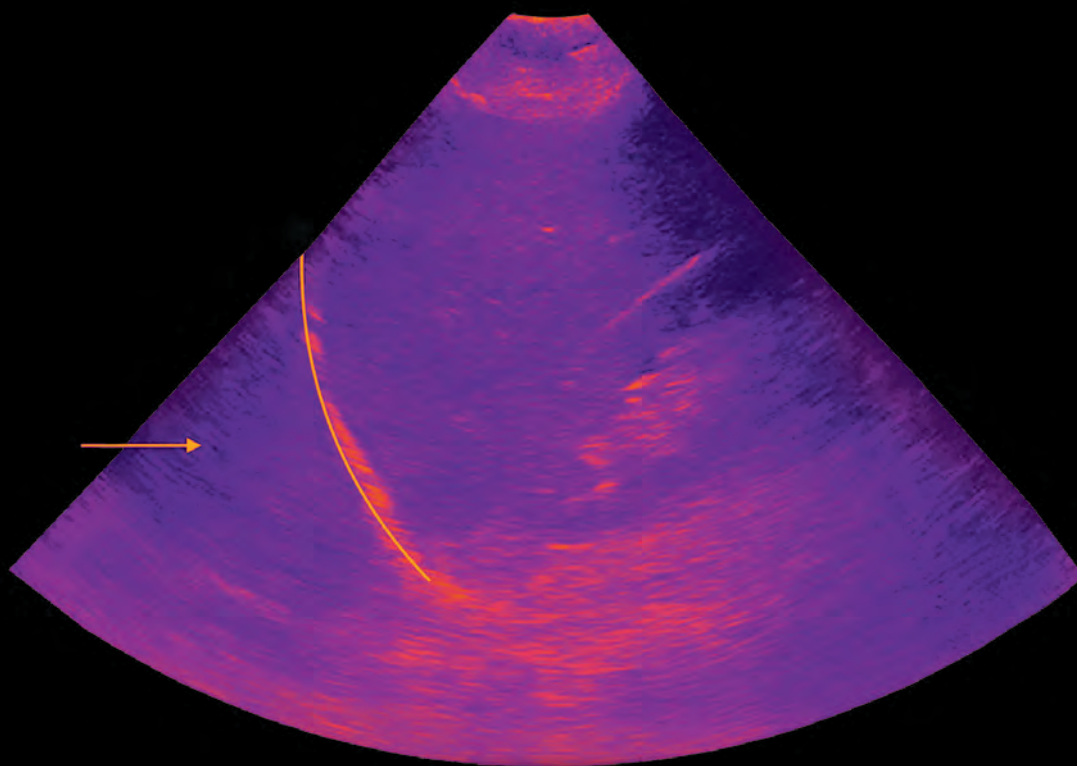


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AppliedRadiology®

The Journal of Practical Medical Imaging and Management

SA-CME
Lung Ultrasound:
A Practical Review
for Radiologists



Fighting Obsolescence:
Professional Assessment
in the Era of ChatGPT

Informed Consent:
A Template for Process
Improvement

3D Printing: Bridging
the Gap Between
Radiologists and
Surgeons

Interventions for Spinal
Muscular Atrophy

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-contrast 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.

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.



IN MRI

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.



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 $\geq 0.5\%$) 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 Macrocyyclic 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.

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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-contrast 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 gadopidlenol.

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.

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, arrhythmia, 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 gadopidlenol 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 gadopidlenol 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. Gadopidlenol 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 [¹⁵³Gd]-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 gadopidlenol 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 gadopidlenol 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 gadopidlenol (6 times the recommended dose of Vueway), headache and nausea were the most frequently reported adverse reactions. Gadopidlenol 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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Vol 52 No 3

8 Lung Ultrasound: A Practical Review for Radiologists

Samuel J. Tate, MD; Jeffrey Lin, DO, MPH;
John P. McGahan, MD

Although lung ultrasound is a growing component of patient care, the modality has not traditionally been taught in radiology residency. This review of LUS is aimed at providing radiologists and radiology residents a practical, clinically useful guide to performing and interpreting normal and pathologic ultrasound findings.

SA-CME

20 Fighting Obsolescence: Professional Assessment in the Era of ChatGPT

Lincoln L. Berland, MD; Seth M. Hardy, MD, MBA

The recent release of ChatGPT, a natural language processing technology developed by San Francisco, CA-based OpenAI.com, has excited many across the US with its promise of disruptive innovation in a wide range of fields, including healthcare. ChatGPT, however, is not without risks, particularly with respect to radiology education and assessment.

24 Informed Consent: A Template for Process Improvement

Evan Ruppell, DO; David Gerson, MD;
Steven J. Baccei, MD

The radiology department at the University of Massachusetts Medical School/UMass Memorial Medical Center in Worcester, Massachusetts, recently undertook to improve its informed consent processes. The authors share the challenges they faced and steps they took to adopt standardized, digitally based documentation to facilitate more consistent, and potentially more accurate, informed consent processes.

EDITORIAL

6 Can You Have It All?

Erin Simon Schwartz, MD, FACR

FIRST IMPRESSIONS

28 Networking for Success

Yasha Parikh Gupta, MD

RADIOLOGY MATTERS

30 3D Printing: Bridging the Gap Between Radiologists and Surgeons

Kerri Reeves

EYE ON AI

34 Why Radiologists are Key to Maximizing AI's Potential in Healthcare

Elad Walach

GLOBAL HEALTH IMAGING

36 Sustainable Global Outreach Through a Holistic Approach to Virtual Learning

Mai Elezaby, MD; Carley Hansen-Prince, MEd, RT (R) (ARRT);
Jenna MacLaine, RTR, CTIC, CAE, BSc

RADIOLOGICAL CASES

38 Neonatal Thymic Hemorrhage

Jonah A. Wachs; Jade B. Greer, MS; Lavi Nissim, MD;
Angela R. Garcia, PhD; Sudhen B. Desai, MD, FSIR

40 Chronic Periaortitis Mimicking Aortic Intramural Hematoma

Adam Kerestes, DO; Thaddeus Yablonsky, MD

43 Aneurysmal Bone Cyst

Richard Wang, MD; Karen Yuan, MD; Saad Nini, MD; Gaurav Saigal, MD

46 Melorheostosis and Osteopoikilosis

Carmen Popa, MD; Andrei-Catalin Moisin, MD; Ciprian Tanasescu, MD;
Denisa Tanasescu, MD; Mihaela Racheriu, MD

48 Rectourethral Fistula

LeShell Washington, BA; Muhammad Danial, DO; Bhishak Kamat, MD

50 Schistosoma Bladder Infection

Andrew A. Wigger; Alexander J. Towbin, MD; Daniel Morgan, MD;
Richard B. Towbin, MD

53 Interventions for Spinal Muscular Atrophy

Janki Desai; Richard B. Towbin, MD; Carrie M. Schaefer, MD;
Alexander J. Towbin, MD

WET READ

56 "Ask Your Doctor"

C. Douglas Phillips, MD, FACR

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Can You Have It All?

Erin Simon Schwartz, MD, FACR

Recently, I was invited to deliver a lecture titled, “Work-Life Balance: Can You Have It All?” My first instinct was to approach the podium, announce the title, say “No,” and sit back down.

Tempting as that would have been, it would not be entirely accurate. Or professional. Or respectful of the organizers. But it would be funny.

All joking aside, I did feel the need to revise the title. The term “work-life balance” is a well-worn phrase, that is true. But for me, it brings to mind a seesaw, with work on one side, life on the other, and a continuous struggle to keep it perfectly even.

Most of us know that’s not reality.

I have long preferred to call it “work-life integration.” There are times – like right now as I write this on an airplane taking me far from my family— when we should be 100 percent focused on work. And there are other times—on days off, on vacation, enjoying time with friends —when we should be entirely focused on life.

My goal is to integrate my personal and professional demands in such a way that they enhance my well-being over the long haul.

It’s been argued that work-life balance is a continuous cycle of re-assessment and adjustment, not an achievement; that a balanced life “integrates the personal and the professional in a healthy way, supporting an identity that includes the career, but doesn’t necessarily revolve around it.”^{1,2}

Studies show that professionals who report the highest levels of happiness are those who are able to “compartmentalize, to disconnect, to switch off without guilt from work.”²

That all sounds great. But, for me, being accessible to colleagues via cellphone, email, text, drop-ins, and applications like Slack makes disconnecting from work virtually impossible. They also make separating from my “life” during work hours equally challenging, especially when working from home.

It is a tough time for radiologists. Case volumes are sky high at many places, with little to no hope among those in academia for lower research and education obligations. Add roles like journal editor, division chief, medical director, and society president, and it’s enough to make your (my!) head spin.

Yes, these are positions that I have actively chosen, but that doesn’t mean they aren’t exhausting at times. I have also chosen my roles as spouse and parent, and they are also exhausting at times. But I could not succeed in any of my work roles without the support of my family, who are my life.

Some experts argue that one’s goal should be to avoid working too much.³ Sadly, their definition of “too much” is laughable in healthcare. Remember the battles over cutting trainees down to 80 hours a week? For many of us, 45 hours a week is practically part-time. And yet working beyond that has been shown detrimental to physical and mental well-being.³

Our performance relies on optimal brain function, which in turn requires strong physical and mental well-being. We cannot achieve either by furiously working in airports to meet deadlines, checking email on vacation, or taking on yet another professional role.

To paraphrase an old advertisement, we may have come a long way, baby. But we still have a long way to go.

References

- 1) <https://hbr.org/2021/01/work-life-balance-is-a-cycle-not-an-achievement>. Accessed April 28, 2023.
- 2) <https://www.bbc.com/worklife/article/20230227-what-does-work-life-balance-mean-in-a-changed-work-world>. Accessed April 28, 2023.
- 3) <https://www.forbes.com/sites/maurathomas/2022/07/26/what-does-work-life-balance-even-mean/?sh=402e31072617>. Accessed April 28, 2023.

Lung Ultrasound: A Practical Review for Radiologists

Description

Lung ultrasound (LUS) has become a powerful bedside tool in diagnosing pathology, guiding procedures, and directing management. Knowledge and interpretation of artifactual patterns, true parenchymal structures, and signs unique to LUS will allow providers to utilize this modality in their care of patients. This activity is designed to educate radiologists about basic findings of lung ultrasound to help interpret images and refine differentials with this modality.

Learning Objectives

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

- Describe the technique of obtaining an adequate lung window on ultrasound.
- Identify typical normal and abnormal patterns of the lung on ultrasound.
- Differentiate similar ultrasound findings of interstitial syndrome based on distribution, pleural line findings, and concomitant ultrasound findings.

