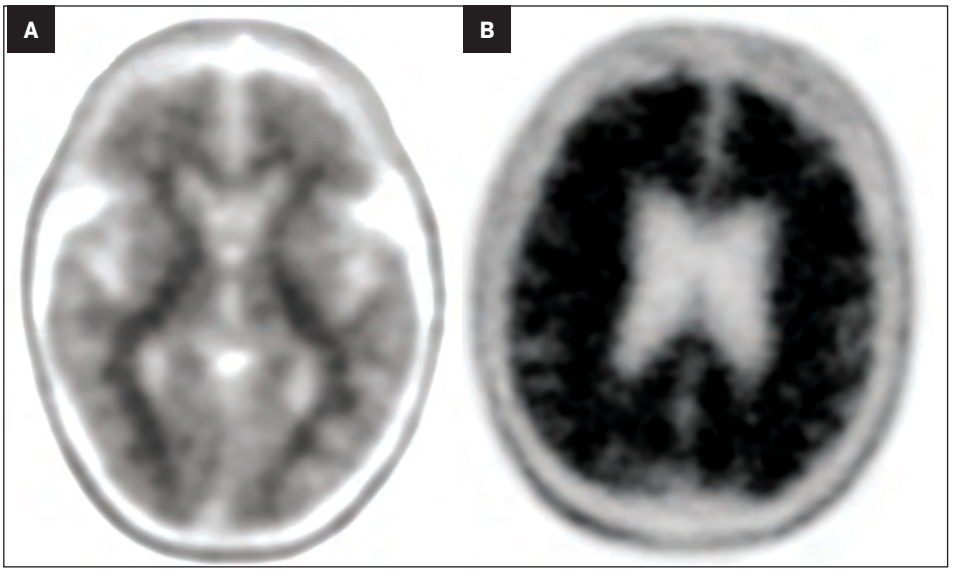


Figure 1. Amyloid PET. (A) Grayscale image of a negative amyloid PET in a patient with frontotemporal dementia, demonstrating the lack of binding of the amyloid tracer to the cortex, with preservation of gray-white matter differentiation. (B) For comparison, grayscale image of a positive amyloid PET in a patient with AD, demonstrating diffuse binding of the amyloid tracer throughout the cerebral cortex, with loss of gray-white matter differentiation.

Figure 2. Positive amyloid PET study demonstrating diffuse binding of the amyloid tracer to the Aβ plaque in the brain as demonstrated at the level of the frontal and parietal lobes. (A,B) Amyloid PET-CT fusion images; (C,D) Amyloid PET-MR fusion images (with axial T2 used for MR fusion).

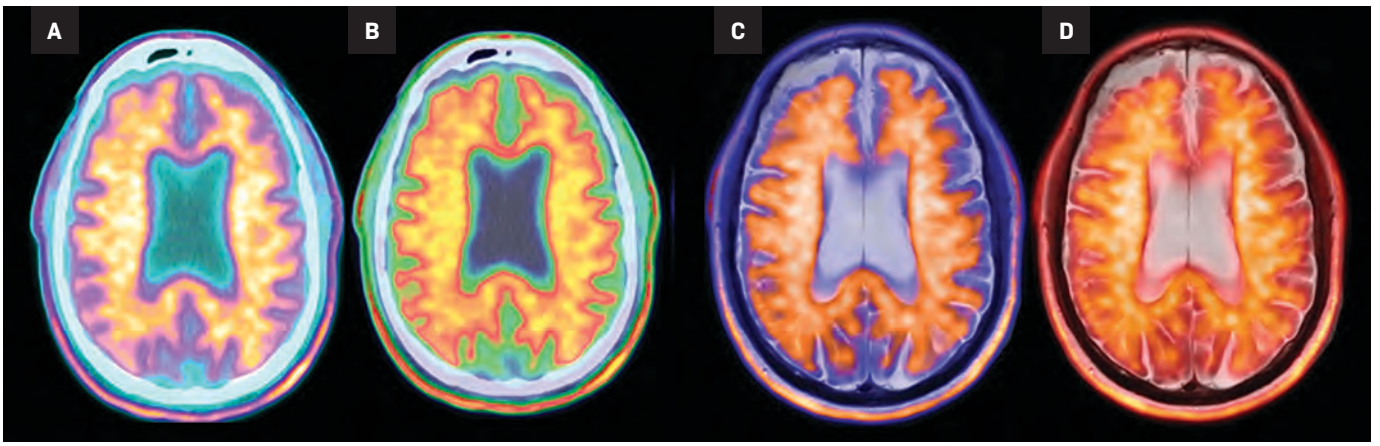


Figure 3. Positive FDG PET study demonstrating statistically significant cortical hypometabolism in the bilateral mesiotemporal lobes. (A,B) FDG PET-CT fusion images; (C,D) FDG PET-MR fusion images (with axial T2 used for MR fusion).

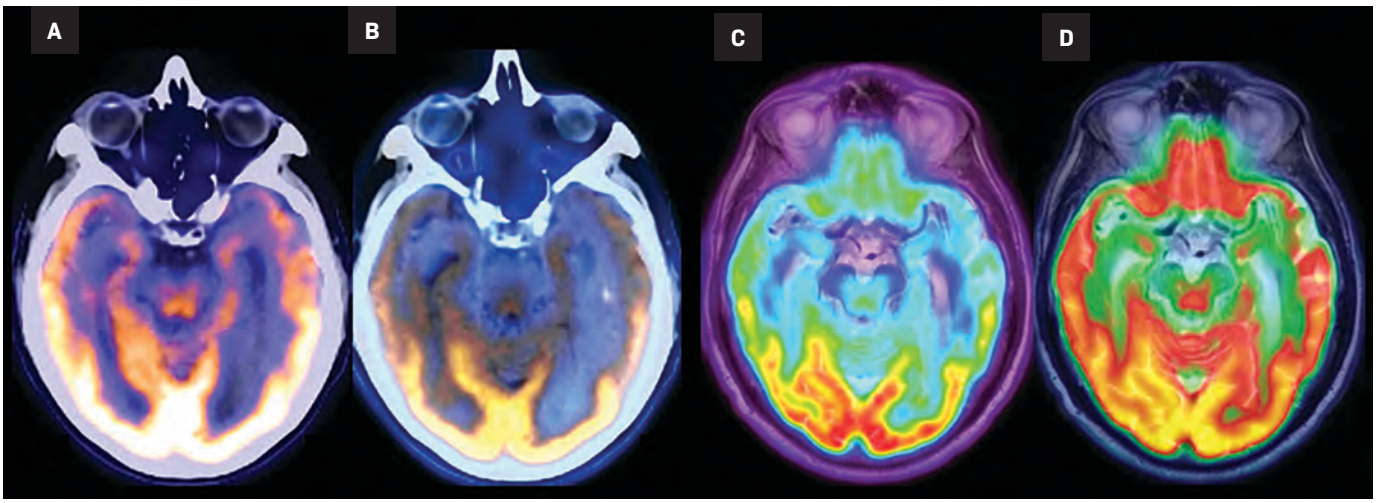


Figure 4. Positive amyloid PET study demonstrating diffuse binding of the amyloid tracer to the Aβ plaque in the cortex. Left (A,B) Amyloid PET-CT fusion images at the level of the temporal lobes; (C,D) Amyloid PET-MR fusion images at the level of the frontal and parietal lobes (with axial T2 used for MR fusion).

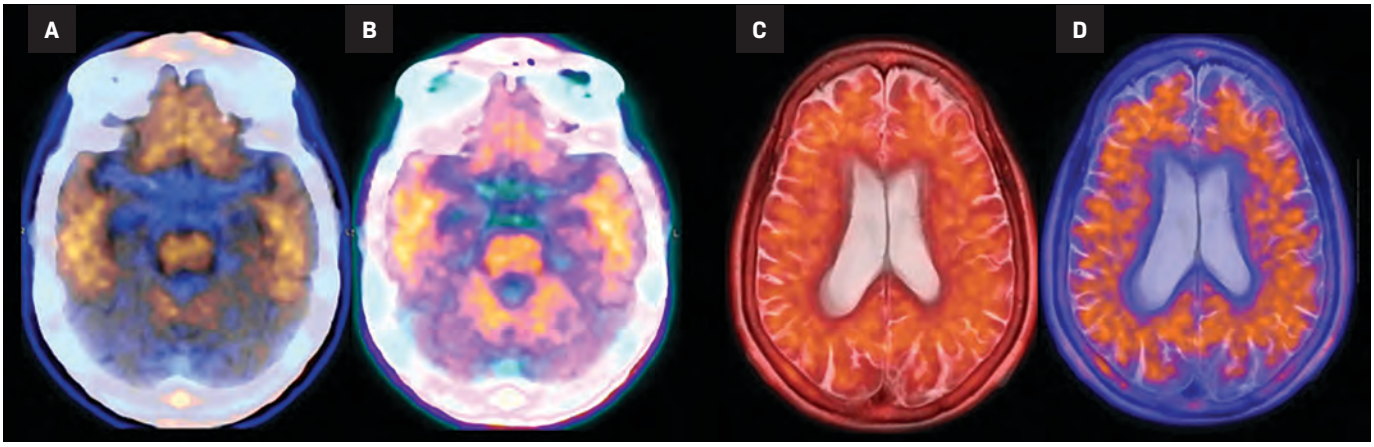
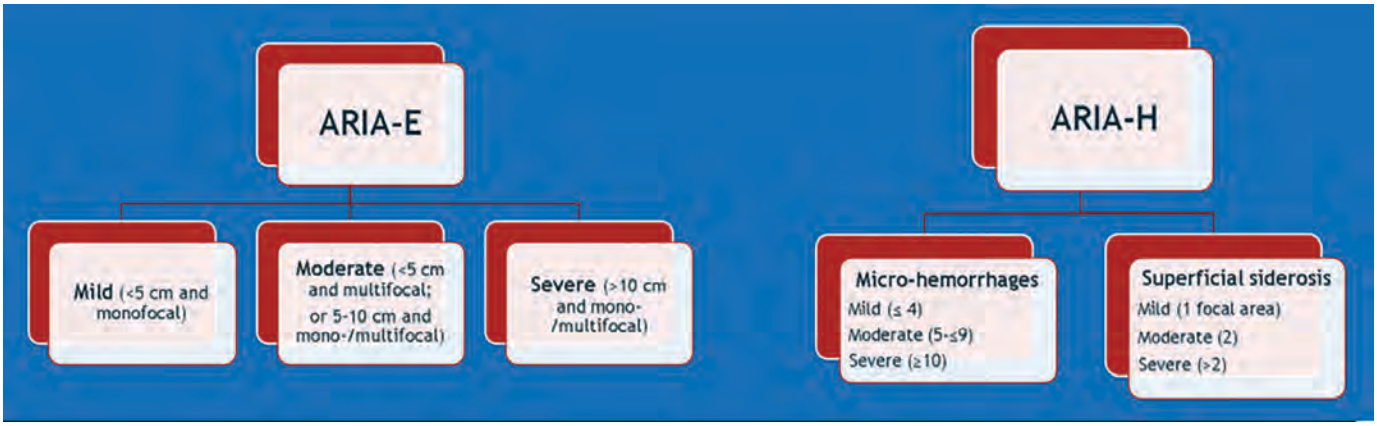


Figure 5. MRI ARIA grading criteria.



Treatment Progress

In the phase 3 CLARITY-AD trial published in January 2023,[4] lecanemab met the primary efficacy endpoint by slowing the rate of cognitive decline by 27% over 18 months based on the Clinical Dementia Rating-Sum of Boxes (CDR-SB).

In the phase 3 TRAILBLAZER-ALZ 2 trial published in July 2023,[5] donanemab (Eli Lilly) met the primary efficacy endpoint by slowing the rate of cognitive decline by 35% over 18 months. Additionally, nearly half (47%) of donanemab participants had no disease progression at one year, based on the CDR-SB. Patients with less advanced disease (low/medium tau burden) outperformed those with more advanced disease (high tau burden), confirming that the earlier treatment is initiated the higher the clinical benefit.

In both trials, the secondary endpoints were also met. Specifically, therapy resulted in effective clearance of Aβ plaque, a hallmark of AD, as imaged with amyloid PET.

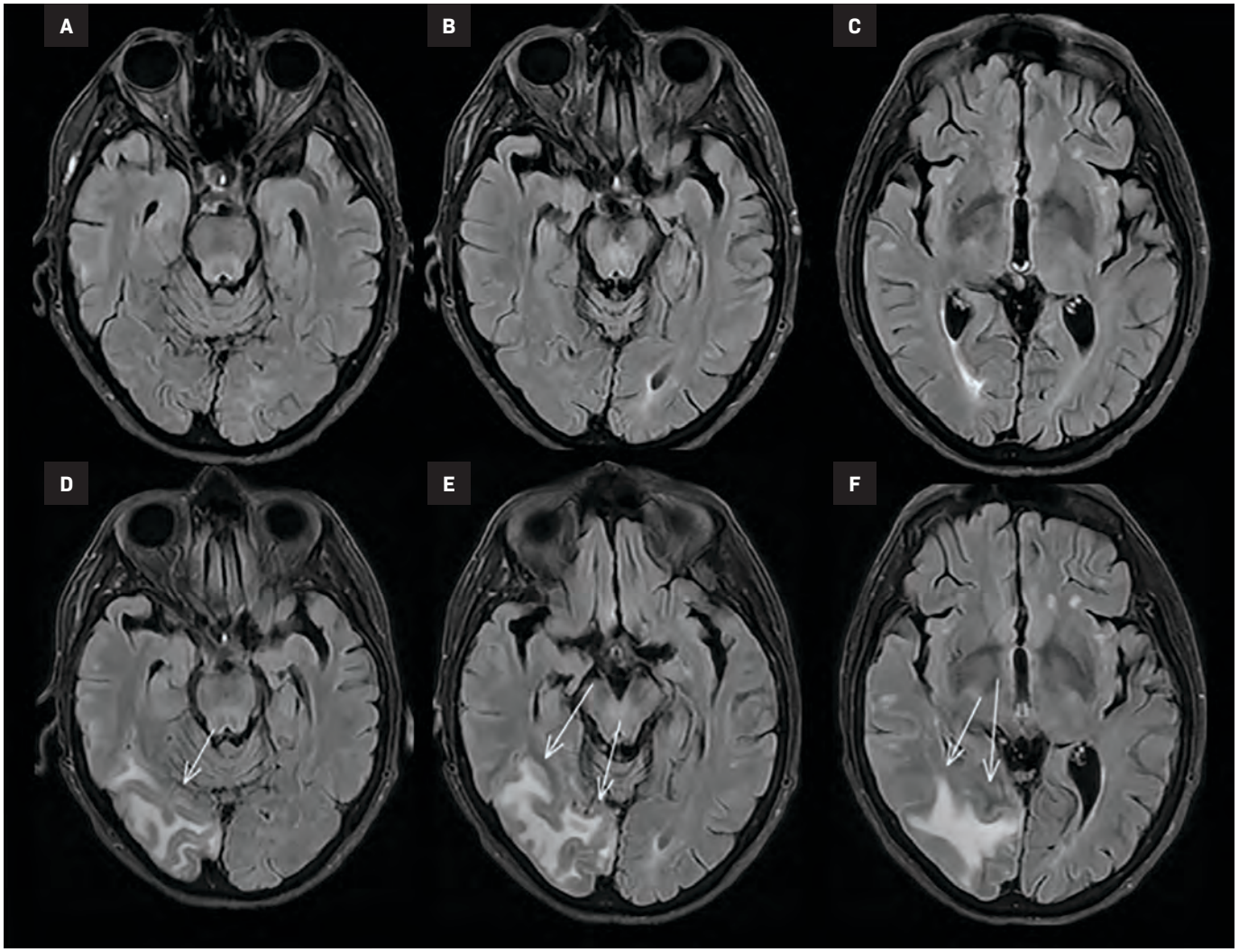
Numerous other trials are ongoing, including disease prevention trials such as the Dominantly Inherited Alzheimer Network Trials Unit (DIAN-TU). Several trials focus on pharmacological targeting and monitoring of other biomarkers for the disease such as neurofibrillary tangles, which can be imaged with tau PET. The National Institute of Aging currently funds more than 450 active clinical dementia trials.

Side Effects

A side effect of these MAB-based therapies that target and mobilize Aβ plaque is the development of drug-induced amyloid-related imaging abnormalities (collectively known as ARIA, subdivided into ARIA-E and ARIA-H). ARIA-E is characterized by edema and/or sulcal effusions. ARIA-H is characterized by microhemorrhages and/or superficial siderosis (Figure 5).

ARIA can clinically present as headaches, confusion, nausea, or visual disturbance. ARIA risk is highest in the initial treatment period, at high dose, and in those with APOE ε4 homozygote carrier status. Caution should be exercised when considering the use

Figure 6. ARIA-E clinical example. An elderly patient with memory loss and confirmed Aβ plaque. The baseline screening MRI demonstrated only mild microvascular ischemic disease on FLAIR (A-C). The standard surveillance exam prior to the fifth infusion of lecanemab demonstrated development of moderate ARIA-E (parenchymal edema) with regional mass effect on FLAIR in the right occipital lobe (arrows, D-F). Treatment was suspended until resolution was established on subsequent MRI. (Images courtesy of Rachael Gordon, MD).



of lecanemab in patients with factors that increase the risk of cerebral hemorrhage, such as concomitant anticoagulation or baseline cerebral amyloid angiopathy.[6]

If the patient develops ARIA symptoms (moderate or severe symptoms for ARIA-E or any symptoms for ARIA-H) or asymptomatic radiographic moderate or severe ARIA, treatment is temporarily held until a follow-up MRI demonstrates resolution of ARIA-E and stability of ARIA-H (Figure 6). In trials, the overall incidence of ARIA was 41% for aducanumab, 37% for donanemab, and 21% for lecanemab.[4,5,7]

The good news is that most patients who develop ARIA are asymptomatic. Symptomatic ARIA occurs in less than 3% of all patients on lecanemab.[4] Additionally, ARIA-E is temporary and typically resolves over the course of weeks to months.[4,5,7] Of note, the rate of symptomatic ARIA was higher for aducanumab (26%) and donanemab (6%) than with lecanemab (<3%).[4,5,7]

Homozygous APOE ε4 carriers have a higher incidence of symptomatic, serious, and severe radiographic ARIA, compared to heterozygote carriers and noncarriers.[6] Therefore, APOE ε4 screening is recommended (but not required) prior to initiating lecanemab treatment to inform the risk of ARIA.[6] Among the general US population, 25% carry one APOE ε4 allele (heterozygous), which portends a 3-times higher risk of developing AD.[8,9] An estimated 2-3% of the population carries both APOE ε4 alleles (homozygous), which portends a 12-times higher risk for the disease.[8,9] About 15% of AD patients are APOE ε4 homozygotes.[8,9]

Infusion-related reactions occur in approximately 10% of patients, often

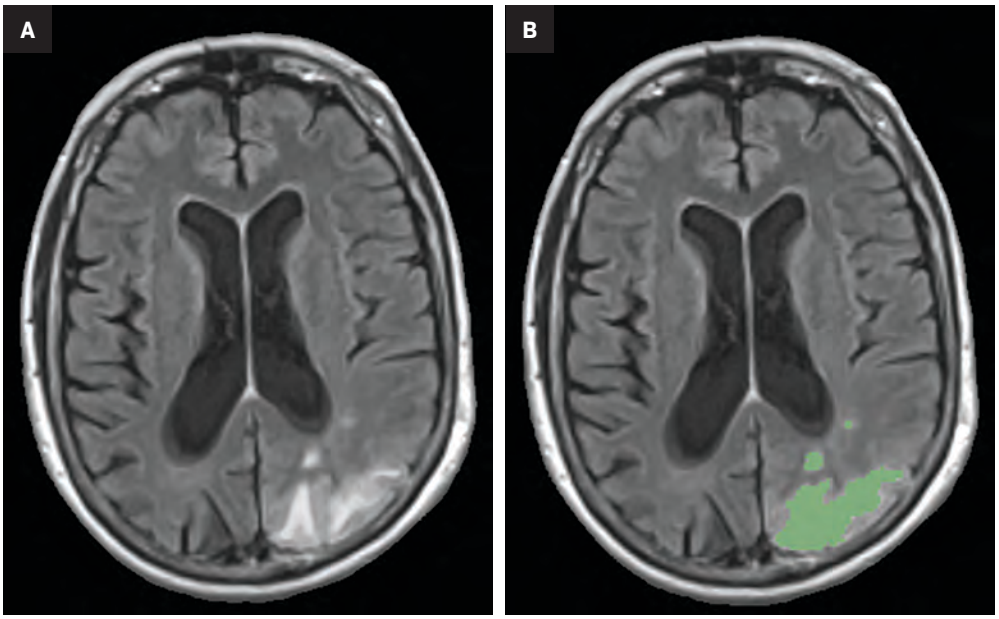


Figure 7. Left parietal lobe ARIA-E (parenchymal edema) on axial FLAIR without (A) and with AI-based segmentation (green, B).

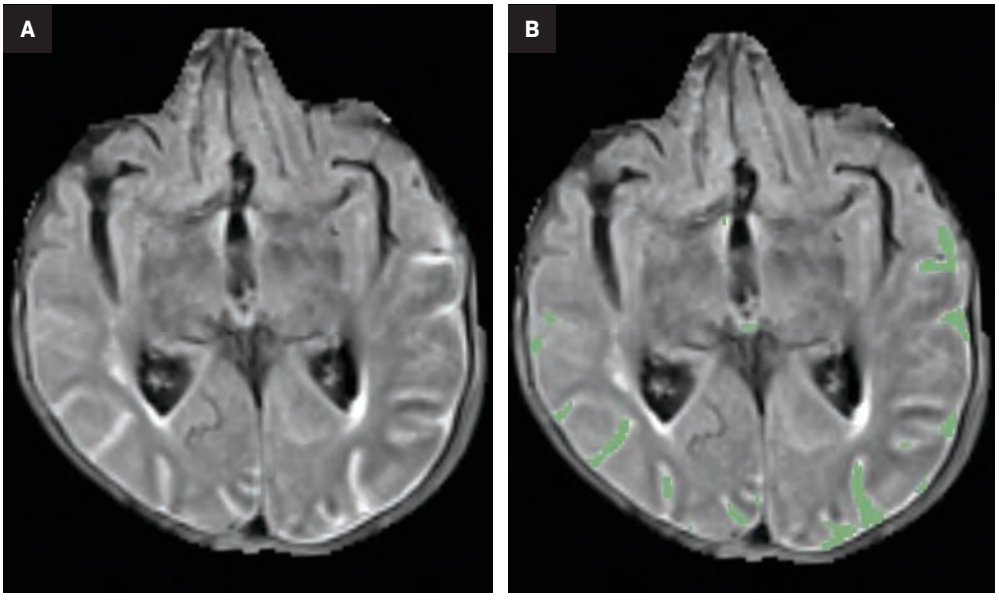


Figure 8. ARIA-E (sulcal effusion) on axial FLAIR involving the bilateral temporal and occipital regions without (A) and with AI-based segmentation (green, B).

presenting with fever and flu-like symptoms.[6] Lecanemab is administered intravenously (IV) every two weeks during treatment.[6] Donanemab is a once monthly IV infusion.[5] Trials are underway to evaluate the efficacy of a subcutaneous injection mode of delivery for lecanemab which would enable home administration and negate the risk of infusion reactions.[10] Preliminary results of subcutaneous injection trials are promising for similar efficacy with the added anticipation of reduced ARIA-E rates.[10]

Impact on Imaging Enterprises and Neuroradiologists

Higher MRI Volume

Imaging centers around the country are gearing up for an anticipated steep increase in the number of brain MRI requests. Magnetic resonance imaging is required at baseline and prior to the 5th, 7th, and 14th infusions because of ARIA risk.[6] The baseline MRI must be recent to accurately screen for exclusionary findings and microhemorrhages. Appropriate use recommendations for lecanemab published by the Alzheimer's Disease and Related Disorders Therapeutics Work Groups also suggest an additional MRI prior to the 26th infusion (week 52).[11] Patients on treatment who develop neurologic symptoms which could portend ARIA will require an additional brain MRI that may be requested on an urgent basis. If ARIA is present, follow-up MRI scans are recommended every two to four

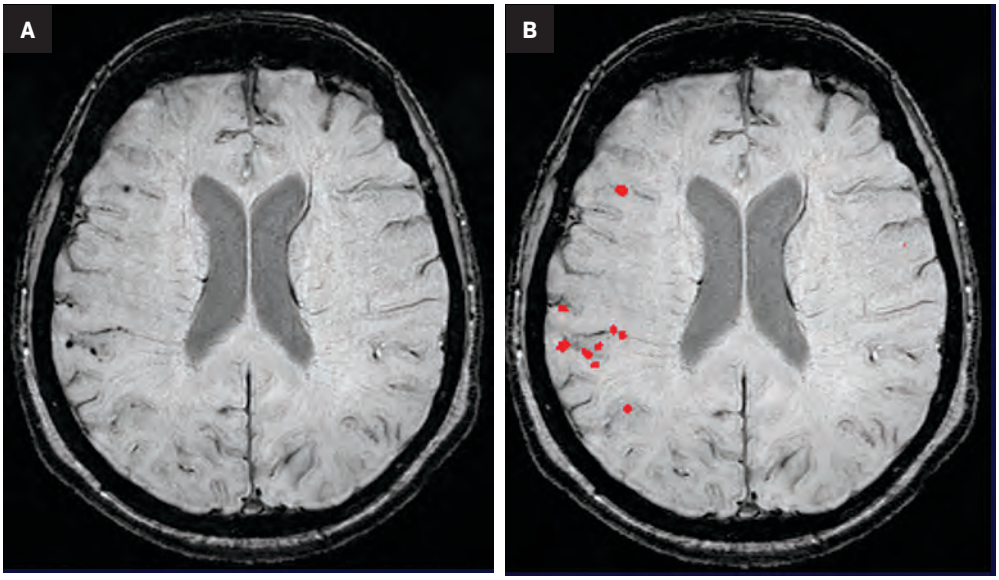


Figure 9. ARIA-H (parenchymal hemorrhage) on axial GRE involving the right frontal and right parietal lobes without (A) and with (red, B) AI-based segmentation.

Figure 10. Sample ARIA-E (left) and ARIA-H (right) AI-based screening reports. Grading is based on classification criteria per lecanemab label.

months until ARIA-E has resolved, and ARIA-H has stabilized.[6]

The anticipated increase in scan volume is expected to widely impact outpatient and inpatient imaging enterprises.[12,13] Organizations can estimate this increase by evaluating their regional demographics and number of patients with MCI or mild AD being treated locally. One example is cited in a white paper from the Alzheimer/ARIA leadership group of the American Society of Neuroradiology (ASNR) (in press — Cogswell, P, Benzinger T, et al): The local Olmsted County, Minnesota, population is approximately 160,000; per latest census data, about 30% (48,000) are 55 years or older. Assuming 15% have MCI (7,200) and a 50% rate of presentation for evaluation, one could

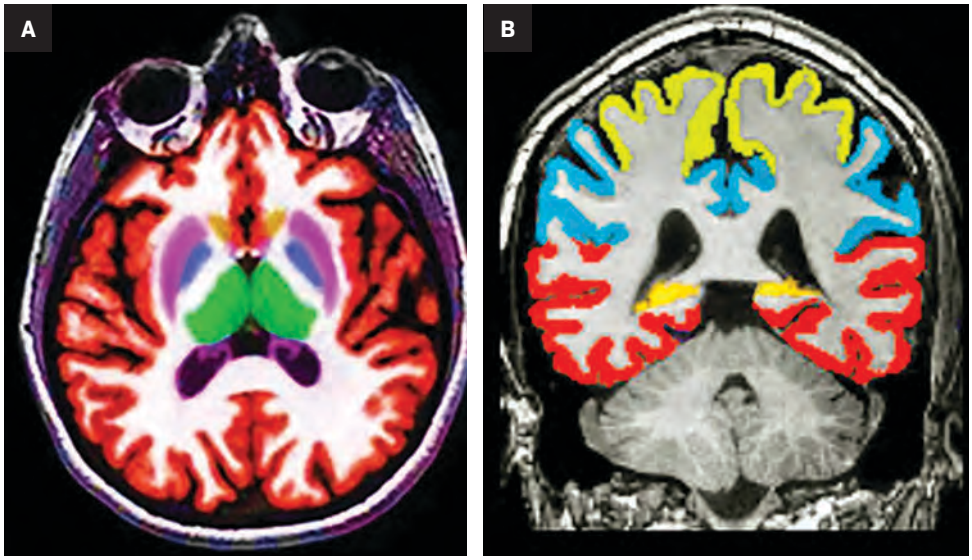


Figure 11. Representative brain substructure segmentation with QMRI on 3D T1 in the axial (A) and coronal (B) planes.

estimate 3,600 additional patients presenting for evaluation at some level of the regional health system. MRI equipment manufacturers anticipate increased new system orders to accommodate this demand.