Target Audience

- Radiologists
- Related Imaging Professionals

Authors

Samuel J. Tate, MD; Jeffrey Lin, DO, MPH; John P. McGahan, MD

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Lung Ultrasound: A Practical Review for Radiologists

Samuel J. Tate, MD; Jeffrey Lin, DO, MPH; John P. McGahan, MD

Although lung ultrasound (LUS) is a growing component of patient care, the modality has not traditionally been taught in radiology residency.¹ The 2022 diagnostic radiology program requirements of the Accreditation Council for Graduate Medical Education state that, “residents must demonstrate competence in the generation of ultrasound images using the transducer and imaging system.” However, a recent survey of radiology residents found that only 26% believed they received adequate training to perform their own ultrasounds scans.²

The goal of this focused review of LUS is to provide radiologists and radiology residents a practical, clinically useful guide to performing and interpreting normal and pathologic ultrasound findings.

History of Lung Ultrasound

The medical application of ultrasound emerged around the halfway point of the 20th century. In 1959, Crawford et al used a device consisting of a transmitting transducer on the anterior chest and a receiving

transducer on the posterior chest to describe differing decibel transmissions through the chest with inspiration and expiration.³ Subsequent clinical studies focused primarily on the pleural space or findings just deep to the pleural line and demonstrated LUS utility in identifying and assessing pleural effusions after thoracentesis. Specifically, LUS showed echogenic changes at the periphery of the lung, suggesting ischemic zones consistent with pulmonary emboli, and demonstrated its utility in guiding peripheral pulmonary mass biopsy.⁴⁻⁶

As the field evolved, investigators moved from evaluating structure to interpreting artifacts produced by ultrasound’s interaction with the pleural line and the lung behind it. A major advancement in our collective understanding of the utility of LUS came with the exploration of these artifacts and their subsequent patterns, culminating in publication of the BLUE Protocol in 2008.⁷ This publication helped to define LUS patterns for specific diseases such as chronic obstructive pulmonary disease, pulmonary edema, pneumothorax, and pneumonia. Additionally, it offered an algorithmic decision tree for diagnosing one of these disease processes based on a handful of LUS findings and their distribution within the thorax. This gave the bedside

provider a tool to rapidly assess and diagnose the cause of respiratory distress in real time. Lung ultrasound has since gained significant traction in clinical practice.

Scanning Technique and Normal Lung Findings

Lung ultrasound can be performed with a low-frequency phased array or curvilinear probe to highlight artifactual patterns. The linear probe can highlight pleural pathology. The bright hyperechoic pleural line is identified between ribs within intercostal spaces (Figure 1). With breathing the visceral pleura moves in relationship to the parietal pleura. This is best appreciated in real time and has been termed “lung sliding.” This sign is important, as it defines the periphery of the lung parenchyma, which must be avoided during biopsy of the subdiaphragmatic liver lesion or while performing thoracentesis.

The absence of lung sliding may be indicative of a pneumothorax resulting from trauma, a thoracic and/or abdominal biopsy, or drainage procedures. In the normal lung, deep to the pleural interface, are horizontal hyperechoic lines called “A” lines, which are reverberation artifacts occurring between the transducer and the parietal/visceral pleural

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Conflicts of Interest: None

Figure 1. Normal pleural line (dotted arrow). Note the subtle A-line (reverberation artifact) present with decreased brightness posterior to the pleural line (curved arrows). These are visualized between two ribs, showing anterior rib cortex with posterior acoustic shadowing (solid arrows).

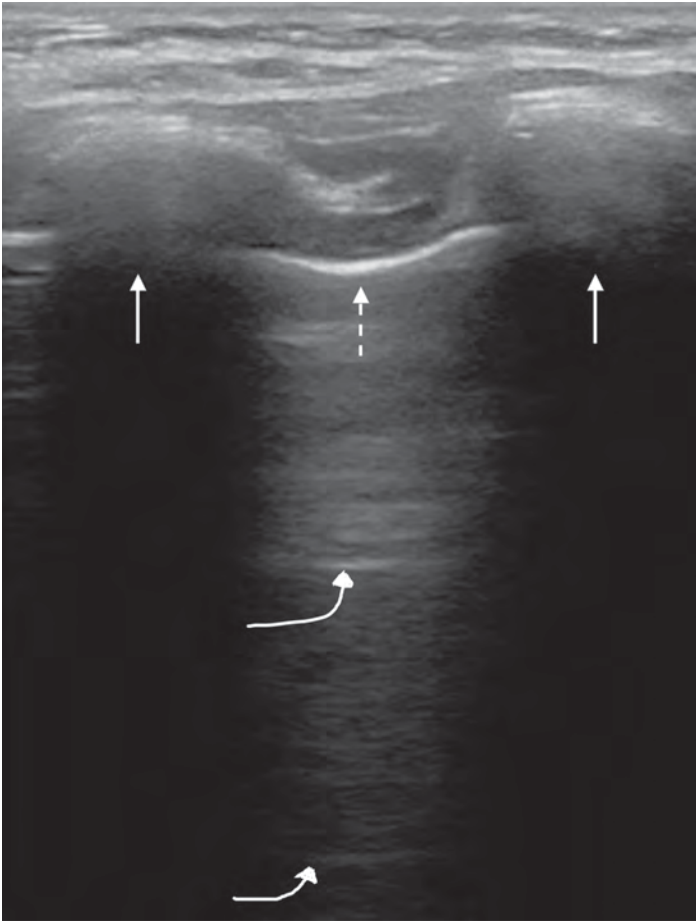


Figure 2. A-lines. Equidistant horizontal reverberation artifacts of the pleural line (thick arrow) visualized deep to the pleural interface (thin arrows). These lines are of decreasing brightness with each subsequent line.

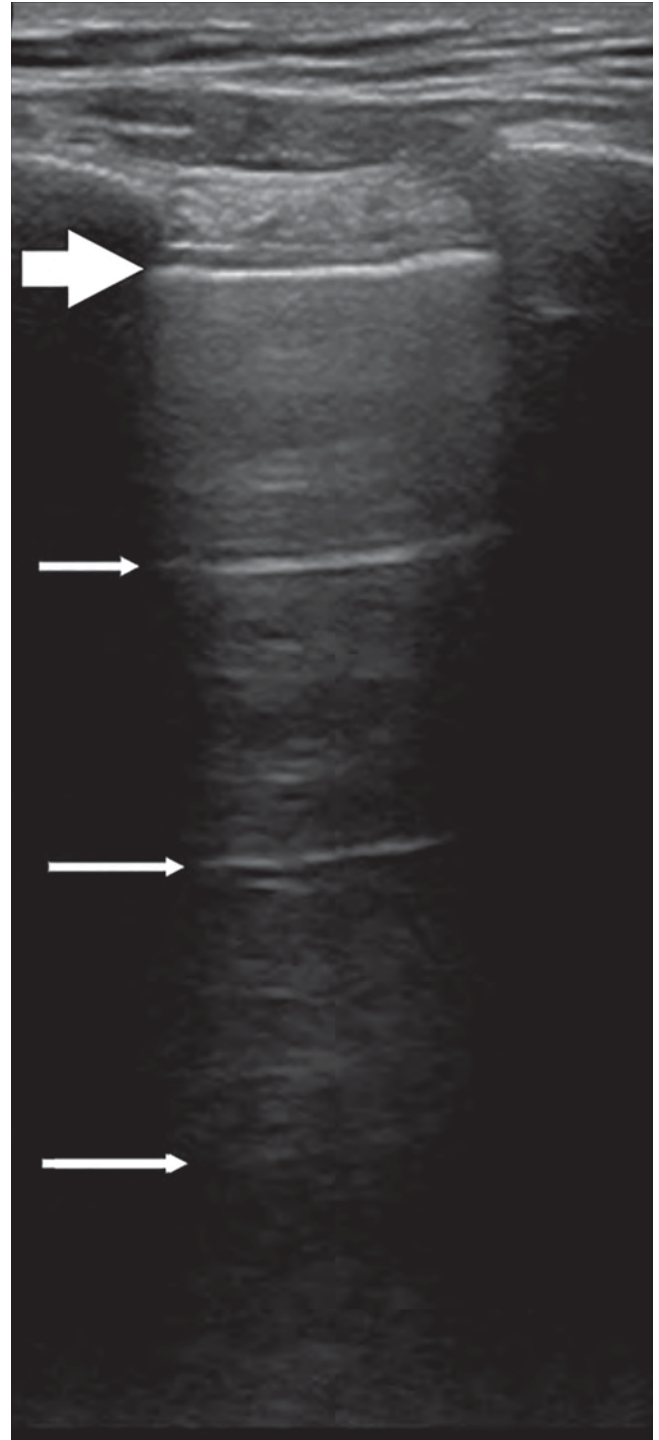


Figure 3. Mirror image artifact. This artifact is generated at tissue boundaries due to a strong reflector such as the diaphragm. Superior to the diaphragm (white curved line) there appears to be liver parenchyma (arrow). The artifact should have the same acoustic texture as the liver. On color Doppler the color in the liver will be artifactually seen above the diaphragm.

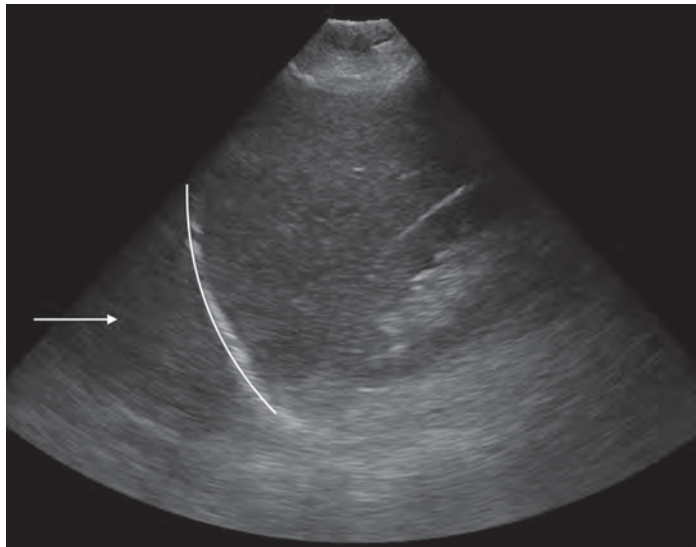


Figure 4. (A) Curtain sign-inhalation. Normal pleural line (arrow) obscures the view of intraabdominal structures in the costophrenic recesses at the diaphragm-lung interface due to the presence of air during the respiratory cycle. (B) Curtain sign-exhalation. The lung moves out of view during exhalation allowing better visualization of intraabdominal structures in the costophrenic recess.