Higher Amyloid PET Volume

With the recent proposal to remove the CMS NCD restricting amyloid PET coverage, imaging practices can expect to see an uptick in amyloid PET studies to confirm Aβ. In the clinical trials, amyloid PET scans were used to confirm therapeutic candidates and perform longitudinal analysis of Aβ clearance.[4,5,7] In clinical practice, neurologists may choose to order additional amyloid PET studies beyond baseline to assess disease progression and drug efficacy. Medical enterprises should ensure sufficient scanner availability and enough radiologists familiar with amyloid PET to interpret these studies.

New Imaging Protocols

Standardized, appropriate protocols for dementia therapeutic imaging are critically important.[13,14] It is essential for local neurologists to include DMT information in imaging requests in a way that alerts schedulers and neuroradiologists, perhaps by offering "AD therapeutic baseline" or "AD therapeutic monitoring" as the study indication. Both 1.5T and 3T scanners can be used for imaging, but in challenging patient populations open 1.2T systems may also be employed in practice. Ideally, patients should be imaged on the same field-strength scanner throughout surveillance. If quantitative imaging tools are being used for analysis, imaging may best be performed on the same scanner, although this may not always be practical.

Minimum imaging protocols for screening and surveillance should include GRE, FLAIR, and DWI, but most radiologists will simply employ their routine brain protocol. A 3D T1 sequence should be included if quantitative analysis of brain volume is desired. A conventional 2D GRE scan is mandatory, as it was the standard method to assess microhemorrhages in the trials,[4,5,7] but some may choose to add 3D susceptibility weighted imaging (SWI) for greater sensitivity to blood products. The ASNR has partnered with equipment manufacturers to present optimized AD therapeutic imaging protocols, which are posted on the ASNR website at www.asnr.org.

Neuroradiology Educational Initiatives

ARIA can be subtle and the requirements in reporting are specific to the needs of treatment. An educational initiative is ramping up throughout the neuroradiology community, as radiologists and imaging enterprises are poised to play a critical role in therapeutic dementia imaging. Educational resources and ARIA training are available through multiple sources, including the ASNR website, AlzImaging.com, expert forums,[13,14] and recent publications.[15]

Artificial Intelligence Tools

Artificial intelligence (AI) solutions like deep learning-based image reconstruction can maximize scanning efficiency by enabling 50-70% faster acquisition, which will help to accommodate increased MRI scan volumes. The faster scan times are also advantageous for motion-prone dementia patients, who may also be suffering from confusion and anxiety.[16,17]

A recent survey sent to the 2,700 members of ASNR revealed that 63% of responding neuroradiologists are interested in utilizing an AI-based quantitative tool to aid in ARIA detection and longitudinal follow-up. Multiple vendors are working to develop

quantitative ARIA screening solutions to aid neuroradiologists in efficient and accurate ARIA segmentation (Figures 7-9) and reporting (Figure 10).[12] These products should detect and quantify ARIA-H and measure the volume of ARIA-E, as well as highlight changes that occur during surveillance.[12] It is anticipated that the tools will provide standardized classification and automated ARIA grading, eg, mild, moderate, or severe.

The TRAILBLAZER-ALZ 2 trial found better preservation of brain volumetry in the treatment limb than in the placebo limb,[5] so quantitative assessment of brain volumes (Figure 11) may also be beneficial as a quantitative structural biomarker in determining longitudinal treatment efficacy.[18] In the interest of enhancing workflow, prepopulated quantitative MRI (QMRI) reporting templates may facilitate standardization and efficiency.[18]

New CPT Codes for QMRI

The American Medical Association issued new CPT Category III codes, 0865T and 0866T, for QMRI analysis of the brain in July 2023, representing a significant milestone in enhancing AD diagnosis and, more importantly, improving patient care.[19] These vendor-neutral, standardized temporary codes, which take effect Jan. 1, 2024, will hopefully create a path to reimbursement for comprehensive QMRI analysis for lesion identification, characterization, and quantification, as well as for brain volumetry. As is typically the case with novel codes, payments are expected to be inconsistent initially. Billing studies correctly under these codes, rather than employing common workarounds, is important for driving conversion to Category I and universal payment.

Agility Required

It is becoming increasingly apparent that the dynamic landscape of AD diagnosis and treatment is profoundly impacting healthcare. Neuroradiologists will play a key role in clinical decision making regarding patient eligibility for and continuance of DMT. Radiologists and their enterprises will require the agility to quickly adapt to changing demands and opportunities at this pivotal time in AD diagnosis and treatment.

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A New Era for Quantitative Brain MRI Analysis

Wim Van Hecke, PhD, and Lawrence N. Tanenbaum, MD

Radiology has been among the early adopters of advances in technology, whether they are new scanner technologies, novel imaging sequences, machine-assisted acquisition and reconstruction techniques, or new tools for image interrogation. Technological advances in medicine over the last decade have been driven largely by artificial intelligence (AI), and radiology is leading the pack in the number of AI-based medical devices cleared by the US Food and Drug Administration.[1]

AI-fueled solutions already impact imaging at numerous points, ranging from scheduling through reporting. Deep learning-based tools improve the quantitative analysis of studies, triage urgent examinations for prioritized attention, and are beginning to emerge with branded FDA clearance for true diagnostic support.

In the coming years and decades, the need for imaging will only grow, driven in part by the nation's aging population. In addition, with the availability of new disease-modifying therapies, there is an urgent need for AI-based assistive solutions that can quantify health — particularly brain health — and monitor therapeutic progress in patients. The July 2023 FDA approval of Leqembi® (developed by Eisai and Biogen), the only disease-modifying treatment shown to reduce the rate of cognitive and functional decline in Alzheimer disease, offers potentially life-changing impacts for those with dementia and their loved ones.[2] Physicians, healthcare systems, and payers will need to prepare for the numerous implications.

Leqembi® is expected to substantially increase the need for MRI capacity, given the large population of people expected to require therapy as well as those seeking imaging to assess early cognitive impairment. Per FDA guidance, treatment with Leqembi® is appropriate only in patients with early disease, putting a premium on early identification. However, at the moment, Alzheimer disease is diagnosed three years after the appearance of symptoms in 80% of patients.[3] Hence, AI-driven quantitative MRI analysis tools have the potential to support differentiating Alzheimer disease from other dementia subtypes and normal aging.

In addition, amyloid targeting therapies are associated with amyloid related imaging abnormalities (ARIA), such as edema and sulcal effusions termed ARIA-E, as well as microhemorrhages and siderosis referred to as ARIA-H. As a result, the FDA currently mandates a recent pre-treatment brain MRI as well as surveillance MRI scans prior to the fifth, seventh, and fourteenth biweekly Leqembi® infusions.[2]

As ARIA reading may be new to many radiologists, physician education would be beneficial. Findings may be subtle and thus, reliable and consistent disease identification and quantification is required. For example, radiologists will need to quantify the number of new microhemorrhages and the longest axis of an edema focus.[4] Hence, there is an important role for AI algorithms that can assist in ARIA reading and severity assessment. Because a standardized, quantitative, and accurate assessment of ARIA is critical for treatment safety and efficacy, AI solutions of the highest standard of validation and accuracy will have the best chance of routine adoption. In this context, several AI tools specifically for ARIA monitoring are being developed and/or under active FDA review (Figure).

A last hurdle standing in the way of day-to-day adoption of quantitative imaging AI solutions, is a

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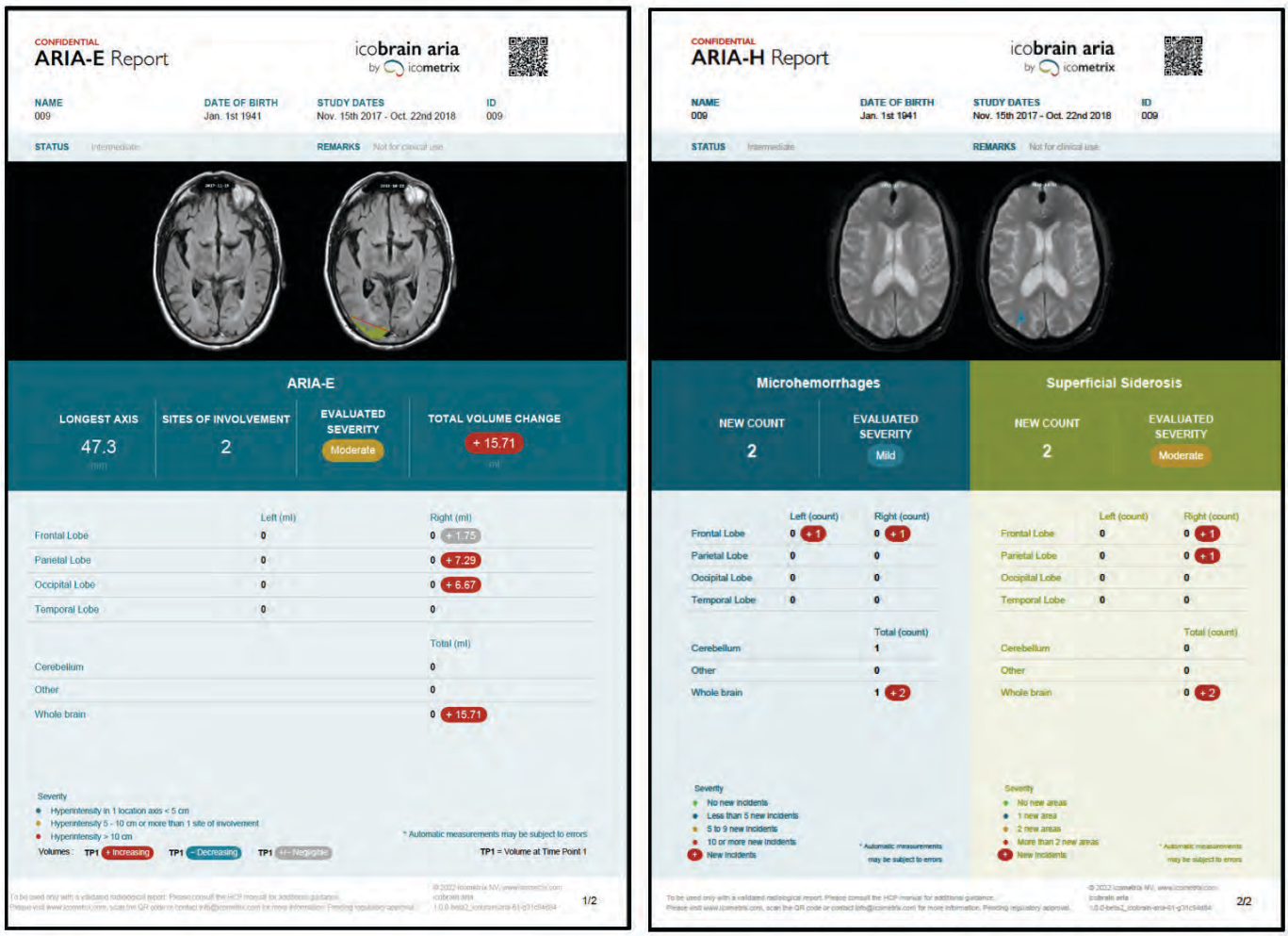

Example radiology report provided by icometrix via icobrain aria, an investigational AI-based digital health solution for the potential assessment of ARIA.

sustainable business model for users and providers. As we experienced with 3D visualization tools two decades ago, a dedicated current procedural terminology (CPT) billing code is needed to elevate adoption to standard of care. Today, we indeed cannot imagine *not* using a 3D visualization solution for modalities like CT angiography. Fortunately, just as this wave of brain scans requiring evaluation begins flooding healthcare systems, a new CPT III code for MRI brain scan quantification has recently become available. Through the efforts of icometrix, a company which offers the icobrain™ suite of solutions for brain MRI and CT, the American Medical Association on July 1, 2023, issued CPT III codes 0865T and 0866T. The widespread use of these codes for billing is the next critical step toward routine and reimbursement.

In summary, radiologists should anticipate a wave of brain MRI study requests in light of new therapeutic options and the imminent arrival of reimbursement for AI-based quantification. The time is now for radiologists to adopt these AI solutions for next-level clinical care.

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A Guide to the Fellowship Match

Yasha Parikh Gupta, MD

Most radiology residents pursue a fellowship,[1] and many would agree that the process truly could not be more confusing.

Some subspecialties utilize the Electronic Residency Application Service, while some follow the National Residency Matching Program match system, and still other subspecialties employ their own "universal application." And, of course, every fellowship program has its own application requirements. To add to the confusion, some programs are accredited by the Accreditation Council for Graduate Medical Education (ACGME) while others are not (more on that later).

So the question becomes: where do you start? The first step is to visit the primary website for the sub-specialty you are pursuing and read its guidelines for application. For example, you can find the guidelines for breast imaging fellowships at the Society of Breast Imaging website, https://www.sbi-online.org/

In addition, the Society of Academic Chairs in Radiology recommends a specific timeline during which fellowship programs can accept applications, conduct interviews, and make offers.2 They are only recommendations, however, and not all programs follow the them. Be sure to check when pursuing a fellowship in your chosen subspecialty.

Three Keys to Success

A key component of the application process—in my opinion, the most important—is your letters of recommendation. You may have heard that residency is one long job interview; I would agree. Securing three strong letters of recommendation from your mentors is a major key to a successful fellowship match.

I recommend obtaining at least one subspecialty letter, a letter from your program director, and a letter from someone of your choice who knows you well. In addition, the letter's content is paramount. The letters should be personal and speak to your character, accomplishments, and what you will bring to radiology. Radiology is already a very small world, and its subspecialties are even smaller. These letters can often lead to personal phone calls between program directors and your mentors, especially if they are already familiar with each other.

I also strongly recommend focusing on your research and publishing experience. While not everyone desires to enter academia, completing at least one significant project during residency typically improves one's chances of obtaining a fellowship match. Remember, most fellowships are in large academic centers, so demonstrating interest in contributing to the department can help you stand out from the pack.

Third, put thought into your personal statement, where you will explain why you are pursuing the fellowship. Many residents choose fellowships based on familiarity (home program), geography (nearby family and support system), specific research projects, and of course, job prospects at the

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institution and/or nearby. The personal statement is your opportunity to discuss these important points and potentially overcome any geographical biases if you are seeking a fellowship located far from your current medical school.

Frequently Asked Questions

Here is a brief list of questions that I am often asked about obtaining fellowships and answers based on my experience:

- **Does core exam score matter?**
  No. You will not receive your core exam score before rank lists are finalized.
- **Do step scores or medical school grades matter?**
  Yes and no. Neither were brought up at any of my interviews. Indeed, most fellowship applicants have already completed Step 3 of the US Medical Licensing Examination and there's no way to go back and change medical school grades, so they are essentially out of your control. Focus on what you can improve and be ready to talk about any low scores in the event they are brought up in the interview.
- **Does ACGME accreditation matter?**
  It depends. Baker et al nicely outline what accreditation means for fellowships and what it could mean for you.[1] As far as job prospects, I have yet to see the issue come up in conversation, and I have not included it in my curriculum vitae.
- **How many programs should I apply to?**
  This is personal and depends largely on your desires for location and job preferences. Anecdotally, most residents I have spoken to have applied to between 15 and 20 programs.