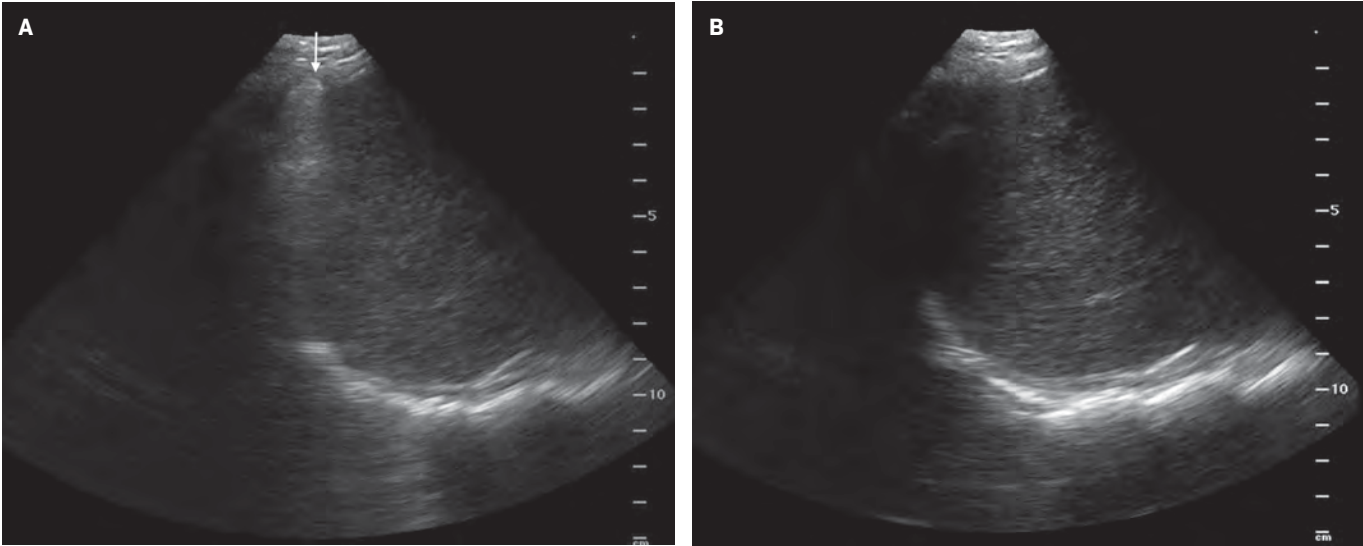


Table 1. Normal Artifacts in Ultrasound.	
Definition	
A - Lines	A-lines are reverberation artifacts. These equidistant horizontal lines propagate deep to the pleural line and decrease in intensity with depth.a,b Seen in normal lung as well as in states of pathology.
Mirror Artifact	Mirror image artifact occurs when the beam hits a highly reflective curvilinear border such as the diaphragm. The beam is redirected as it encounters a specular reflector. When viewed from inferior to the diaphragm through the liver or spleen, the sound waves are reflected off the diaphragm, creating a false, duplicated image superior to the diaphragm in the setting of well aerated, normal lung.
Curtain Sign	The curtain sign occurs when normal lung obscures the view of intraabdominal structures in the costophrenic recesses at the diaphragm-lung interface due to the presence of air. When seen in the setting of normal lung, it dynamically moves with respiration and the lateral aspect of the diaphragm is obscured.

a. Stassen J, Bax JJ. How to do lung ultrasound. *Eur. Heart J. Cardiovasc. Imaging*. 2021;23(4):447-449. doi:https://doi.org/10.1093/ehjci/jeab241

b. Soldati G, Demi M, Smargiassi A, Inchingolo R, Demi L. The role of ultrasound lung artifacts in the diagnosis of respiratory diseases. *Expert Rev. Respir. Med*. 2019;13(2):163-172. doi:https://doi.org/10.1080/17476348.2019.1565997

c. Lee FCY. The Curtain Sign in Lung Ultrasound. *J. Med. Ultrasound* 2017;25(2):101-104. doi:https://doi.org/10.1016/j.jmu.2017.04.005

interface. They are displayed at equidistant intervals within the lung and, if accompanied by lung sliding, indicate no pneumothorax is present in this region (Figure 2). The ribs are seen as hyperechoic structures with dense shadowing deep to the ribs and overlying the pleura. Thus, the pleural interface cannot be identified posterior to the ribs because of the acoustic shadowing.⁸

Lung ultrasound relies on the sonographer's ability to identify the presence or absence of true structures and artifacts. Fully aerated lung scatters ultrasound waves, preventing

visualization of the parenchyma and instead creating an artifactual representation.⁹ One artifactual pattern of normal tissue is mirror image artifact, which occurs when a false image of the liver or spleen superior to the diaphragm is created by the subdiaphragmatic ultrasound beam hitting a highly reflective curvilinear border, in this case the diaphragm (Figure 3).¹⁰ The "curtain sign" is another helpful artifact that distinguishes the inferior border of well-aerated lung from the costophrenic recess. As it moves inferiorly during inspiration, the aerated lung covers the liver and spleen like a

window curtain, preventing visualization of deeper abdominal structures (Figure 4). These normal lung artifacts are further explained in Table 1.

Lung Ultrasound in Medical Pathology

Although disease processes can overlap, the combination of the distribution and pattern of ultrasound findings, along with the clinical context, can help to diagnose specific pathologies.¹¹ Table 2 highlights pathologic findings used to build the signature of a disease process.

Table 2. Lung Pathology	
B-lines	Vertical, hyperechoic, discrete artifacts arising from the pleural line and extending to the bottom of the screen without fading. They move with the lung during the respiratory cycle and erase the A-lines. When present, they confirm there is no pneumothorax present.
Pleural Thickening	In healthy lung, the pleura should be thin (<0.2-0.5 mm) with pleural sliding and a typical A-line pattern. In some disease processes, such as ARDS, interstitial pneumonia, and pulmonary fibrosis, the pleural line itself will appear thickened.
Subpleural (Small) Consolidations	Hypoechoic regions just deep and adjacent to the pleural line of various sizes. They move with lung during respiration.
Pleural Effusion	An anechoic fluid collection superior to the diaphragm with characteristic extension of the thoracic spine superior to the diaphragm, known as the spine sign. In normal lungs, the spine is obscured above the diaphragm due to the high acoustic impedance of the lungs.
Hepatization	Consolidated lung suggestive of infection or contusion may appear as dense tissue that looks similar to the echogenicity of liver tissue.
Sonographic Air Bronchogram	Hyperechoic tubular structures representing the small airways within consolidated lung. In normal lung these cannot be seen.

a. Volpicelli G, Elbarbary M, Blaivas M, et al. International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med.* Apr 2012;38(4):577-91. doi:10.1007/s00134-012-2513-4

b. Lichtenstein D. Lung ultrasound in acute respiratory failure an introduction to the BLUE-protocol. *Minerva Anesthesiol.* May 2009;75(5):313-7.

c. Musolino AM, Toma P, De Rose C, et al. Ten Years of Pediatric Lung Ultrasound: A Narrative Review. *Front Physiol.* 2021;12:721951. doi:10.3389/fphys.2021.721951

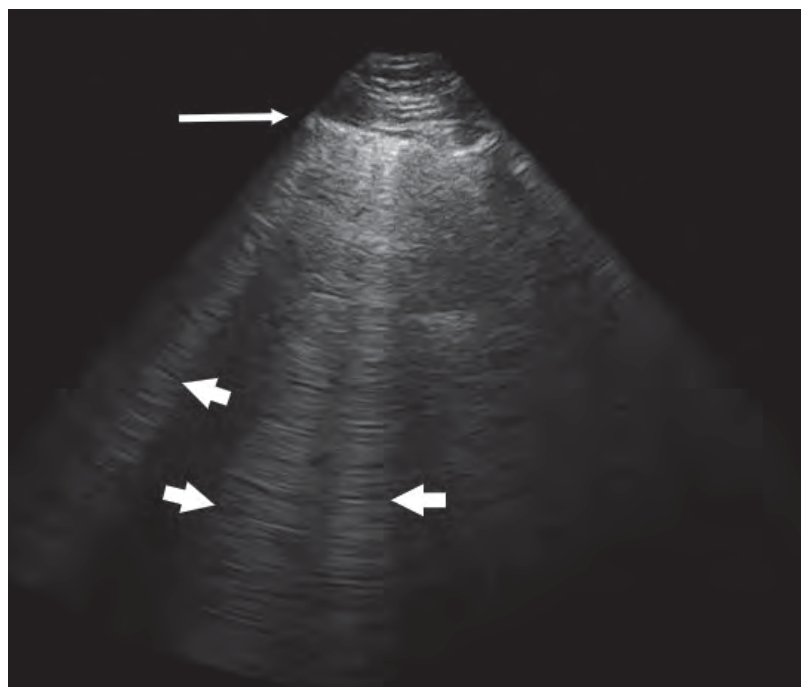
d. Gravel CA, Neuman MI, Monuteaux MC, Neal JT, Miller AF, Bachur RG. Significance of Sonographic Subcentimeter, Subpleural Consolidations in Pediatric Patients Evaluated for Pneumonia. *J Pediatr.* Apr 2022;243:193-199 e2. doi:10.1016/j.jpeds.2021.12.052

e. Dickman E, Terentiev V, Likourezos A, Derman A, Haines L. Extension of the Thoracic Spine Sign. *J Ultrason.* 2015;34(9):1555-1561. doi:10.7863/ultra.15.14.06013

f. Bhoil R, Ahluwalia A, Chopra R, Surya M, Bhoil S. Signs and lines in lung ultrasound. *J Ultrason.* Aug 16 2021;21(86):e225-e233. doi:10.15557/JoU.2021.0036

g. Unlukaplan IM, Dogan H, Ozucelik DN. Lung ultrasound for the diagnosis of pneumonia in adults. *J Pak Med Assoc.* Jun 2020;70(6):989-992. doi:10.5455/JPMA.3390

Figure 5. B-lines. A thin pleural line (long arrow) is seen anteriorly. Note how the B-lines extend to the bottom of the screen, erasing potential A-lines.



B-Line Normal and Abnormal

B-lines are vertical, hyperechoic lines that begin at the pleural line, extend to the depth of the image, and move with lung sliding. They are hyperechoic artifacts that have

been described as “comet tails” or “spotlights in the fog.” The B-lines erase the A-lines and run from the top to the bottom of the screen. (Figure 5) Occasionally, thin B-lines can be identified in normal lung, especially in the bases.¹² However, the presence

of multiple B-lines (more than three between two ribs in a single image) in two or more lung regions bilaterally defines interstitial syndrome. Interstitial syndrome describes heterogeneous clinical pathologies with similar ultrasound findings that are thought to have decreased air content and increasing lung density with a diffuse pattern of B-lines.¹¹ Interstitial syndrome is not itself a sign of interstitial lung disease; instead, it has a much broader differential of pathological processes. Those associated with areas of multiple B-lines include pulmonary edema, interstitial pneumonia or pneumonitis, and diffuse parenchymal lung disease such as pulmonary fibrosis.¹³ B-lines can be found focally (therefore not meeting the criteria for interstitial syndrome) in pneumonia, atelectasis, pulmonary contusion, pulmonary infarction and neoplasia, so care should be taken to identify the distribution of these B-lines within the thorax.

In general, the distribution of B-lines, effects on the pleural line, and concomitant ultrasound findings such as echo and inferior vena cava evaluation can help differentiate

Figure 6. Thickened pleural line (white arrow) >0.2-0.5 mm with B-lines emanating and extending deep to the pleural interface. This finding would make cardiogenic pulmonary edema less likely.

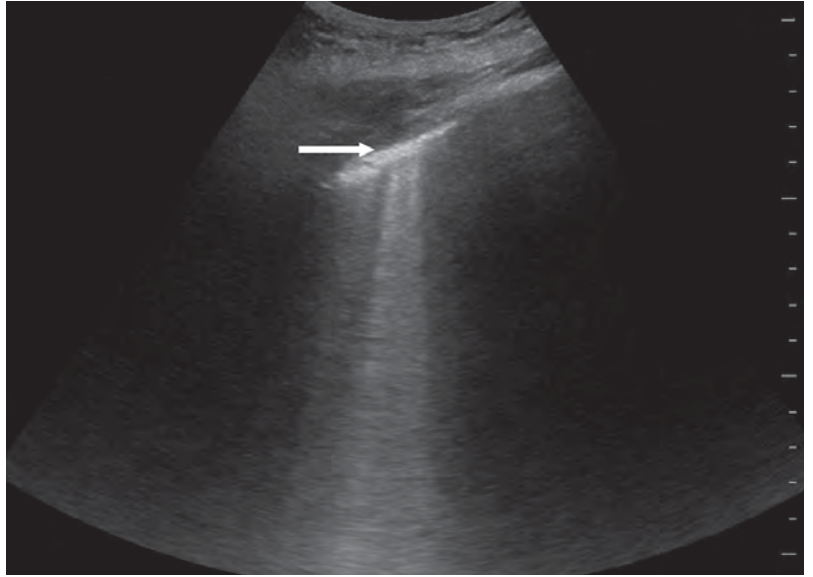


Figure 7. Subpleural consolidation. Hypoechoic areas just beneath the parietal pleura consistent with subpleural consolidations (arrows). In the video correlate, notice how these hypoechoic areas move with respiration, helping distinguish consolidation from a small pleural effusion.

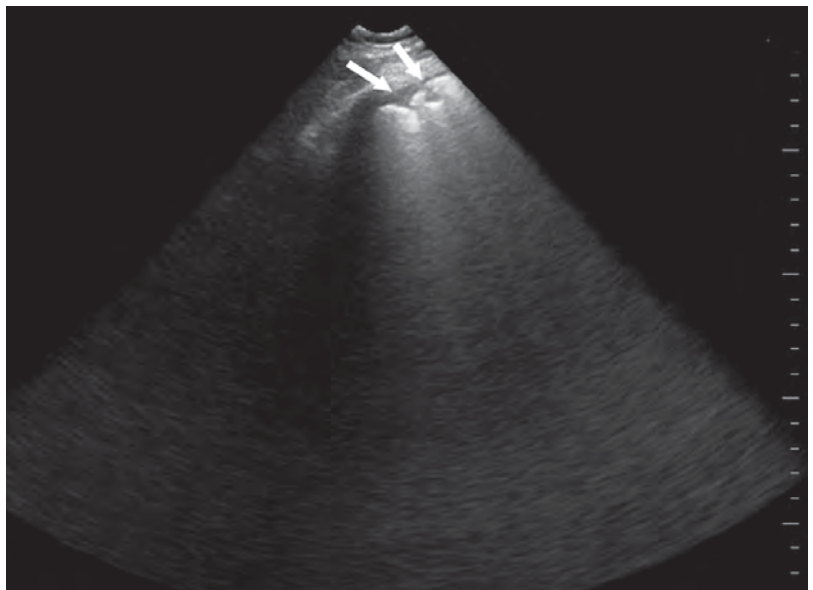


Table 3. Echo Signatures of Interstitial Syndrome

	Distribution of Bilateral B-Lines	Pleural Line	Concomitant Imaging Findings
Pulmonary Edema (Cardiogenic)	Homogeneous, superior lung less affected. No spared areas.	Generally not affected; thin with normal lung slide preserved.	Pleural effusions common, not insignificant in size. Evidence of heart failure on echo and plethoric IVC.
ARDS	Nonhomogeneous, "spared areas" of normal lung.	Irregular, thick; anterior subpleural consolidations; absence or reduction of lung sliding, often with lung pulse.	Areas of consolidation at bases with air bronchograms.
Interstitial Pneumonia	More common in lower lung.	Thickened, irregular.	No change with diuresis on repeat scan.
Pulmonary Fibrosis	Diffuse, nonhomogeneous.	Irregular, fragmented with subpleural abnormalities often present.	Correlates with CT signs of fibrosis.

a. Volpicelli G, Elbarbary M, Blaivas M, et al. International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med.* Apr 2012;38(4):577-91. doi:10.1007/s00134-012-2513-4

b. Copetti R, Soldati G, Copetti P. Chest sonography: a useful tool to differentiate acute cardiogenic pulmonary edema from acute respiratory distress syndrome. *Cardiovasc Ultrasound.* Apr 29 2008;6:16. doi:10.1186/1476-7120-6-16

c. Dietrich CF, Mathis G, Blaivas M, et al. Lung B-line artefacts and their use. *J. Thorac. Dis.* 2016;8(6):1356-1365. doi:10.21037/jtd.2016.04.55

d. Asano M, Watanabe H, Sato K, et al. Validity of Ultrasound Lung Comets for Assessment of the Severity of Interstitial Pneumonia. *J Ultrasound Med.* Jun 2018;37(6):1523-1531. doi:10.1002/jum.14497

Figure 8. White lung. Coalescing B-lines wash out all of the potential A-lines. When B-lines take up the entire intercostal space, the diffuse hyperechoic result (between dotted lines) deep to the pleural line (thick arrow) is called white lung.

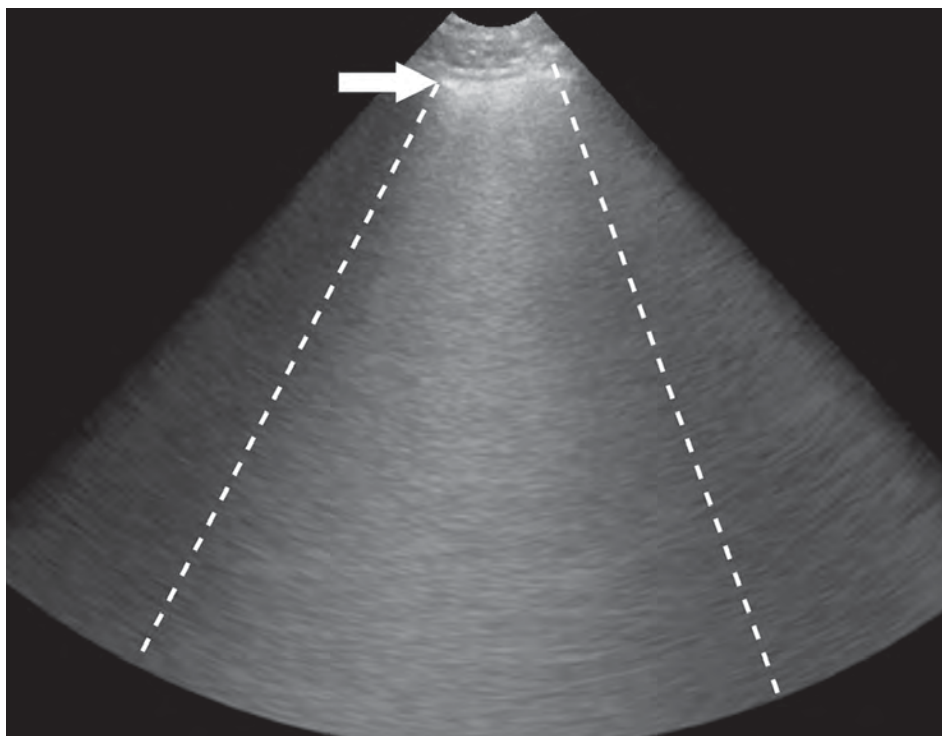
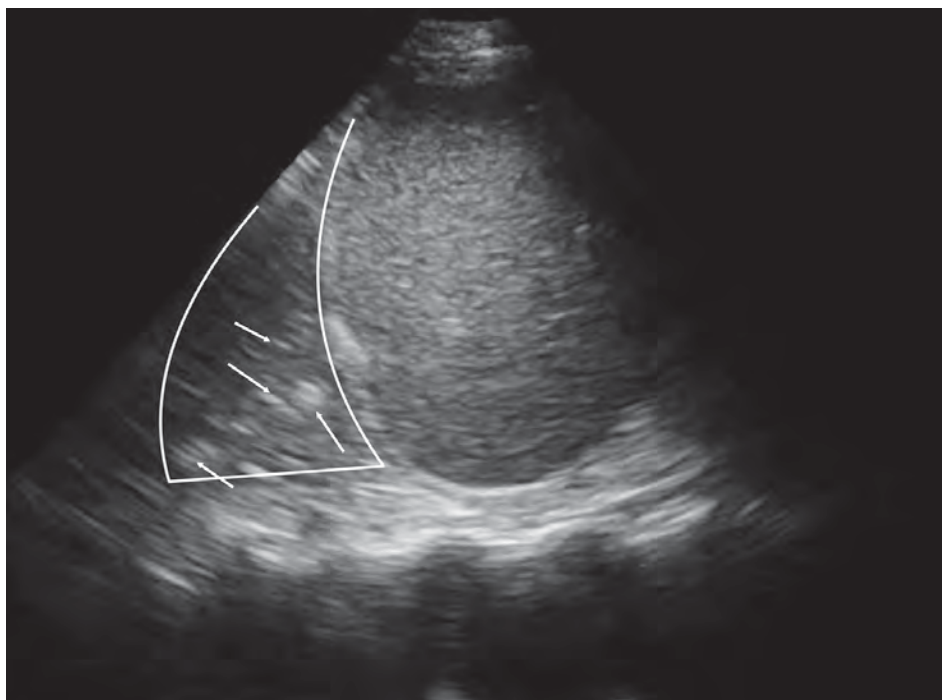


Figure 9. Hepatization. Consolidated lung (bordered by white lines) suggestive of infection with a similar appearance to liver parenchyma. However, note discrete echogenic areas that may represent air bronchograms within the consolidated lung (arrows), which help to differentiate this from the mirror image artifact.



these diseases. Although significant overlap exists between interstitial processes, cardiogenic pulmonary edema (CPE) and noncardiogenic interstitial syndrome (NCIS) can be differentiated. One consistent characteristic of CPE is a normal, thin pleural line, whereas a thickened pleural line is more characteristic of NCIS (>0.2 - 0.5 mm, Figure 6).^{14,15} Additionally, hypoechoic, subpleural, and echo-poor areas that move with the lung are consistent with consolidation and much less likely with CPE. Their presence would, therefore, build a case for an alternative cause of interstitial syndrome (Figure 7).^{13,14} Table 3 describes typical LUS findings of common causes of interstitial processes and should help

to refine the differential diagnosis of an interstitial syndrome.