A fellowship can be one of the most rewarding experiences of your career but obtaining one can be challenging. Carefully planning your steps and doing your due diligence can help make the process easier and more successful.

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Subspecialty Teleradiology: Good or Bad for Medical Imaging?

Kerri Reeves

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

Teleradiology emerged in the 1990s as a major disrupter of medical imaging. No longer bound by the need to employ their own radiologists 24/7, hospitals could leverage the services of radiologists from other parts of the country — even overseas — to read their images.

More than a quarter-century later, sparked in part by the COVID-19 pandemic, subspecialty teleradiology is causing similar disruption. A growing number of health systems are turning to subspecialty teleradiology providers for round-the-clock reading help in neuroradiology, musculoskeletal imaging, and other areas.

This has sparked some discussion over whether the advantages of subspecialty teleradiology outweigh the disadvantages.

Evolution of Subspecialty Reads

The emergence of general teleradiology services some 30 years ago proved especially helpful to facilities located in rural areas and those without sufficient patient volume to warrant in-house overnight coverage. Radiologists who joined third-party teleradiology providers, meanwhile, enjoyed improved quality of life owing to greater autonomy in scheduling and work-from-anywhere capabilities.

"Traditional teleradiology is a distinct specialty and generally attracts people who [are] moving toward retirement, seeking lifestyle flexibility, or [aren't] interested in engaging much with other docs in the clinical setting," says Lawrence N. Tanenbaum, MD, vice president and chief technology officer of Radnet, a provider of outpatient imaging services based in New York, New York.

Subspecialty image reading followed soon after but really began expanding about 12 years ago when nighttime final reads became standard operating procedure and there was an explosion of stroke imaging, says Samir Shah, MD, chief clinical officer of teleradiology and senior vice president of radiology at Envision Physician Services of Nashville, Tennessee.

"These factors pushed a need for more neuroradiologists at night," Dr Shah says. "Then … we saw more and more requests for pediatric subspecialty reads on neonatal films, as well as a general push for MSK [musculoskeletal] radiology expertise."

Both general and subspecialty teleradiology services experienced a significant upswing in popularity as the COVID-19 pandemic took hold and many businesses, including healthcare systems, began implementing work-from-home arrangements.

"With the onset of COVID-19, remote reading of images suddenly got much more common," Dr Tanenbaum says, adding that urban flight and mass retirements left many organizations in need of reading help. Third-party subspecialty teleradiology services, he says, helped to meet those needs.

Taj Kattapuram, MD, a diagnostic and interventional radiologist at Gundersen Health System, has worked in numerous practice settings over her career.

Lawrence N. Tanenbaum, MD, is vice president and chief technology officer of Radnet, which completes more than 9 million outpatient imaging procedures annually.

Samir Shah, MD, is chief clinical officer of teleradiology and senior vice president of radiology at Envision Physician Services, where more than 500 radiologists perform over 8 million annual reads, combining on-site radiology and subspecialist teleradiology

Thinking About Outsourcing? Some Things to Consider

Teleradiology services operate under a range of performance standards, agreements and contracts, and technology platforms that enable varying degrees of collaboration.

Hospitals looking to outsource should be sure to:

- **Carefully assess the qualifications and experience of the teleradiology service's radiologists;**
- **Request sample reports and documentation;**
- **Analyze the type and number of images intended for outsourcing; and**
- **Analyze the projected revenue of these cases against the costs of outsourcing.**

Health systems also should not rule out making internal changes that could generate the intended results without outsourcing. "I caution people to try to do your best work with your current radiologists. Work with the docs and try to figure out if there's a solution that will keep everyone happy," Dr Kattapuram advises.

"With COVID, we saw in many ways that people do not have to be in house—physically present at the hospital site—to read imaging studies and get the workflow done," adds Taj Kattapuram, MD, a diagnostic and interventional radiologist at Gundersen Health System in La Crosse, Wisconsin. "Without a commute, it saved people a lot of time. In terms of quality of life and satisfaction, we saw a big happiness boost for a lot of radiologists."

Dr Shah notes that the pandemic helped subspecialty teleradiology gain greater credibility with healthcare institutions.

"It was only after the pandemic that remote reading became fully accepted," Dr Shah says. "And

[T]he optimal medical imaging approach will combine the versatility of general radiologists with in-person and remote subspecialty radiologists to handle cases spanning a wide range of complexity.

as teleradiology groups, it's taken us this long to … have the right workflows in place that mimic on-site, daytime work to provide that optimal degree of subspecialization."

Now, he says, there's an increasing expectation for remote subspecialty image reading even during the day. Some hospitals in rural and other areas with limited access to advanced imaging consider subspecialty teleradiology services a necessity. Their general radiologists may not have the expertise to handle complex cases in the cardiac or neuro realm, for example, and outsourcing these reads is the most convenient, affordable option, he says.

For their part, Drs Tanenbaum and Kattapuram say complex cases constitute only a small portion of third-party interpretations.

"A really good general radiologist, especially in a rural setting, isn't going to see those 'crazy zebra' cases," Dr Kattapuram says. "They've learned the vast majority of things as a resident and it's sufficient." She adds that patients are better off being referred to the closest major academic medical center in such cases.

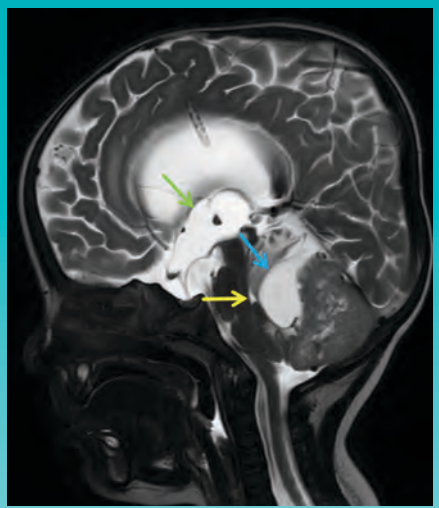
And then there are financial realities to consider. Payors determine reimbursement rates for imaging services, complicating the economics of subspecialty teleradiology for many institutions. This, in turn, impacts teleradiology services themselves.

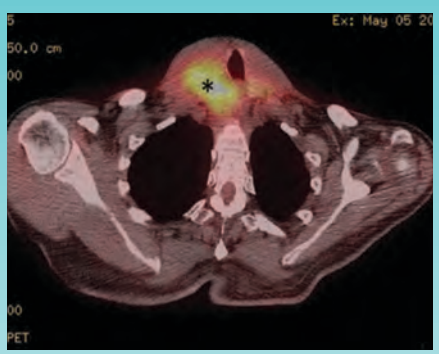
"The fundamental problem is that for many organizations reimbursements are low—getting ever lower—and margins are very tight. Practices can't outsource reading if the costs exceed revenues," says Dr Tanenbaum. This price pressure forces teleradiology salaries down, he adds. "How is a teleradiology concern going to recruit an 'expert' if they can't pay an appropriate salary? Volume is the key to teleradiology, but there isn't a lot of margin to retain the best people."

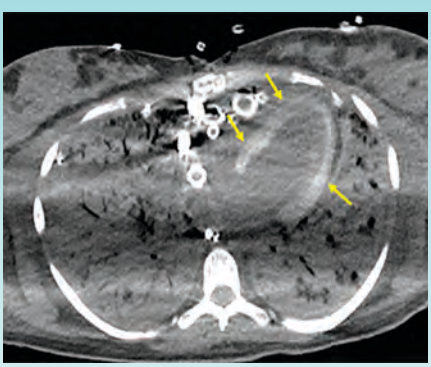
Forecasting the Future

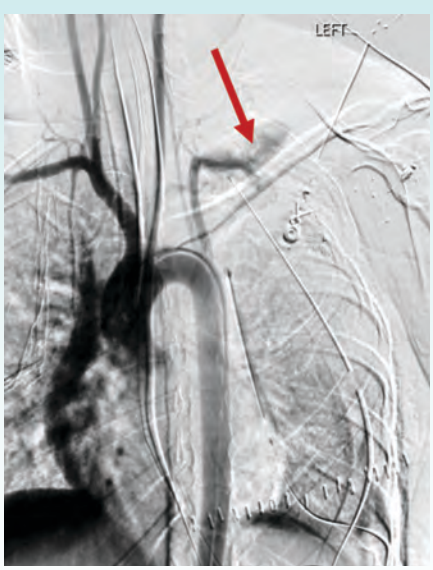
Going forward, some say the optimal medical imaging approach will combine the versatility of general radiologists with in-person and remote subspecialty radiologists to handle cases spanning a wide range of complexity.

"We're at a crossroads right now with subspecialty teleradiology because we're seeing hospitals move to remote models, yet there's no question that the local radiologist is still valued by health system and by referring physicians. They're not going to disappear," Dr Shah says.









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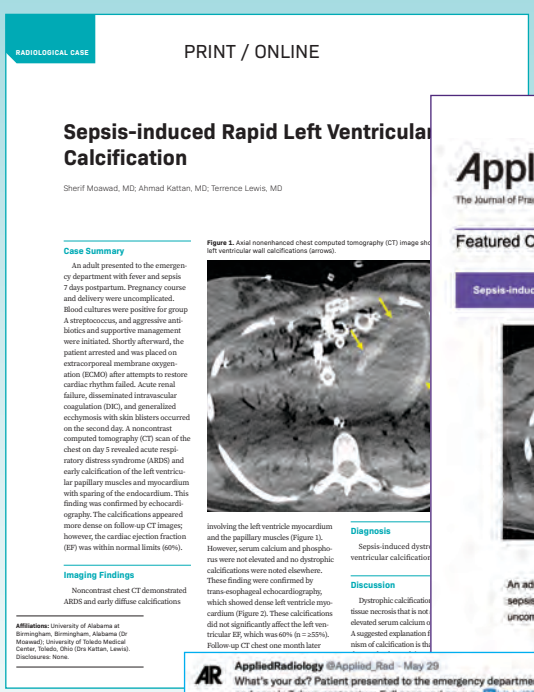
RADIOLOGICAL CASE

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

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Disclosures: None.

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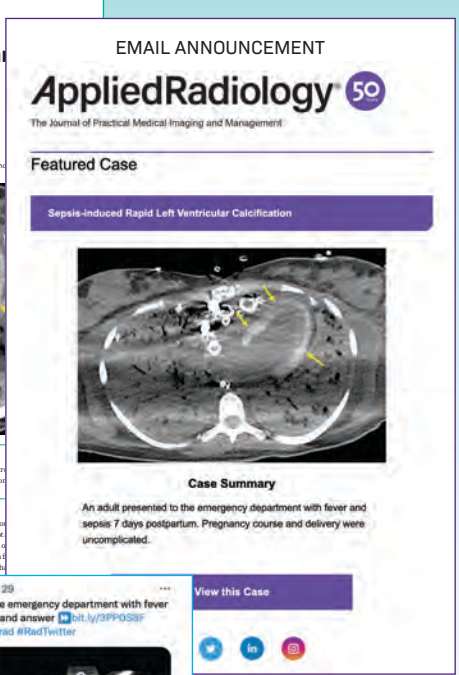
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Sepsis-induced Rapid Left Ventricular Calcification

Case Summary

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Meeting the Need for Breast Imaging Training in Tanzania

Toma S. Omofoye, MD; Zuhura Nkurumbih, MD, MMed; Frank J. Minja, MD

Breast cancer is the most common cancer in sub-Saharan Africa and a major cause of cancer mortality among women in Tanzania, second only to cervical cancer.[1,2] The five-year survival rate of breast cancer in Tanzania is 45%, compared to 90% in the United States.[3] In Tanzania, 80% of cases are diagnosed at later stages (III or IV), compared to only 35% in the United States.[2-5] Furthermore, breast cancer incidence and mortality in Tanzania are projected to increase by 80% by 2030.[2]

Improving breast cancer mortality requires early detection, accurate diagnosis and staging, and tissue sampling to determine receptor status and guide chemotherapy.

Multiple barriers delay the presentation of breast cancer patients in in Tanzania. These include a lack of basic knowledge and awareness, stigma associated with the disease, and financial and local healthcare system barriers.[5] Local barriers, such as limited access to diagnostic services, a lack of trained personnel able to recognize early signs of breast cancer, and broken referral pathways, lead to diagnostic delays and improper management, even when patients present with early-stage disease.[5] Patient management is largely limited to mastectomy and axillary lymph node dissection; chemotherapy, when available, is often non-targeted because of the limited ability to determine breast cancer receptor status.[3]

Breast imaging specialists are essential to each of these steps; as such, high-quality radiologist training programs in breast imaging are fundamental to improving the care of patients with breast cancer in Tanzania.

Phased Implementation Approach to Breast Cancer Management in Tanzania

In 2017, the Tanzania Ministry of Health (MoH) commissioned a comprehensive report on breast cancer that recommended a resource-stratified and phased implementation approach to addressing detection, diagnosis, and treatment.[2] The report recommended starting with systematic triaging and diagnosis of palpable breast disease while working toward building the healthcare system's capacity to diagnose and manage nonpalpable breast disease. The report acknowledged standardized guidelines, protocols, and a trained healthcare workforce as prerequisites to this approach; however, it did not specify breast imaging specialists as critical to the effort.

The MoH released the first edition of the National Cancer Treatment Guidelines in 2020. They incorporated evidence-based advances in breast cancer management[7] and included the 2017 recommendations for a phased approach to implementation, with phase 1 consisting of triaging and diagnosing palpable breast disease, and phase 2 consisting of resource-adapted, stage-appropriate treatment planning.[2] The guidelines put breast imaging expertise at the center of every step of management of patients with palpable breast disease: detection, diagnosis, staging, and tissue sampling for breast cancer receptor status.

Previously, patients with suspicious lesions were only referred for clinical breast exams, but they are now required to undergo imaging as part of their initial workup. Various imaging modalities are recommended for staging before any intervention is undertaken. Core needle biopsy under ultrasound or stereotactic guidance is now recommended for tissue sampling, whereas fine needle aspiration (FNA) should be reserved for screening; abnormal FNA results require histopathology confirmation. Each step of this process now requires a breast imaging expert.

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The worldwide shortage of radiologists is even more acute in Tanzania, with only about one radiologist per 1 million residents.