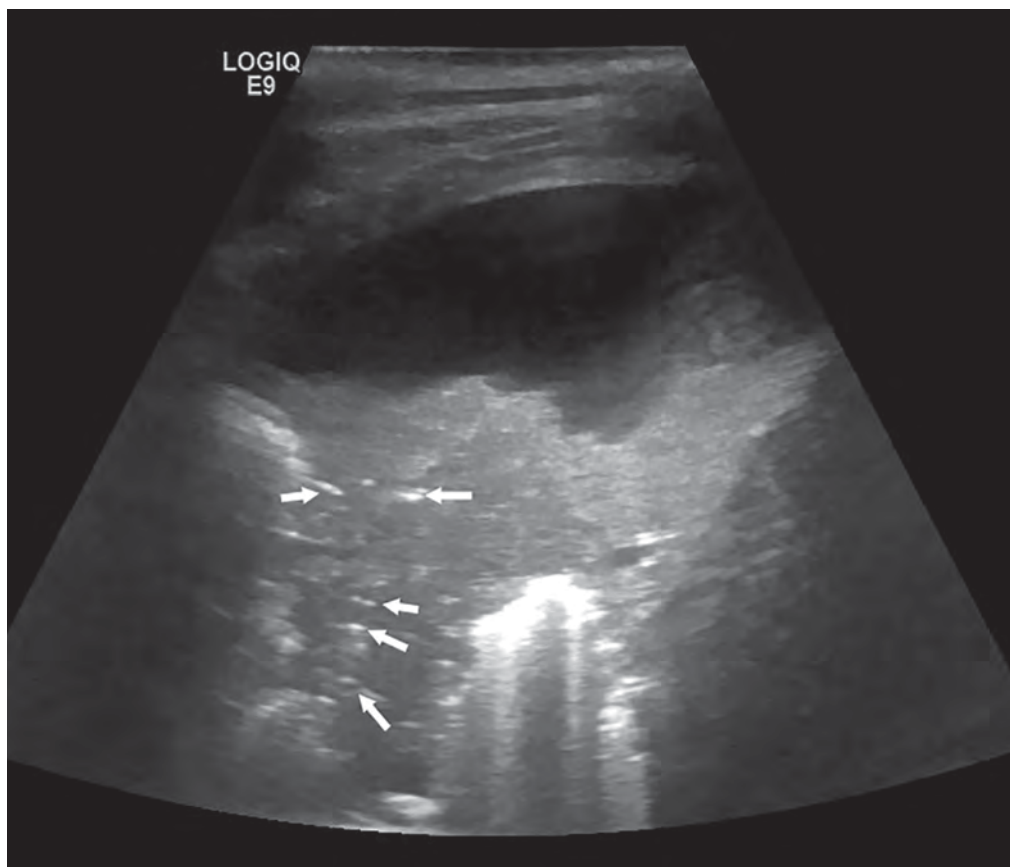
Pneumonia

Lung ultrasound has been shown to have improved sensitivity compared to x-ray in the detection of

pneumonia.^{16,17} Focal pneumonia may appear with various findings.

As discussed previously, the appearance of B-lines in particular areas compared to their absence in others can suggest infection. A patient with a diffuse, multifocal

Figure 10. Air bronchograms. Moderate-size pleural effusion with adjacent atelectatic lung with bright internal echoes (arrows) described as ultrasound air bronchograms.



pneumonia may have more persistent B-lines throughout multiple areas of the lung.¹⁷ As these areas become progressively less aerated, the B-lines tend progressively worsen.

As lung aeration declines, the number of B-lines will increase and they will coalesce into thick bands that ultimately take up the entire intercostal space, a condition referred to as “white lung” (Figure 8).^{18,19}

Finally, when aeration is at its lowest, B-line artifact is replaced by a real image of lung consolidation. Consolidated lung may sometimes appear as dense tissue similar to liver tissue in echogenicity. This is known as hepatization of the lung (Figure 9) and can signify consolidation in areas where infection is present.²⁰ Sonographic air bronchograms may also be visualized in consolidated lung; these appear as hyperechoic tubular structures within lung tissue (Figure 10).

COVID-19 Pneumonia

Since the COVID-19 pandemic, LUS has been a useful bedside tool for assessing viral pneumonia caused by the SARS-CoV-2 virus. It is able to identify the pattern consistent with COVID pneumonia, to correlate uncommon findings with disease severity, and to identify signs of recovery.^{21,22} A recent meta-analysis found that LUS had a sensitivity of 87% and a specificity of 69.5% for COVID pneumonia.²³

The ultrasound findings of COVID-19 reflect the continuum of severity—the more severe the findings, the more severe the clinical condition.²⁴⁻²⁸ Several findings can help to make the diagnosis as well as gauge pneumonia severity. First, the pleural line is assessed for thickening which may be interrupted or discontinuous. Second, B-lines are assessed on a continuum ranging from well-defined, discrete B-lines through

dense coalescence, or “white lung.” Third, B-line distribution can vary from focal or multifocal to confluent patterns across the chest wall.

Finally, small subpleural through larger lobar or translobar consolidations can be seen as disease severity increases.^{21,24} Given the extent and breadth of findings, many studies have proposed a 12-zone protocol (anterior, lateral, and posterior regions, each divided bilaterally into superior and inferior fields), with an associated scoring system describing the extent of disease. Each portion of the lung is scored progressively based on the artifact pattern; from an A-line predominant pattern to worsening B-lines to consolidation, each pattern receives progressively more points.^{22,25-28} The scores are then added together to produce a lung ultrasound severity score or other similar quantified metric.^{26,29} Some scoring systems include the pleural line findings that are

Figure 11. Seashore sign. Upper panel shows B-mode image with M-mode cursor highlighted (thin arrow). Lower panel shows the M-mode tracing demonstrating multiple horizontal lines, which occurs without movement. The pleural line (thick arrows) is thought to represent the beginning of the beach. The region below the pleural line without horizontal lines shows movement and has been described to represent the shoreline.

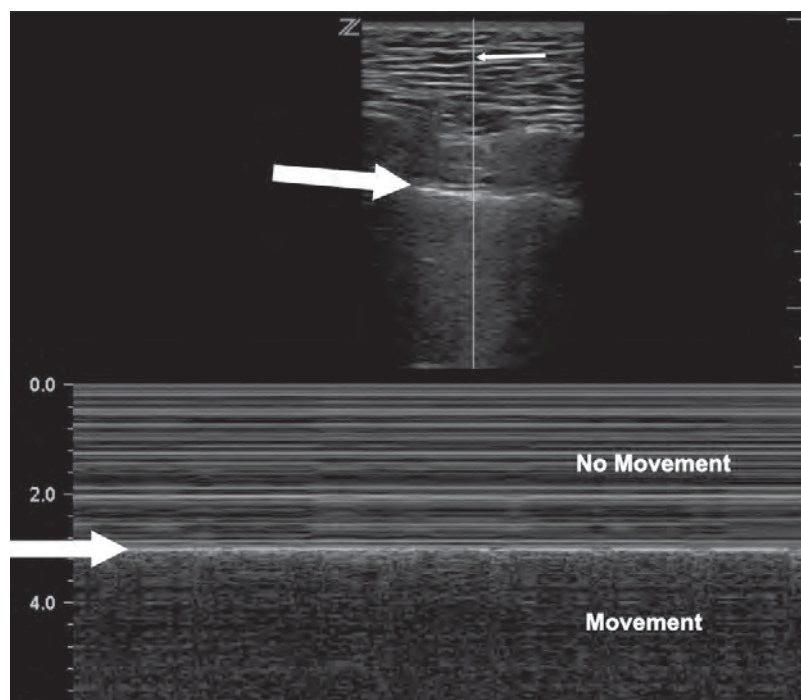
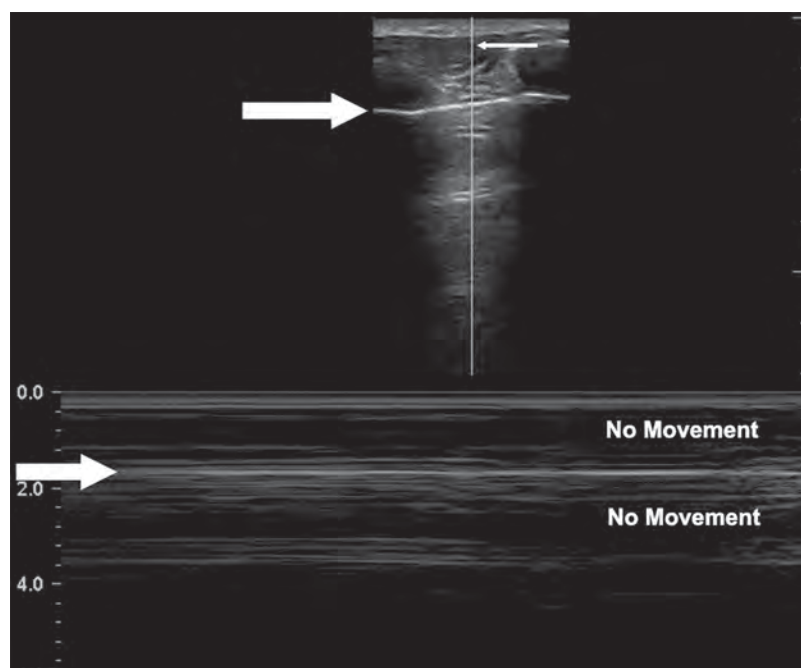


Figure 12. Stratosphere/barcode sign. Upper panel shows B-mode image with M-mode cursor highlighted (thin arrow). On the M-mode (bottom image), no movement is present superficial to the pleural line (thick arrows), represented by horizontal lines, and there is also no movement below the pleural line. Note A-lines are present on the B-mode image, but no movement is seen in the M-mode image. This pattern is consistent with pneumothorax, although other etiologies associated with absence of lung movement should still be considered.



independently correlated with severe COVID-19 disease.^{24,27}

Clinically, high scores have been associated with low partial-pressure-of oxygen to fraction-of- inspiratory-oxygen concentration (PaO₂/FiO₂) ratios, adverse clinical events, incidence of acute respiratory distress syndrome (ARDS), intensive care

unit (ICU) length of stay, and even mortality.²⁵⁻²⁷ Interestingly, pleural effusions are rare in COVID-19 pneumonia and portend poor prognosis when present.^{24,28}

Pneumothorax

Lung ultrasound has transformed pneumothorax evaluation in critically

ill patients who are too unstable to be transported for advanced imaging and in those with trauma or undergoing procedures.^{7,9,30-36} Its utility has been shown in identifying, ruling out, and quantifying the relative size of pneumothorax, as well as in identifying pneumothoraces missed by chest X-ray.³⁴⁻³⁶

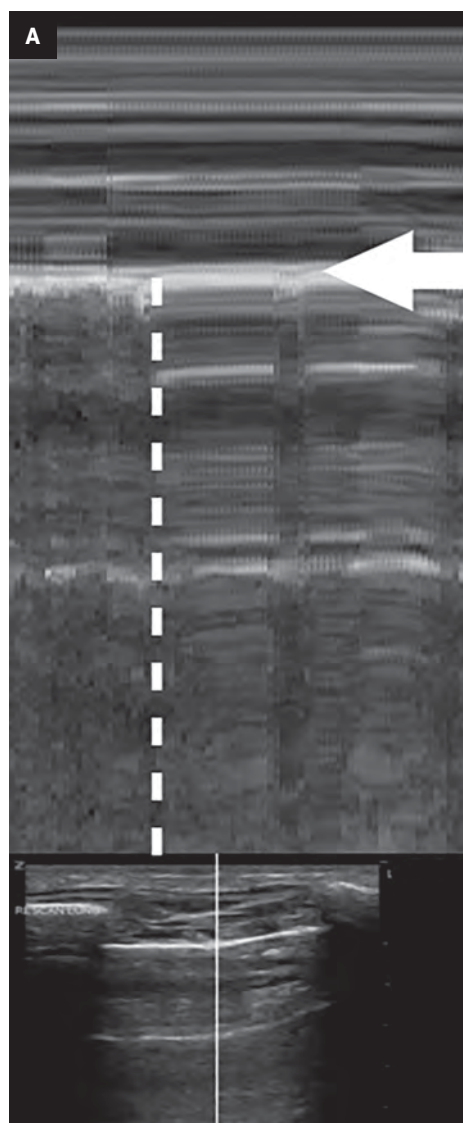
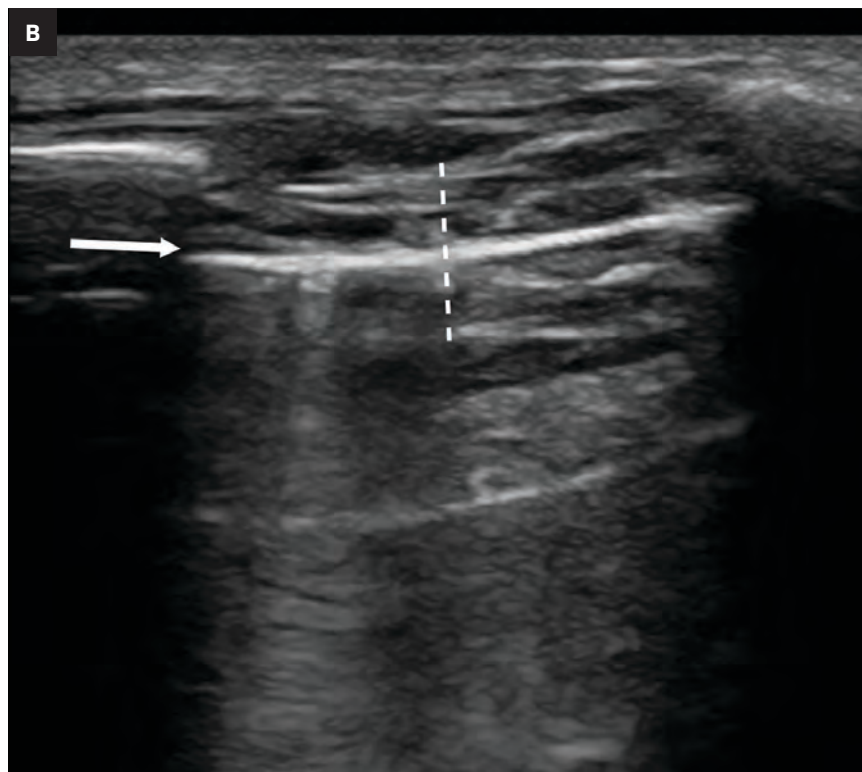


Figure 13. (A) Lung point. There is movement of the pleural line (arrow) to the left, but no movement of the pleural line to the left of the dotted line (better seen on corresponding online video clip). (B) Lung point, M-mode. The same image as in A displayed in M-mode, showing movement deep to the pleural line (thick arrow) left of the dotted line, while there is no movement to the right of the dotted line. This is consistent with a lung point and a pneumothorax.



Evaluating pneumothorax with ultrasound requires the absence of lung sliding. In the presence of pneumothorax, A-lines still emanate from the parietal pleura, requiring careful evaluation. Using a high frequency linear probe can increase accuracy.³⁷

M-mode has also been found to help distinguish normal lung slide from pneumothorax. With M-mode, one vertical segment of the B-mode image is mapped to create a tracing of the segment along the y-axis and its changes across time along the x-axis. When lung sliding is present, the most superficial portion of this graph, representing the skin and subcutaneous tissue, will remain still

across time, leading to static, horizontal lines superficial to the pleura while showing persistent movement below the pleura. The appearance has been likened to the static from poor signals on old television screen.

The movement below the pleural line with no movement above the line is called the “seashore sign,” and represents normal lung slide (Figure 11). Conversely, in the absence of lung slide M-mode will display horizontal lines both above and below the pleural line. This is called the “stratosphere” or “bar code” sign (Figure 12).³³ These findings get their names from the horizontal lines seen both above and below the pleural

line that make the M-mode image appear as layers of the stratosphere or a bar code. A lack of lung slide can be consistent with pneumothorax, but it may also be consistent with other circumstances in which the lung is not moving; these include breath holding, mainstem intubation, diaphragmatic paralysis, and non-ventilation of the side being evaluated.

The presence of a lung point has shown high specificity for pneumothorax.³³ This finding is the point at which the visceral and parietal pleura no longer appose one another. This alternating pattern of lung slide/no lung slide occurs in the same interspace delineating

Figure 14. Pleural effusion with spine sign. What has been described as the posterior spine with acoustic shadowing (arrows) can be seen as the ultrasound waves projecting through the fluid in the pleural space. The effusion shows anechoic fluid, suggesting simple effusion or very acute hemothorax (within dotted lines).

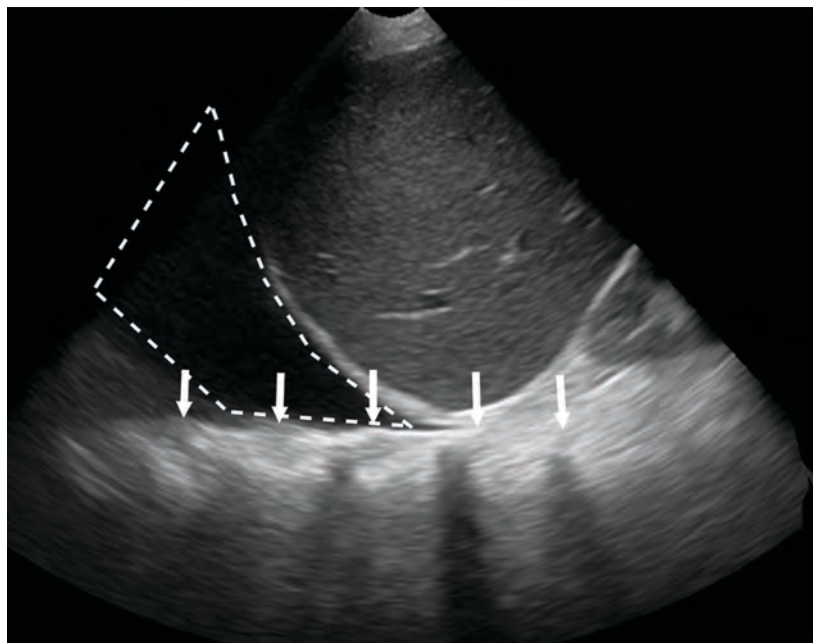
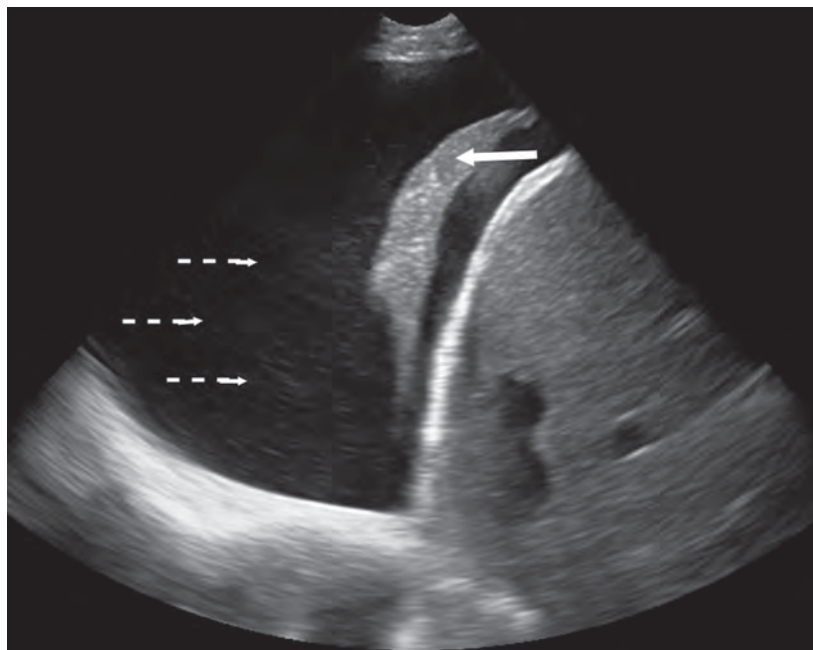