Breast Imaging Training Program

Unfortunately, no clear plan was presented for recruiting or training such specialists. The worldwide shortage of radiologists is even more acute in Tanzania, with only about one radiologist per 1 million residents.[8] Tanzania and other low-to-middle income countries (LMICs) cannot afford to recruit breast imaging experts, especially those from high-income countries. Creating in-country breast imaging training programs offers one pragmatic solution for LMICs.

In 2021, RAD-AID began working with key stakeholders in Tanzania, including the MoH, the Muhimbili University of Health and Allied Sciences (MUHAS), Muhimbili National Hospital (MNH), and Ocean Road Cancer Institute, to establish a two-year Master of Science in Women's Imaging Fellowship to focus on the training of radiologists specifically in breast and cervical cancer imaging.

The team's efforts are organized and supported by the Radiological Society of North America Global Learning Center program in Tanzania. Led by volunteer international faculty from RSNA and hosted at the MUHAS/MNH complex, the fellowship enrolled its inaugural cohort of three Tanzanian fellows in 2022.

The fellowship consists of a four-semester curriculum that mirrors the phased implementation of the MoH's recommendations. It focuses on palpable breast disease during the first year of training (Introduction to Breast Imaging in semester 1, and Breast Ultrasound in semester 2); and building competence in nonpalpable breast disease during their second year (Mammography in semester 3 and Breast MRI and Other Modalities in semester 4). The fellowship also provides a mentored clinical diagnosis and breast biopsy service for patients presenting with palpable breast disease. This in-country training also allows the fellows to develop cross-discipline partnerships with other healthcare providers, strengthening the professional networks required to comprehensively treat breast cancer patients in Tanzania.

Conclusion

Breast cancer patients in Tanzania face already-high incidence and mortality that are projected to more than double by 2040.[9,10] Breast imaging specialists are urgently needed to lead the country's phased-implementation approach to treatment and management. Collaboration with international partners to create and support in-country training programs is one pragmatic solution that can help to birth the local breast imaging experts who will lead the effort and train breast imaging experts of the future. Lessons learned from this experience, moreover, could likely be applied to other LMICs facing similarly high impacts from an otherwise highly treatable disease.

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Congenital Pulmonary Airway Malformation

Erica Li; Richard B. Towbin, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Case Summary

A pregnant patient presented at 35 weeks' gestation for further evaluation of a previously diagnosed fetal congenital pulmonary airway malformation (CPAM). The baby was asymptomatic at near-term delivery and discharged home. At 9 months of age a left-sided thoracoscopy and left lower lobectomy for resection of the CPAM was performed.

Imaging Findings

Prenatal ultrasound (Figure 1) showed a 2.7 × 1.9 × 1.2 cm left-sided mass with a single cyst. The CPAM volume ratio (CVR) was 0.1 and had increased in size from a prior study, when it was 0.06. This clinically important ratio can help predict which fetuses will be more likely to develop fetal hydrops, a CVR < 1.6 being associated with a lower likelihood.

Chest radiography (Figure 2) performed at 1 month of age showed a relative lucency in the posterior aspect of the left lower lobe. There was no pneumothorax, pleural effusion, or mediastinal shift.

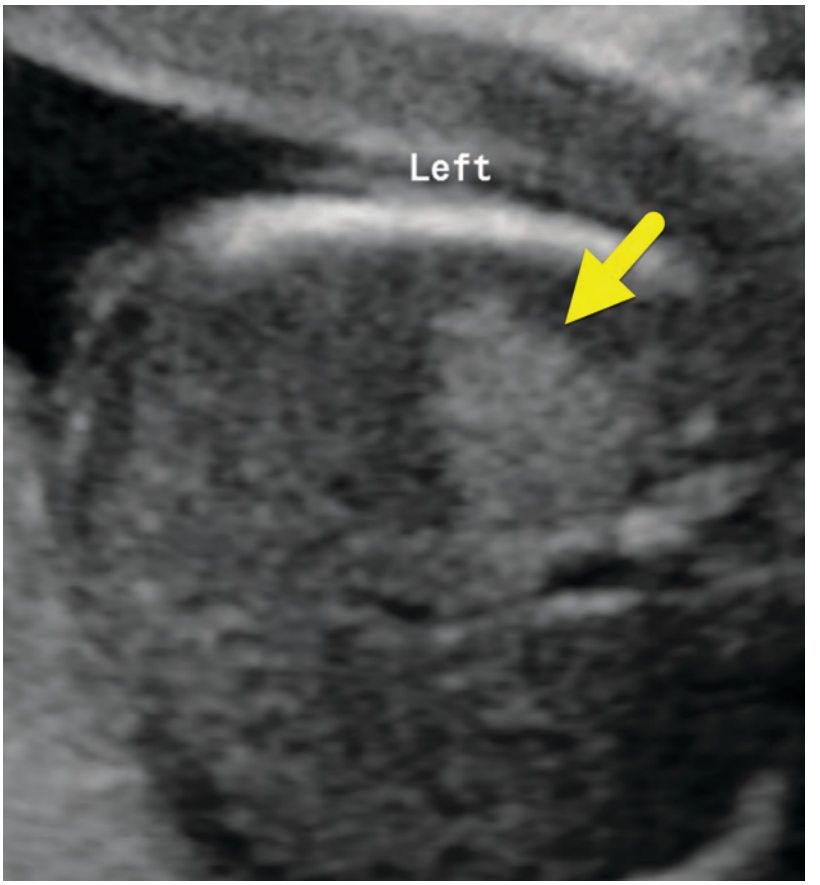

Figure 1. Prenatal ultrasound shows a well-defined echogenic lesion (arrow) in the left lung.

Contrast-enhanced chest CT (Figure 3) performed at 5 months showed a 3.6 × 3.3 × 3.8 cm lesion in the left lower lobe that contained multiple air-filled cysts within a soft-tissue mass and an associated atretic bronchus. There was no systemic arterial supply.

Diagnosis

Congenital pulmonary airway malformation.

Differential diagnoses include pulmonary sequestration, congenital lobar overinflation, and a bronchogenic cyst.[1]

Affiliations: University of California Riverside School of Medicine, Riverside, California (Ms Li); Department of Radiology, Phoenix Children's Hospital, Phoenix, Arizona (Drs Schaefer, R Towbin); Department of Radiology, Cincinnati Children's Hospital; Department of Radiology, University of Cincinnati College of Medicine, Cincinnati, Ohio (Dr A Towbin).

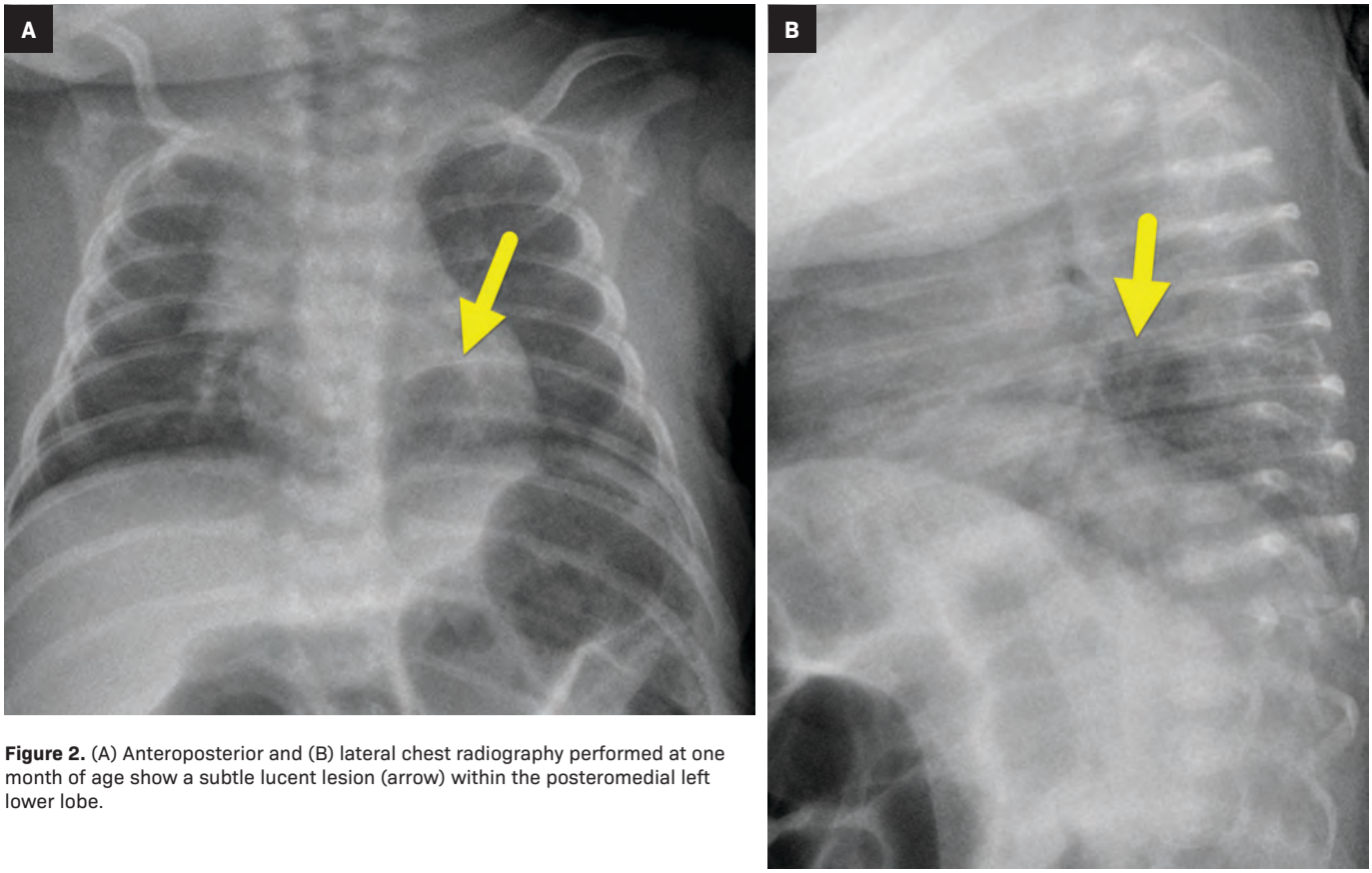

Figure 2. (A) Anteroposterior and (B) lateral chest radiography performed at one month of age show a subtle lucent lesion (arrow) within the posteromedial left lower lobe.

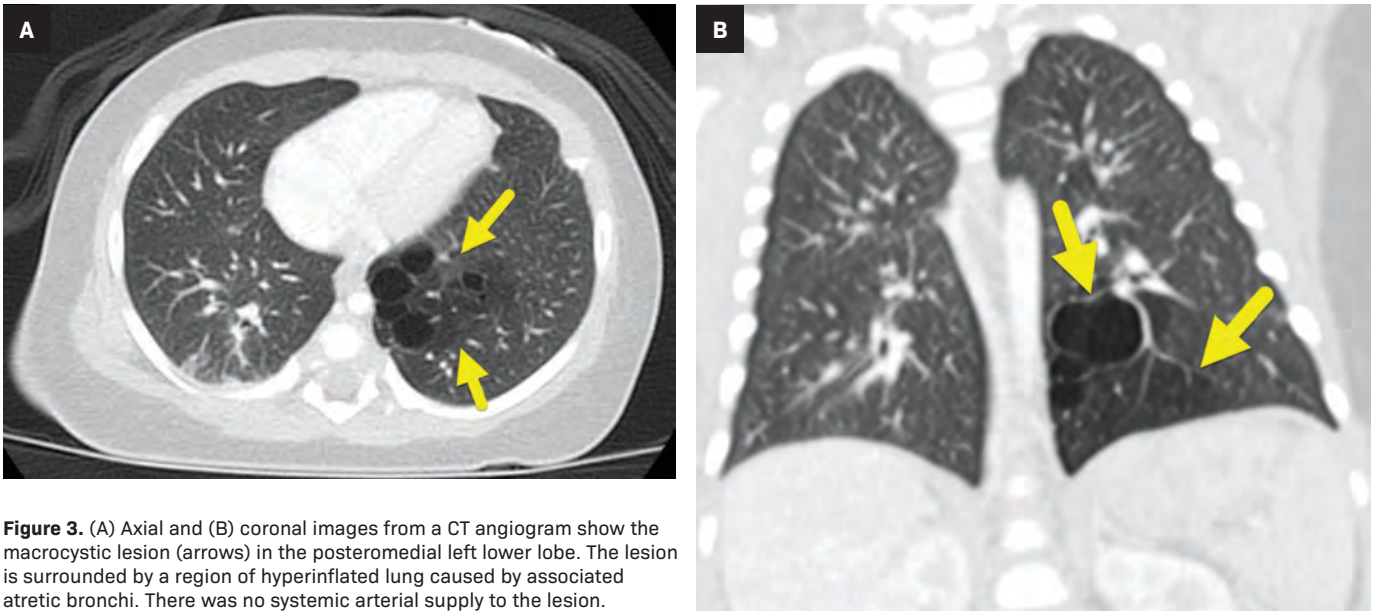

Figure 3. (A) Axial and (B) coronal images from a CT angiogram show the macrocystic lesion (arrows) in the posteromedial left lower lobe. The lesion is surrounded by a region of hyperinflated lung caused by associated atretic bronchi. There was no systemic arterial supply to the lesion.

Discussion

Congenital pulmonary airway malformation is the most common congenital lung lesion of the lower respiratory tract. It was formerly known as congenital cystic adenomatoid malformation (CCAM).[1] The name was changed to better conform to the histologic variety.

CPAM occurs with a reported incidence of 1 in 10,000-35,000 births. The condition may be diagnosed in utero, in the neonatal period or later, or while the patient is undergoing

thoracic imaging for an unrelated reason.[2]

Five Types of CPAMs

CPAMs can be classified histologically or by antenatal sonographic appearance. The Stocker classification is based on histologic features and specifies five types of lesions. Each type is derived from a component of the bronchial tree which informs the histopathology. The often-fatal type 0, which originates in the trachea or bronchi, is characterized by cartilage, smooth muscle, glands, and mesenchyme. Type 1 CPAMs stem from the bronchi and/or bronchioles and is the most common form of of the condition. It is characterized by large pulmonary cysts lined with mucus cells and pseudo-stratified columnar epithelium.