Figure 15. Hemothorax with plankton sign. Mixed echogenic fluid in the pleural cavity suggestive of hemothorax (dotted arrows). The plankton sign refers to swirling internal echoes within an otherwise anechoic pleural effusion and should be highly suspicious for hemothorax as a potential etiology in the setting of trauma. This can also be seen in exudative pleural effusions. Atelectatic lung is present, floating in the hemothorax (solid arrow).



the border of the pneumothorax (Figure 13, *online video*).^{33,38} This can also be observed on M-mode where, within the same intercostal space, the seashore and stratosphere signs are intermittently present, revealing the point at which the visceral and parietal surfaces diverge, confirming a pneumothorax.³⁹ A false lung point may occur when evaluating peridiaphragmatic portions of the lung, as temporary visualization into

abdominal structures may falsely cause similar findings.⁴⁰

As noted previously, lung sliding may not be present without a pneumothorax in certain situations, such as atelectasis, ARDS, right mainstem intubation, among others (false positives). If B-lines or a lung pulse are present, no pneumothorax exists at this level. A lung pulse is a vertical pulsation of the pleural line in concordance with the heartbeat

that excludes pneumothorax at a given location in the intercostal space; both findings require the pleura to be in contact with each other (*online video*).^{20,31}

Pleural Effusion

Pleural effusion was one of the first pathologies studied for the utilization of LUS.⁴ In one study of intensive care patients, LUS showed a sensitivity and specificity of 100%

for pleural effusion.⁴¹ Proper assessment of pleural fluid, particularly in the aerated lung, can help guide safe thoracentesis and reduce the risk of pneumothorax and other complications.⁴²

Pleural effusions are characteristically dependent fluid between the visceral and parietal pleura superior to the diaphragm.⁴³ Simple effusions are anechoic and take the shape of their surrounding borders, typically the chest wall, lung surface, and the diaphragm. They are best visualized in intercostal spaces on dependent chest wall. The probe often will be placed in the superior abdomen, just inferior to the diaphragm and angling superiorly into the chest. Typically, sound waves through normal lung are scattered, owing to high acoustic impedance that obscures the spine superior to the diaphragm. However, if there is fluid or lung with high water content occupies the costophrenic recess (such as in the settings of pleural effusion or hemothorax), the sound waves will propagate to the spine. The spine will then be visualized superior to the diaphragm, a condition referred to as the “spine sign” (Figure 14).⁴⁴⁻⁴⁶ In the setting of trauma, fluid in the lung in the costophrenic recess of a supine patient supports the presence of blood. When clotted blood or exudative material is seen in the hemithorax, anechoic fluid will often have debris seen as hyperechoic particles floating in the fluid. This is referred to as the “plankton sign” (Figure 15).⁴⁷

Conclusion

Lung ultrasound has become useful in bedside imaging across a variety of specialties. Its strengths have been documented through decades of research, and it has proven to be especially effective in diagnosing and assessing lung pathology. This practical review can serve as

a quick reference to the ultrasound findings that can be used to identify pathology, to guide procedures, and to change patient management.

Online Videos

Links to videos corresponding to many of the images in this article can be found in the online version of this article at www.appliedradiology.com.

References

- Marini TJ, Rubens DJ, Zhao YT, et al. Lung ultrasound: the essentials. *Radiol Cardiothorac Imaging*. Apr 2021;3(2):e200564. doi:10.1148/ryct.2021200564
- Mansoori B, Golnari P, Sharifi A, et al. Ultrasound training in radiology residency Programs. *Journal of Ultrasound in Medicine*. 2021;40(4):731-740. doi:10.1002/jum.15443
- Crawford HD, Wild JJ, Wolf PI, Fink JS. Transmission of Ultrasound Through Living Human Thorax. *IRE Transactions on Medical Electronics*. 1959;ME-6(3):141-146. doi:10.1109/iret-me.1959.5007940
- Joyner CR, Jr., Herman RJ, Reid JM. Reflected ultrasound in the detection and localization of pleural effusion. *JAMA*. May 1 1967;200(5):399-402.
- Miller LD, Joyner CR, Jr., Dudrick SJ, Eskin DJ. Clinical use of ultrasound in the early diagnosis of pulmonary embolism. *Ann Surg*. Sep 1967;166(3):381-93. doi:10.1097/00000658-196709000-00006
- Chandrasekhar AJ, Reynes CJ, Churchill RJ. Ultrasonically Guided Percutaneous Biopsy of Peripheral Pulmonary Masses. *Chest*. 1976;70(5):627-630. doi:10.1378/chest.70.5.627
- Lichtenstein DA, Mezière GA. Relevance of Lung Ultrasound in the Diagnosis of Acute Respiratory Failure*: The BLUE Protocol. *Chest*. 2008;134(1):117-125. doi:10.1378/chest.07-2800
- Stassen J, Bax JJ. How to do lung ultrasound. *Eur Heart J Cardiovasc Imaging*. Mar 22 2022;23(4):447-449. doi:10.1093/ehjci/jeab241
- Mojoli F, Bouhemad B, Mongodi S, Lichtenstein D. Lung Ultrasound for Critically Ill Patients. *Am J Respir Crit Care Med*. Mar 15 2019;199(6):701-714. doi:10.1164/rccm.201802-0236CI
- Lobo V, Weingrow D, Perera P, Williams SR, Gharahbaghian L. Thoracic Ultrasonography. *Critical Care Clinics*. 2014;30(1):93-117. doi:10.1016/j.ccc.2013.08.002
- Dietrich CF, Mathis G, Blaivas M, et al. Lung B-line artefacts and their use. *Journal of Thoracic Disease*. 2016;8(6):1356-1365. doi:10.21037/jtd.2016.04.55
- Volpicelli G, Caramello V, Cardinale L, Mussa A, Bar F, Frascisco MF. Detection of sonographic B-lines in patients with normal lung or radiographic alveolar consolidation. *Med Sci Monit*. Mar 2008;14(3):CR122-8.
- Volpicelli G, Elbarbary M, Blaivas M, et al. International evidence-based recommendations for point-of-care lung ultrasound. *Intensive Care Med*. Apr 2012;38(4):577-91. doi:10.1007/s00134-012-2513-4
- Heldeweg MLA, Haaksma ME, Smit JM, Smit MR, Tuinman PR. Lung ultrasound to discriminate non-cardiogenic interstitial syndrome from cardiogenic pulmonary edema: Is “gestalt” as good as it gets? *J Crit Care*. Feb 2023;73:154180. doi:10.1016/j.jcrc.2022.154180
- Musolino AM, Toma P, De Rose C, et al. Ten Years of Pediatric Lung Ultrasound: A Narrative Review. *Front Physiol*. 2021;12:721951. doi:10.3389/fphys.2021.721951
- Unlukaplan IM, Dogan H, Ozucelik DN. Lung ultrasound for the diagnosis of pneumonia in adults. *J Pak Med Assoc*. Jun 2020;70(6):989-992. doi:10.5455/JPMA.3390
- Gibbons RC, Magee M, Goett H, et al. Lung Ultrasound vs. Chest X-Ray Study for the Radiographic Diagnosis of COVID-19 Pneumonia in a High-Prevalence Population. *J Emerg Med*. May 2021;60(5):615-625. doi:10.1016/j.jemermed.2021.01.041
- Smith MJ, Hayward SA, Innes SM, Miller ASC. Point-of-care lung ultrasound in patients with COVID-19 – a narrative review. *Anaesthesia*. 2020;75(8):1096-1104. doi:10.1111/anae.15082
- Soldati G, Demi M, Smargiassi A, Inchingolo R, Demi L. The role of ultrasound lung artifacts in the diagnosis of respiratory diseases. *Expert Rev Respir Med*. Feb 2019;13(2):163-172. doi:10.1080/17476348.2019.1565997
- Bhoil R, Ahluwalia A, Chopra R, Surya M, Bhoil S. Signs and lines in lung ultrasound. *J Ultrason*. Aug 16 2021;21(86):e225-e233. doi:10.15557/JoU.2021.0036
- Clevert D-A, Sidhu PS, Lim A, et al. The role of lung ultrasound in COVID-19 disease. *Insights into Imaging*. 2021;12(1):doi:10.1186/s13244-021-01013-6
- Loke TK, Earl N, Begbey ACH, et al. Lung ultrasound as a tool for monitoring the interstitial changes in recently hospitalised patients with COVID-19 pneumonia - The COVIDLUS study. *Respir Med*. Mar 3 2023;210:107176. doi:10.1016/j.rmed.2023.107176
- Matthies A, Trauer M, Chopra K, Jarman RD. Diagnostic accuracy of point-of-care lung ultrasound for COVID-19: a systematic review and meta-analysis. *Emerg Med J*. Mar 3 2023;doi:10.1136/emered-2021-212092