Type 2 CPAMs consist of multiple small cysts that originate from bronchiolar areas. These lesions are often associated with renal, cardiovascular, and skeletal abnormalities. Type 3 CPAMs are bulky, solid lesions that can cause mediastinal shift. They also originate from the bronchiolar regions. Finally, type 4 CPAMs originate from acinar lung tissue and contain variably sized cysts with type 1 and type 2 alveolar cells.[1-4]

Diagnosis

CPAM is frequently diagnosed with fetal ultrasound during the second trimester; the Adzick classification is used to sonographically categorize the lesions.[1] In this classification, type 1 lesions are macrocystic with one or more cysts > 5 mm and type 2 (microcystic) lesions contain cysts < 5 mm. The larger cysts in type 1 CPAM appear cystic with hypoechoic fluid. Type 2 lesions are solid-appearing and echogenic.[2, 5]

Pulmonary sequestration is typically part of the differential diagnosis for an echogenic fetal lung lesion. Pulmonary sequestration differs from CPAM in that it reflects an isolated portion of lung that receives its blood supply from an abnormal systemic artery and does not communicate with the bronchial tree. CPAM, in contrast, maintains communication with the bronchial tree and has a normal pulmonary blood supply. Fetal ultrasound with color Doppler evaluation can help distinguish these vessels.

Other entities in the differential diagnosis of an echogenic fetal lung lesion include congenital lobar overinflation and bronchogenic cysts. Congenital lobar overinflation creates mass effect and can compress neighboring structures. It is caused by an intrinsic bronchial epithelial defect or external obstruction that leads to air trapping. Bronchogenic cysts are unilocular cysts filled with fluid or mucus and lined by pseudostratified ciliated columnar respiratory epithelium and hyaline cartilage.[2]

CPAM identified in utero may spontaneously resolve, regress, or progress. A retrospective review of 100 fetuses with congenital lung lesions found that vanishing lung lesions were more likely to occur with microcystic lesions or in those with a low CVR.[6] Even when a lesion has resolved in utero, postnatal imaging is recommended to confirm resolution and characterize any sonographically occult residual.

Potential associated abnormalities are assessed on prenatal imaging; these include mediastinal shift, fetal hydrops, hydramnios, and fetal demise. The CVR was developed by Crombleholme, et al, to assess risk for CPAM-related complications. It represents the ratio between the prenatal sonographic estimate of CPAM volume (length × height × width × 0.52) and head circumference. A value greater than 1.6 is associated with an 80% higher risk of fetal hydrops.

Follow-up fetal ultrasound frequency is based on the CVR.[1,2,8] Postnatal imaging begins with a chest X-ray, repeated six months later to assess for lesion stability. On chest radiography a CPAM typically appears as a lucent mass with varying areas of radio-opacity depending on CPAM type. CT angiography (CTA) will characterize the lesion, facilitate surgical planning and identify the arterial supply (pulmonary vs systemic).[1,7] Specimen analysis after surgical resection is the most reliable method for histological confirmation and typing.[1,2]

If not diagnosed antenatally, CPAM is usually diagnosed following chest imaging for unrelated reasons or for pulmonary symptoms.

Treatment Options

Treatment can be considered antenatally and postnatally and should be guided by the presence of complications. Ideal evaluation for antenatal treatment includes fetal MRI for lesion and vascular characterization and echocardiography to evaluate for valvular regurgitation or impaired ventricular function.[1] Treatment options include maternal steroids, percutaneous laser ablation of the lesion, minimally invasive and/or open fetal surgery.[1,2]

For microcystic lesions with hydrops, maternal administration of steroids is associated with fewer complications than open surgery. Macrocystic CPAM with hydrops can be treated with fetal thoracocentesis; however, thoracoamniotic shunting is the most effective treatment, as it prevents re-accumulation of fluid. Mediastinal shift resulting from large lung lesions can be addressed with ex-utero intrapartum treatment procedure if fetal lung development is sufficient.[1]

Postnatal treatment of CPAM is surgical (thoracoscopic or open). There is clear benefit for surgical resection in symptomatic patients; however, the optimal management of asymptomatic lesions is less clear, as the natural progression of postnatal

CPAM is not fully understood. Symptomatic patients may present with lesion infection, respiratory distress, pneumothorax, hemorrhage, feeding difficulties, acute hypoxic events, and malignant transformation, although malignancy is relatively rare.[1]

Resection of asymptomatic lesions is often recommended to prevent complications. Additionally, type 4 CPAM cannot be differentiated from pleuro-pulmonary blastoma (PPB) on imaging.[1,9] While PPB is rare, it is an aggressive cancer. Thus, the potential for prevention can be a significant benefit to electively removing an asymptomatic type 4 lesion.[1] Other associated malignancies include bronchoalveolar carcinoma and rhabdomyosarcoma.[2] Another potential advantage of electively resecting an asymptomatic CPAM is a lower rate of surgical complications compared with emergent surgery for symptomatic patients. Observation is an option for asymptomatic patients.[1,2,9,10]

Conclusion

Congenital pulmonary airway malformations form from abnormal airway branching and is the most common congenital lung lesion. Prenatal ultrasound has increased antenatal diagnosis and improved prognosis. CPAM can be classified by its histopathological appearance or sonographic characteristics.

Postnatal diagnosis is typically made after clinical presentation of infection or respiratory distress. Chest radiography and CTA can characterize CPAM. However, diagnosis is most reliably made with specimen analysis, which can differentiate CPAM from rare but aggressive lesions.

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Periventricular Schwannoma

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Case Summary

A previously healthy child presented with left upper and lower extremity weakness and numbness.

Imaging Findings

Brain MRI demonstrated a large, right periventricular mass protruding into the lateral ventricle, with surrounding vasogenic edema, producing mass effect and resulting in subfalcine herniation and midline shift (Figure 1). Histopathologic examination demonstrated a well-delineated tumor with nodules of spindle cells with Verocay bodies, hyalinized blood vessels, loose Antoni B and compact Antoni A regions, and diffusely positive S100 immunohistochemistry (Figure 2). Findings were consistent with a pathological diagnosis of schwannoma, grade I.

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Diagnosis

Periventricular schwannoma. Although schwannomas have characteristic imaging findings when arising from cranial nerves, this lesion posed a diagnostic challenge due to its atypical location. The differential diagnosis for large, supratentorial intraparenchymal masses in children include glioblastoma, pilocytic astrocytoma, ependymoma, and atypical teratoid rhabdoid tumor.

Discussion

Schwannomas are benign, slow-growing nerve sheath tumors derived from Schwann cells forming the myelin sheath of peripheral nerves.[1] These tumors make up 8% of all primary intracranial tumors in adults and most often arise from cranial nerve VIII.[2,3] About 90% of schwannomas are solitary and sporadic; however, multiple tumors are associated with syndromic conditions such as neurofibromatosis type 2, schwannomatosis, and Carney complex. [4]

Schwannomas located in the periventricular region are rare and, unlike extra-axial schwannomas, they usually present in younger individuals.

Schwann cells are normally only found outside the pia mater surrounding the nerve sheath. They do not exist in the brain parenchyma or ventricles, thus making periventricular schwannomas a rare entity.[5,6] Intraoperative gross examination of this lesion demonstrated a mass originating near the lining of the lateral ventricle with intraparenchymal extension.

It has been hypothesized that a failure in neural crest cell migration during embryogenesis can result in Schwann cell remnants in the parenchyma and lining the ventricles; these cells can undergo neoplastic transformation.[7] Additional theories suggest that perivascular nerve plexi may give rise to schwannomas or that the presence of multipotential mesenchymal progenitor cells in the ventricular walls may differentiate into Schwann cells.[8-10]

Clinical manifestations of intracranial schwannomas vary depending on location and tumor size. Rare cases of periventricular schwannomas have been reported in the literature, manifesting with nonspecific symptoms such as nausea, vomiting,

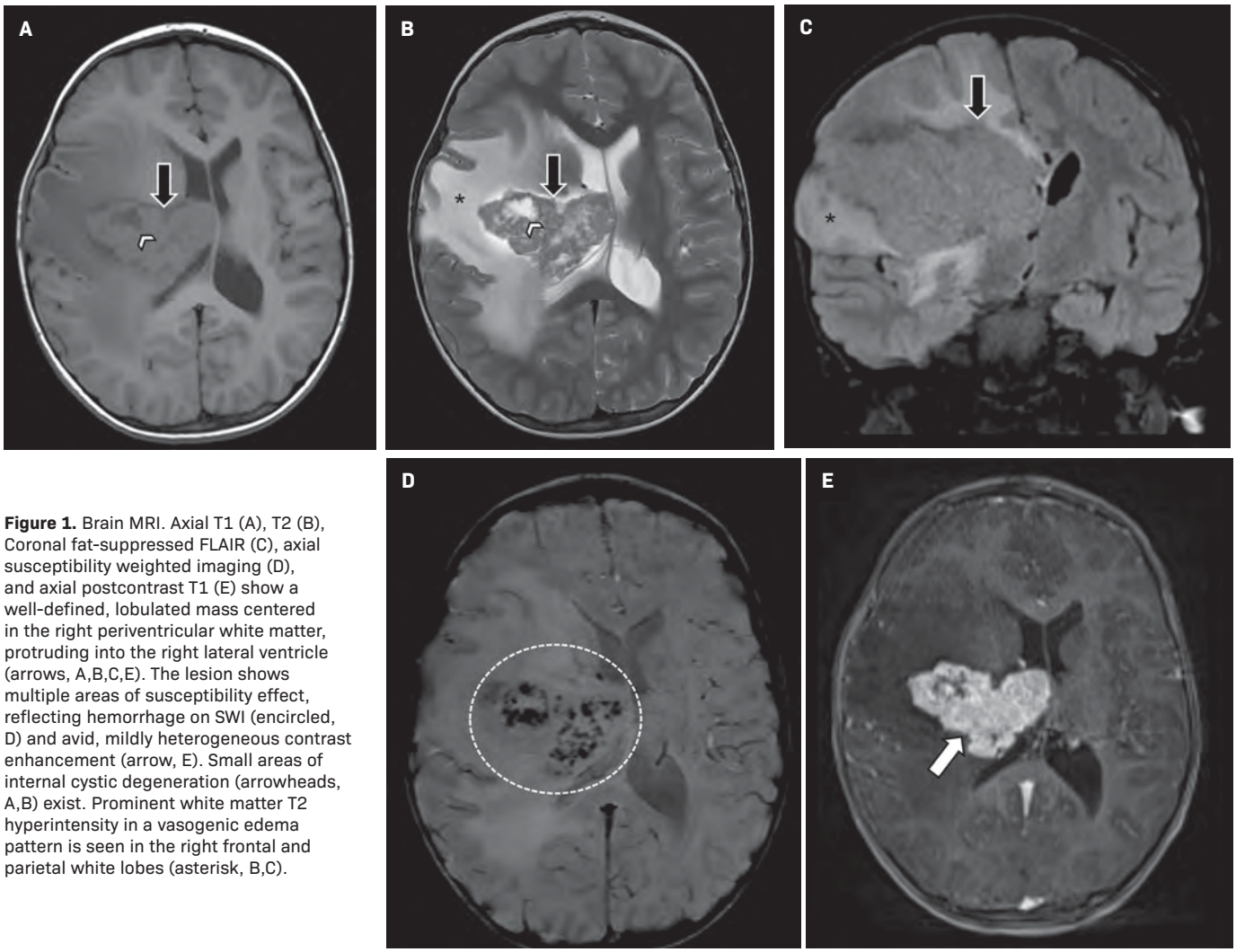

Figure 1. Brain MRI. Axial T1 (A), T2 (B), Coronal fat-suppressed FLAIR (C), axial susceptibility weighted imaging (D), and axial postcontrast T1 (E) show a well-defined, lobulated mass centered in the right periventricular white matter, protruding into the right lateral ventricle (arrows, A,B,C,E). The lesion shows multiple areas of susceptibility effect, reflecting hemorrhage on SWI (encircled, D) and avid, mildly heterogeneous contrast enhancement (arrow, E). Small areas of internal cystic degeneration (arrowheads, A,B) exist. Prominent white matter T2 hyperintensity in a vasogenic edema pattern is seen in the right frontal and parietal white lobes (asterisk, B,C).

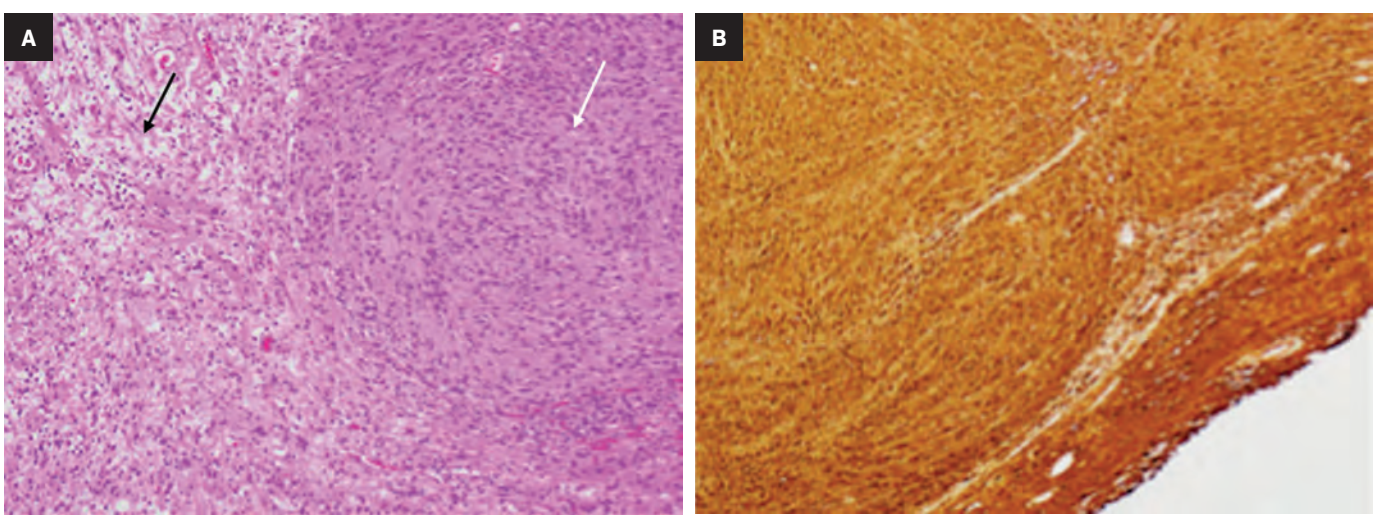

Figure 2. (A) Antoni B (loose, black arrow) and Antoni A (compact, white arrow) regions. (B) S100 immunohistochemistry is diffusely positive.

headache, focal neurological deficit, and/or seizure, depending on their location and extent. They have been reported to arise from any portion of the ventricular system, most commonly the right lateral ventricle.[5,11]

On CT, periventricular schwannomas will appear as isodense masses and may contain cystic degeneration and calcification. On MRI, findings are nonspecific with the mass being T1 hypo-to-isointense and T2 heterogeneously hyperintense. Contrast enhancement is typically avid but heterogeneous; cyst formation may be present. Associated perilesional edema is common; however the etiology remains uncertain in this low-grade lesion.[12,13] The lack of restricted diffusion may help differentiate these masses from highly cellular tumors and regions of susceptibility effect may be seen when the tumor contains calcifications and/or hemorrhagic foci.

Histopathologically, schwannomas show S100 positive cells, compact Antoni A regions, loose Antoni B regions, Verocay bodies, and hyalinized vessels.[1,2]

Surgical resection of periventricular schwannomas is recommended for symptomatic tumors. A very good prognosis and no recurrences have been identified at 24-month follow-up. Postoperative hydrocephalus is the most common complication. Adjuvant therapy is currently not indicated as regrowth recurrence, and/or malignant transformation of periventricular schwannomas are rare. [5,13]

Conclusion

We present a rare case of periventricular schwannoma. Owing to lesion's uncommon location, imaging-based diagnosis can be challenging, requiring histopathological diagnosis. Although the etiology of this tumor remains unproven, recent research suggests an origin from neural crest cells or multipotent mesenchymal progenitor cells along the ventricles.

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Hereditary Hemorrhagic Telangiectasia

Nisha Rehman; Richard B. Towbin, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Case Summary

A teenager had a history of a right temporal lobe stroke. Subsequent bubble echocardiogram was suspicious for a pulmonary arteriovenous malformation (AVM). The patient's parent and parent's sibling had a history of recurrent epistaxis; the parent also had a prior ruptured brain AVM. The history and ultrasound results raised the concern for hereditary hemorrhagic telangiectasia (HHT), prompting chest CT.

Imaging Findings

Contrast-enhanced CT of the chest demonstrated small pulmonary AVMs located in the lingula and right lower lobe (Figure 1). The pulmonary AVMs were successfully treated with embolization using coils (Figure 2).

Diagnosis

Hereditary hemorrhagic telangiectasia

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Discussion

Hereditary hemorrhagic telangiectasia (HHT), also called Osler-Weber-Rendu syndrome, is an inherited disease of vasculature dysplasia characterized by AVMs and telangiectasias throughout the body.[1] In 1896, Rendu was the first to write about the combination of familial epistaxis and telangiectasias separate from hemophilia.[2] In the next 10 years multiple case reports were published, including by Osler and Weber, giving rise to the name of the condition.[2]

HHT is a heterogeneous, autosomal dominant condition where mutations in two genes, *ENG* (Type 1) and *ACVRL1 (ALK1)* (Type 2), are implicated in 85% of cases. However, five different genes have been identified.[1] Patients can present with telangiectasias, which are blanchable, mucocutaneous, red/pink lesions located on the lips, tongue, face, fingers, and/or the nasal, buccal, and gastrointestinal (GI) mucosa.[1] These telangiectasias can sometimes rupture, leading to mild to severe bleeding.[3] Complications of telangiectasias include recurrent epistaxis, which can result in iron deficiency anemia.[4]

AVMs are vascular abnormalities defined as direct communication(s) of arteries to veins, that are often located in the liver, lung, and/or brain. These direct connections lead to more serious complications such as venous emboli entering the arterial circulation, hemoptysis, pulmonary hypertension, gastrointestinal bleeding, brain hemorrhage, strokes, brain abscesses. Myelopathy and back pain may be seen with spinal AVMs.[1]

HHT is diagnosed clinically by identifying multiple telangiectasias or AVMs in various locations throughout the body. The Curacao criteria created a consensus for diagnosis of HHT based on 4 elements: 1) spontaneous recurrent epistaxis, 2) multiple mucocutaneous telangiectasias, 3) visceral AVMs, and 4) a diagnosis in a first-degree relative.[4] A definitive diagnosis is made when three or more criteria are present. A diagnosis of possible or suspected HHT is made when two criteria are present. Diagnosis is unlikely when one or zero findings are present.[4] Genetic testing can confirm the diagnosis in approximately 75-85% of cases.

The lifetime prevalence and incidence of ruptured pulmonary AVMs are 2.7% and 0.16%, respectively.[5] Imaging for hepatic, pulmonary, or central nervous system AVMs is

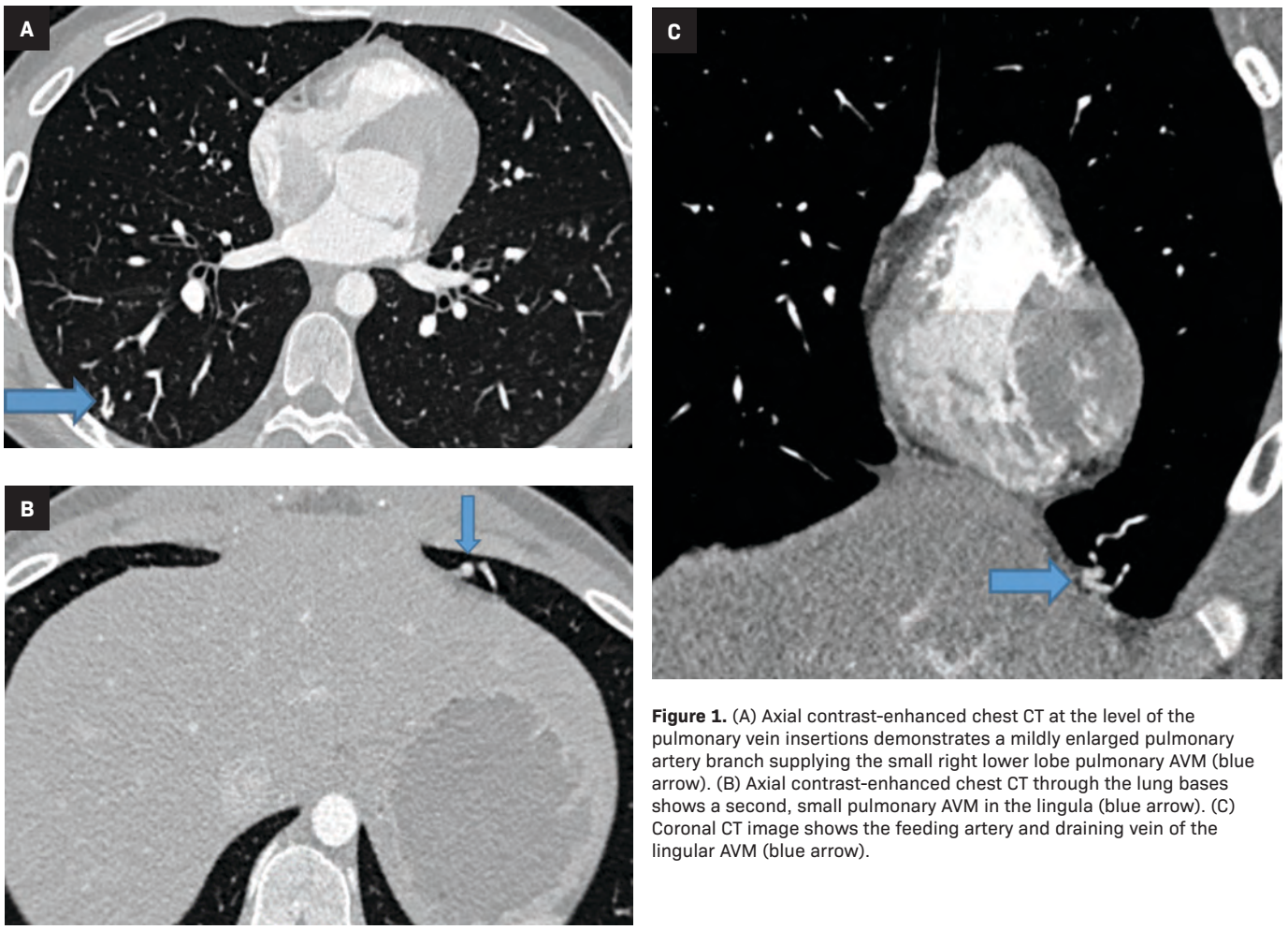

Figure 1. (A) Axial contrast-enhanced chest CT at the level of the pulmonary vein insertions demonstrates a mildly enlarged pulmonary artery branch supplying the small right lower lobe pulmonary AVM (blue arrow). (B) Axial contrast-enhanced chest CT through the lung bases shows a second, small pulmonary AVM in the lingula (blue arrow). (C) Coronal CT image shows the feeding artery and draining vein of the lingular AVM (blue arrow).

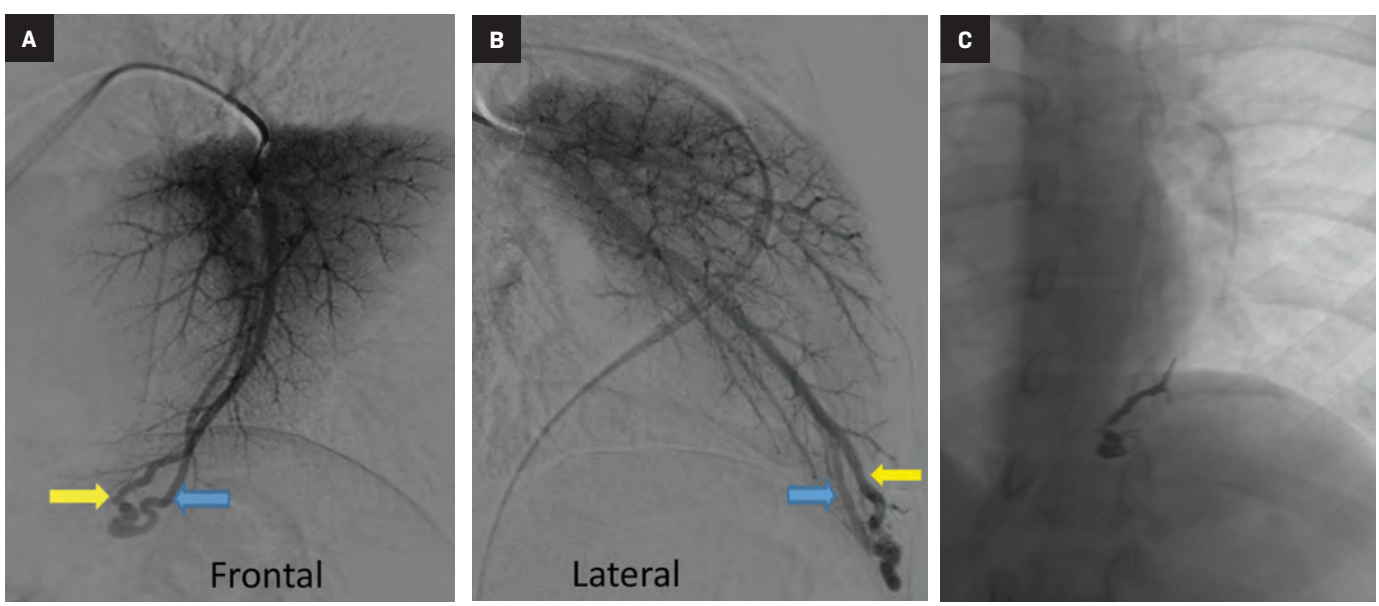

Figure 2. (A) Selective lingular branch pulmonary artery angiography in frontal and (B) lateral projection demonstrates the pulmonary arterial supply (blue arrow) and draining vein (yellow arrow) of the AVM. (C) Following embolization of the feeding artery using microcoils, a static contrast column is evident.

an important part of the workup of patients with suspected or known HHT. Contrast-enhanced echocardiogram (bubble echocardiogram) demonstrating intravenously injected microbubbles within the left atrium can confirm the presence of a pulmonary AVM. Pulmonary CT angiography (PCTA) is then used to identify the location, size, and number of pulmonary AVMs. On PCTA, AVMs will appear as a well-circumscribed vascular mass with one or more enhancing feeding arteries and draining vein(s).[3] Pulmonary AVMs can lead to hemorrhage and hemoptysis. Additional complications include paradoxical emboli, septic emboli, hypoxia, and high output cardiac failure.[6]

Hepatic AVMs occur in as many as 74% of patients with HHT although the majority are asymptomatic.[7] When evaluating patients for liver involvement, ultrasound, CT, or MRI can be used. Catheter angiography is typically not the first-line imaging study, but can be valuable if an intervention is contemplated.[7] These imaging modalities can reveal AVMs in the liver, arteriovenous or portal venous shunts, hepatomegaly, biliary necrosis, and bile leaks.[7] Hepatic AVMs can lead to high-output cardiac failure, portal hypertension, and biliary disease from shunting of the blood away from the peribiliary plexi.[7]

MRI is the preferred modality to identify central nervous system lesions; it can show telangiectasias and AVMs of the brain or spinal cord and any associated aneurysms.[8] Brain and spinal cord involvement can cause headaches, seizures, myelopathy, and hemorrhage.[8]

The GI tract is often evaluated via endoscopy, colonoscopy, or capsule endoscopy. Imaging may be performed if a patient has acute GI bleeding., CT, nuclear medicine-tagged red blood cell scans and catheter angiography are the tests of choice to evaluate active bleeding and embolization can be performed.[9,10]These imaging modalities can reveal AVMs or angiodysplasia in the esophagus, stomach, small bowel, or large bowel, which can be the cause of recurrent bleeding[9,10]

Conclusion

Imaging is necessary to diagnose and treat HHT. Contrast-enhanced chest CT, liver ultrasound, and abdominal, brain, and spine MRI help to identify AVMs, as well as to plan therapy and predict potential complications. CT and catheter angiography can play a role in AVM diagnosis and treatment, respectively. Embolization has become the treatment of choice for occluding AVMs in any organ.

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Bilateral Germ Cell Neoplasia In Situ with Left Testicular Seminoma

James Hwang, BS; Lauren F. Alexander, MD

Case Summary

An adult presented to the urology clinic with persistent scrotal pain approximately four months after emergency evaluation for a traumatic scrotal injury. The clinical exam revealed a nontender right testis with a hydrocele and a normal-size left testis with a barely palpable mass. The patient's alpha-fetoprotein (AFP) level was 2.3 ng/mL and beta-human chorionic gonadotropin (b-HCG) level was <0.6 IU/L, both within normal range.

Imaging Findings

Scrotal ultrasound (US) demonstrated a heterogeneous, mass-like protrusion from the right testis consistent with the history of testicular trauma, and bilateral punctate echogenic foci consistent with microlithiasis (Figure 1). Ultrasound of the left testis showed microlithiasis and a hypoechoic mass measuring 1.0 x 0.7 cm with color Doppler flow (Figure 2).

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Diagnosis

The patient was treated with trans-scrotal repair of the chronic posttraumatic right testicular rupture and with left partial orchiectomy via an inguinal approach. Pathology of the left testicular mass showed classic seminoma and tubular germ cell neoplasia in situ (GCNIS). Neoplastic cells were positive for CD117 and D2-40 and negative for keratin, CD30, and CD45, consistent with seminoma. Pathology of the right extruded testis showed infarct-like necrosis with granulation tissue. Tubular GCNIS was also present, with neoplastic cells positive for CD117. Six-month surveillance US showed expected changes after right repair and left partial orchiectomy (Figure 3); however, 19 months postoperatively, surveillance ultrasound identified two new left testicular lesions, indicating recurrent seminoma, confirmed after left inguinal orchiectomy.

Discussion

Testicular cancer most commonly occurs between the ages of 15 and 40 and accounts for 1% of all cancers in people with testes. Seminoma is the most common testicular tumor and typically presents as a painless mass between 30 and 40 years of age. Nonseminomatous tumors are often a mix of multiple germ cell subtypes and occur about a decade younger. Tumor markers should be obtained prior to treatment and include AFP, b-HCG, and lactate dehydrogenase (LDH). Seminoma can have elevated or normal b-HCG and LDH levels, while an elevated AFP level indicates nonseminomatous components.[1,2]

Germ cell neoplasia in situ, formerly intratubular germ cell neoplasia, increases the risk of germ cell tumor (GCT) formation. Other risk factors include history of contralateral testicular cancer, infertility, cryptorchidism, and disorders of sexual differentiation. GCNIS can be found adjacent to GCTs in nearly all specimens and in 4-8% of contralateral testes,[3] and 70% of patients with GCNIS develop invasive GCT within 7 years.[2]

Ultrasound is the standard imaging test for evaluation of scrotal pain and palpable masses.[4,5] Seminomas are typically homogeneous and hypoechoic on US, with smooth or lobulated borders. Hemorrhage, cysts, and calcification are uncommon but can be found in 10-30% of

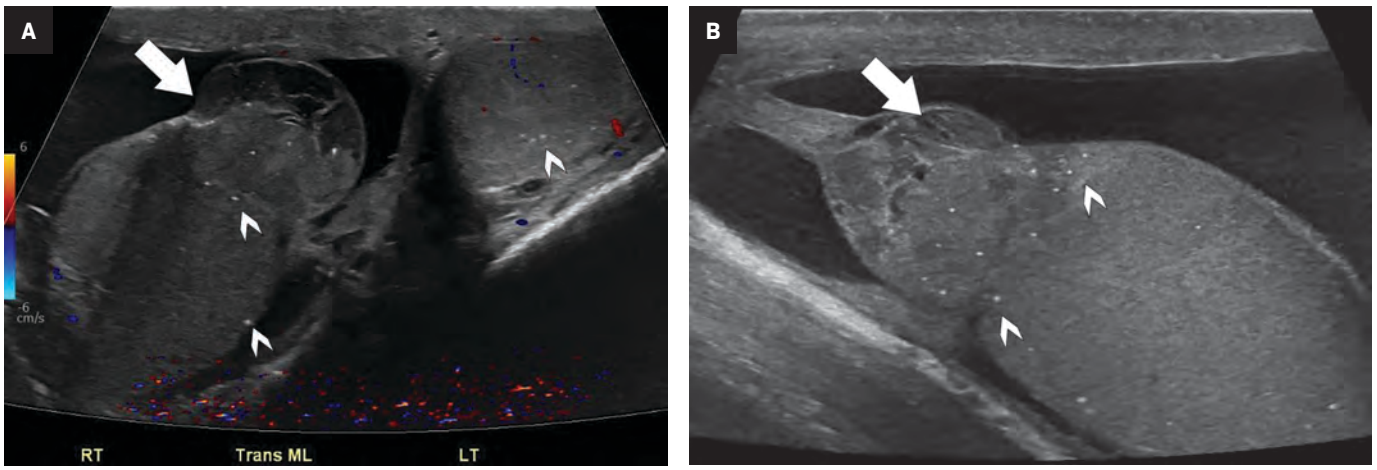

Figure 1. (A) Transverse Doppler US view of both testes demonstrates a heterogeneous, mass-like protrusion (arrow) from the right testis and bilateral punctate echogenic foci consistent with microlithiasis (arrowheads). (B) Longitudinal US image through the right testis shows disruption of the normal echogenic tunica and mass-like protrusion from the superior aspect (arrow) and microlithiasis (arrowheads).

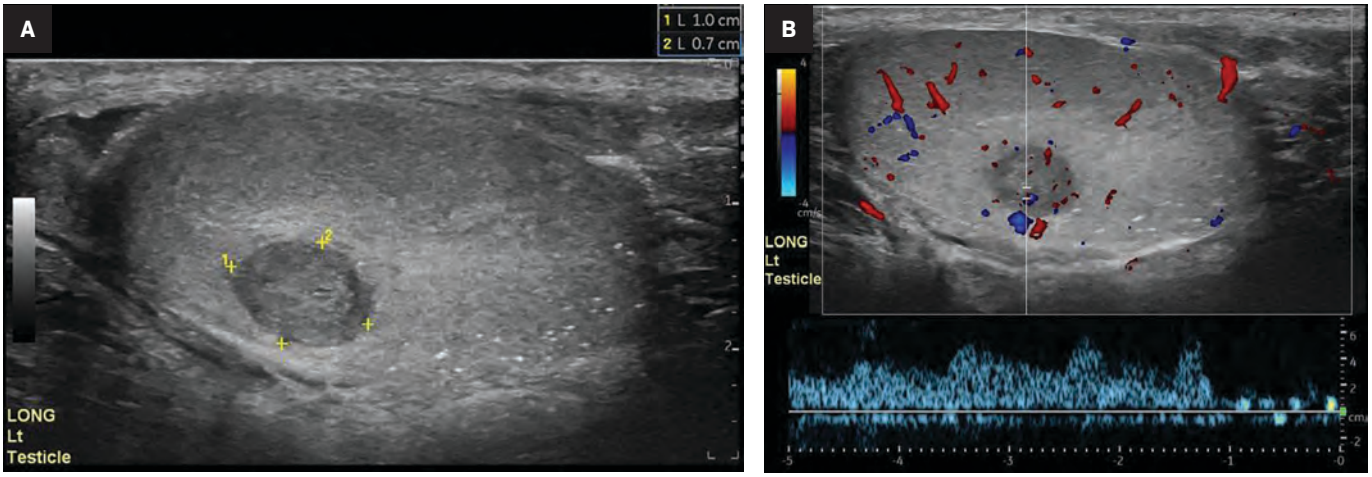

Figure 2. (A) Longitudinal US of the left testis shows microlithiasis and a hypoechoic mass measuring 1.0 x 0.7 cm (calipers). (B) Longitudinal Doppler US of the left testis shows flow in the solid mass.

these tumors.[1,6] Nonseminomatous GCTs have a more heterogeneous appearance owing to the variable tissue composition, and usually have ill-defined margins, internal cystic spaces, or calcifications.[3]

Testicular microlithiasis, or calcium deposition within the seminiferous tubules, is seen at US as echogenic foci in the parenchyma ranging from 1-3 mm in size. These calcifications can be seen with testicular tumors, as well as incidentally when no mass is found, and whether they serve as a risk factor or marker of neoplasm is unclear.[7] The American Association of Urology does not recommend follow up for patients with isolated microlithiasis and no other risk factors for GCT.[8]

Traumatic testicular injuries have several US features to help distinguish them from testicular neoplasms. Acutely, intratesticular hematomas are avascular, may appear isoechoic or heterogeneous in echogenicity, and should change appearance over hours to days as the blood products liquify and become more hypoechoic. Hematomas should rapidly decrease in size but may be heterogeneous owing to necrosis or becoming abscesses. Testicular rupture is identified by irregular contour resulting from disruption of the tunica albuginea.[9]

Radical inguinal orchiectomy is the gold standard treatment for testicular masses. However, testis-sparing surgery has been deemed a reasonable option for tumors smaller than 2 cm in diameter and less than 50% of total testis mass. Because of the risk of seeding with a trans-scrotal approach, a partial or radical orchiectomy is performed through an inguinal approach. Patients treated with partial orchiectomy without adjuvant therapy have a greater incidence of local recurrence compared with those who receive adjuvant radiotherapy.[10]

The prognosis for testicular cancer is excellent, with a 5-year survival rate of about 95% for localized testicular and regionally metastatic tumors. Distant metastatic tumors have a 5-year survival rate of about 72%.[6] After surgery, stage I tumors may be managed with surveillance, while stage IIA and some stage IIB tumors may be treated with radiation. Chemotherapy is used for stage IIB, IIC, and III disease.[1]

Conclusion

Seminoma is the most common testicular tumor and presents as a painless mass between the ages of 30 and 40 years. Ultrasound is the standard imaging test for testicular masses, and seminomas are typically homogeneous and hypoechoic, with smooth or lobulated borders. Microlithiasis may be present, although it is unclear whether this finding serves as a risk factor or marker of neoplasm. Radical inguinal orchiectomy is the gold standard treatment for testicular masses, but testis-sparing surgery is a reasonable option for small tumors. Treatment may also include surveillance, radiation, or chemotherapy, depending on tumor staging. The overall prognosis for patients with testicular cancer is excellent.

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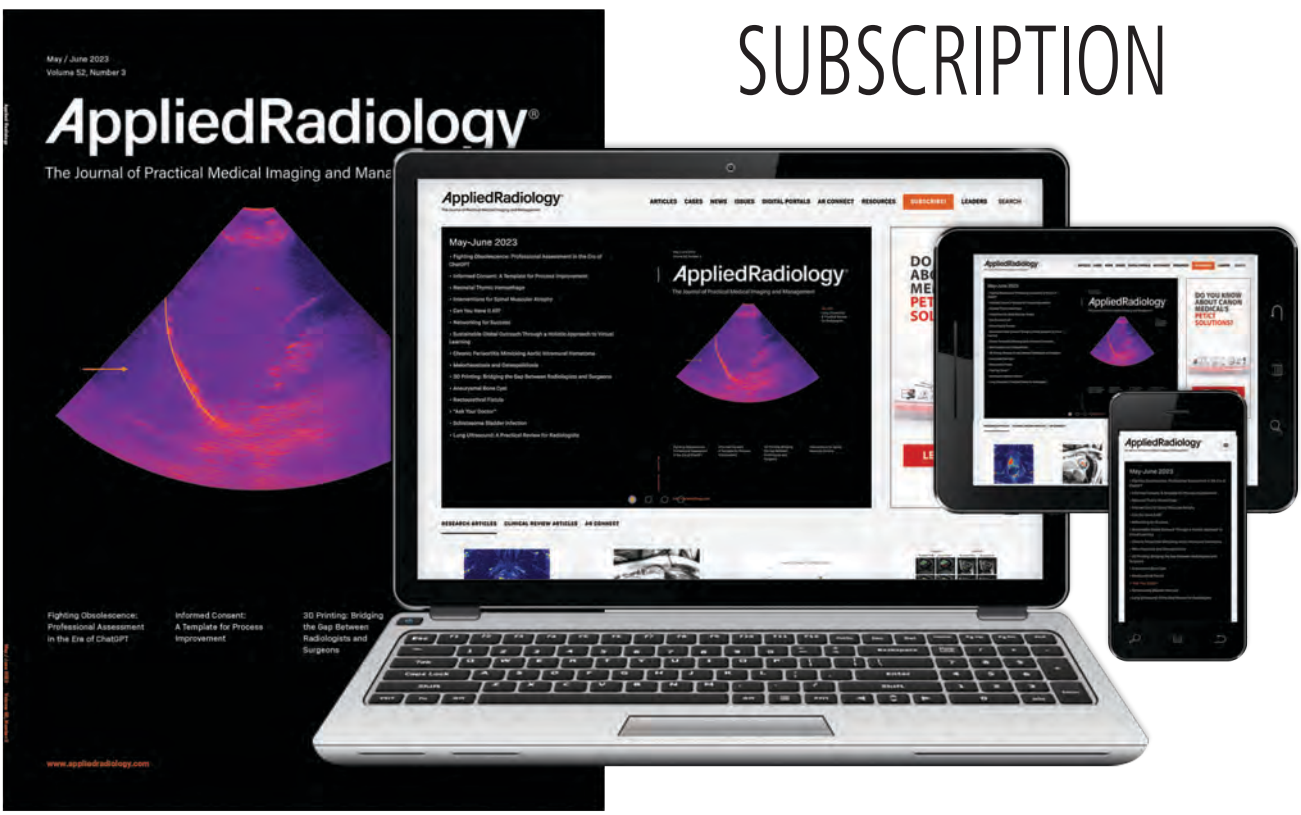

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"Folks are usually about as happy as they make their minds up to be."
—Abraham Lincoln

Wellness Redux

C. Douglas Phillips, MD, FACR

I think Lincoln hit it on the head. Something about the mindset of being happy is self fulfilling in many cases. Not always, but often. We're super concerned about "wellness" these days. I've seen institutions with so-called "deans of wellness," a high-level administrative position (inarguably highly paid) that in my mind is a person in an office with a large-screen TV and a great sound system playing comedy movies on an endless loop while they themselves are throwing darts at a dartboard. They have a scotch cabinet in the corner with a great single malt in their other hand. You may get invited in to have a game, if you're lucky or complain a lot. I digress.

Do you all remember wellness in the prior era? I certainly do:

ME: "I'm not happy."

ADMIN: "You've got a job. You're happy."

ME: "Hmmm, you've got a point there. Thanks for the pep talk."

Now, we fret over everything that someone has in some fashion linked to our job happiness. I'm not saying this is all wrong, please understand. I'm just saying that it seems that the wellness cart may be way out in front of the job/stress horse.

Wellness in the current era:

ME: "I'm not happy."

ADMIN: "Well, obviously it has nothing to do with that ever-expanding worklist, decreased staff, fewer support personnel, and constant demand for higher productivity. Maybe we should get you an hour massage at a local spa this weekend, eh?"

A short list of things that have recently been proposed to me as wellness solutions for radiologists: improved mouse pads, ergonomic keyboards, curved monitors, white-noise generators, stand-up workstations for reading, jogging workstations for reading, low UV lighting, classical music, jazz music, programmed coffee/snack times, shorter workdays, segmented workdays, team-building exercises, bowling outings, sports outings, AI (in every guise possible), auto-dialing services to call clinicians (who won't answer the phone anyway), yoga breaks, Pilates breaks, conversation breaks … . The list goes on, approaching forever at this point.

Gandhi said, "Happiness is when what you think, what you say, and what you do are in harmony." What we do is pretty cool, I think. I've pretty much always liked looking at images and formulating an opinion about the findings and hopefully training some residents and fellows and, as a bonus, working with other clinicians to help patients. I'm all for wellness. I just have other opinions as to how to scratch that itch.

Stay well, seriously.

And 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.

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