- 24) Baloesu C, Weingart GE, Moore CL. Emergency Department Point-Of-Care Echocardiography and Lung Ultrasound in Predicting COVID-19 Severity. *J Ultrasound Med*. Feb 25 2023;doi:10.1002/jum.16205
- 25) Dargent A, Chatelain E, Si-Mohamed S, et al. Lung ultrasound score as a tool to monitor disease progression and detect ventilator-associated pneumonia during COVID-19-associated ARDS. *Heart Lung*. Sep-Oct 2021;50(5):700-705. doi:10.1016/j.hrtlung.2021.05.003
- 26) Heldeweg MLA, Lopez Matta JE, Haaksma ME, et al. Lung ultrasound and computed tomography to monitor COVID-19 pneumonia in critically ill patients: a two-center prospective cohort study. *Intensive Care Med Exp*. Jan 25 2021;9(1):1. doi:10.1186/s40635-020-00367-3
- 27) Ji L, Cao C, Gao Y, et al. Prognostic value of bedside lung ultrasound score in patients with COVID-19. *Crit Care*. Dec 22 2020;24(1):700. doi:10.1186/s13054-020-03416-1
- 28) Lichter Y, Topilsky Y, Taieb P, et al. Lung ultrasound predicts clinical course and outcomes in COVID-19 patients. *Intensive Care Medicine*. 2020;46(10):1873-1883. doi:10.1007/s00134-020-06212-1
- 29) Lieveld AWE, Heldeweg MLA, Schouwenburg J, et al. Monitoring of pulmonary involvement in critically ill COVID-19 patients - should lung ultrasound be preferred over CT? *Ultrasound J*. Feb 26 2023;15(1):11. doi:10.1186/s13089-022-00299-x
- 30) Targhetta R, Bourgeois JM, Chavagneux R, Balmes P. Diagnosis of pneumothorax by ultrasound immediately after ultrasonically guided aspiration biopsy. *Chest*. Mar 1992;101(3):855-6. doi:10.1378/chest.101.3.855
- 31) Lichtenstein DA, Lascols N, Prin S, Meziere G. The "lung pulse": an early ultrasound sign of complete atelectasis. *Intensive Care Med*. Dec 2003;29(12):2187-2192. doi:10.1007/s00134-003-1930-9
- 32) Lichtenstein DA, Menu Y. A bedside ultrasound sign ruling out pneumothorax in the critically ill. Lung sliding. *Chest*. Nov 1995;108(5):1345-8. doi:10.1378/chest.108.5.1345
- 33) Lichtenstein DA, Meziere G, Lascols N, et al. Ultrasound diagnosis of occult pneumothorax. *Crit Care Med*. Jun 2005;33(6):1231-8. doi:10.1097/01.ccm.0000164542.86954.b4
- 34) Kirkpatrick AW, Ng AK, Dulchavsky SA, et al. Sonographic diagnosis of a pneumothorax inapparent on plain radiography: confirmation by computed tomography. *J Trauma*. Apr 2001;50(4):750-2. doi:10.1097/00005373-200104000-00029
- 35) Kirkpatrick AW, Nicolaou S. The Sonographic Detection of Pneumothoraces. In: Karmy-Jones R, Nathens A, Stern EJ, eds. *Thoracic Trauma and Critical Care*. Springer US; 2002:227-234.
- 36) Kirkpatrick AW, Sirois M, Laupland KB, et al. Hand-held thoracic sonography for detecting post-traumatic pneumothoraces: the Extended Focused Assessment with Sonography for Trauma (EFAST). *J Trauma*. Aug 2004;57(2):288-95. doi:10.1097/01.ta.0000133565.88871.e4
- 37) Myers M, Billstrom A, Cohen J, Curtis R. Comparing the Sensitivity of a Low Frequency Versus a High Frequency Probe in the Detection of Pneumothorax in a Swine Model. *Med J (Ft Sam Houst Tex)*. Jul-Sep 2021;(PB 8-21-07/08/09):13-19.
- 38) Wilkerson RG, Stone MB. Sensitivity of bedside ultrasound and supine anteroposterior chest radiographs for the identification of pneumothorax after blunt trauma. *Acad Emerg Med*. Jan 2010;17(1):11-7. doi:10.1111/j.1553-2712.2009.00628.x
- 39) Lichtenstein DA. BLUE-protocol and FALLS-protocol: two applications of lung ultrasound in the critically ill. *Chest*. Jun 2015;147(6):1659-1670. doi:10.1378/chest.14-1313
- 40) Piette E, Daoust R, Denault A. Basic concepts in the use of thoracic and lung ultrasound. *Curr Opin Anaesthesiol*. Feb 2013;26(1):20-30. doi:10.1097/ACO.0b013e32835afd40
- 41) Xirouchaki N, Magkanas E, Vaporidi K, et al. Lung ultrasound in critically ill patients: comparison with bedside chest radiography. *Intensive Care Medicine*. 2011;37(9):1488-1493. doi:10.1007/s00134-011-2317-y
- 42) Dancel R, Schnobrich D, Puri N, et al. Recommendations on the Use of Ultrasound Guidance for Adult Thoracentesis: A Position Statement of the Society of Hospital Medicine. *J Hosp Med*. Feb 2018;13(2):126-135. doi:10.12788/jhm.2940
- 43) Lichtenstein DA. Ultrasound in the management of thoracic disease. *Crit Care Med*. May 2007;35(5 Suppl):S250-61. doi:10.1097/01.CCM.0000260674.60761.85
- 44) Salahuddin M, Ayub S. Spontaneous large volume hemothorax managed with a small-bore chest tube. *Monaldi Arch Chest Dis*. Feb 2 2023;doi:10.4081/monaldi.2023.2496
- 45) Ojaghi Haghighi SH, Adimi I, Shams Vahdati S, Sarkhoshi Khiavi R. Ultrasonographic diagnosis of suspected hemothorax in trauma patients. *Trauma Mon*. Nov 2014;19(4):e17498. doi:10.5812/traumamon.17498
- 46) Pumarejo Gomez L, Tran VH. Hemothorax. *StatPearls*. 2022.
- 47) Han J, Xiang H, Ridley WE, Ridley LJ. Plankton sign: Pleural effusion. *J Med Imaging Radiat Oncol*. Oct 2018;62 Suppl 1:35. doi:10.1111/1754-9485.22_12785

Fighting Obsolescence: Professional Assessment in the Era of ChatGPT

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The recent release of ChatGPT, a natural language processing technology developed by San Francisco, CA-based OpenAI.com, has excited the public with its promise of disruptive innovation.

With its startling ability to answer complex questions coherently (often erroneously), ChatGPT— and competing large language model (LLM) deep-learning (DL) algorithms— has also captured the attention of healthcare leaders, many of whom envision exciting opportunities for its application to physician education and practice.

ChatGPT, however, is not without its risks, particularly with respect to radiology education and assessment. Indeed, the technology's capacity to “pass” professional assessment examinations threatens to make conventional tests obsolete. To head off this threat, radiology leaders must begin preparing now to replace

current examinations with alternative, “authentic” assessment methods that simulate clinical practice and more fully address the broad range of skills required for professional competence.

ChatGPT: Surprising in More Ways than One

Despite the many obvious, rapid advances in artificial intelligence (AI) in recent years, and preexisting systems based on earlier, similar algorithms, the arrival of ChatGPT came as quite a surprise to many in the general public and specialized fields alike. The algorithm also has a startling ability to generate sophisticated, human-like responses to a head-spinning scope of questions and challenges; ChatGPT can recommend a good local restaurant, plan a schedule, describe complex physiologic phenomena, and even compose radiology reports, to name just a few of its many capabilities. Upon its release in November of 2022, ChatGPT attracted over a million users in five days, and 100 million in two months, smashing records for software adoption.

Microsoft, Google, and Meta all have or will be deploying and refining similar algorithms in

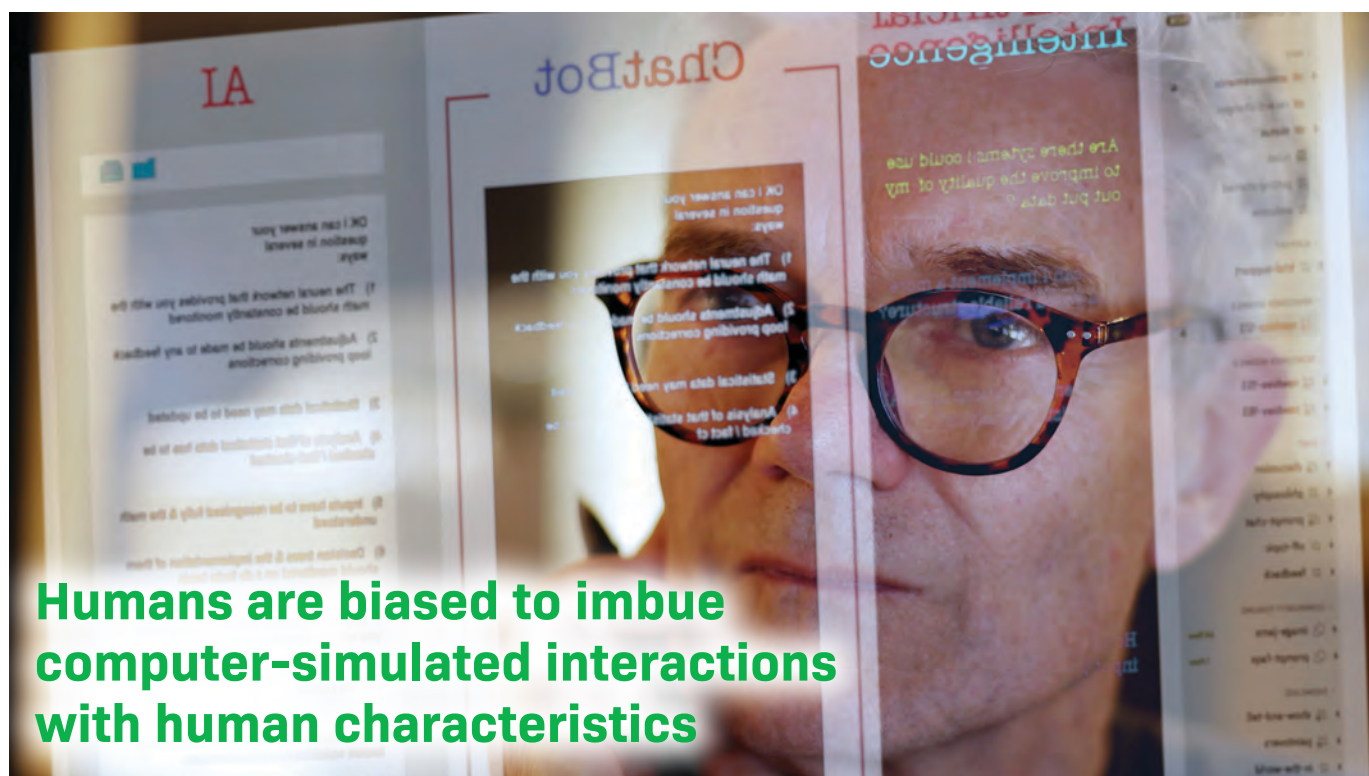
upcoming months and years. Other quickly-evolving AI systems already generate astonishingly realistic, “deep fake” images, videos, audio, and music. Just as it is essentially impossible for a human to visualize the vast distance between planets, stars, and galaxies, humans are also incapable of fully appreciating the scope and volume of data used to construct these LLMs, or the speed at which they can process this information. However, while the broad capabilities of these systems may even appear mystical, our inability to fully understand how they work should not translate to incorrectly concluding, as some have, that they are sentient.

ChatGPT is an artificial (or augmented) intelligence algorithm (also termed a “chatbot”) that uses DL, one class of machine learning that involves training artificial neural networks to learn representations of data. The acronym GPT stands for “Generative Pretrained Transformer,” which is a chat-capable interface based on an LLM and designed to process and generate natural language.¹ Its initial training is “unsupervised,” ie, analyzed without human input or annotation.

GPTs are built upon “Transformer,” a DL neural network architecture^{1,2}

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Humans are biased to imbue computer-simulated interactions with human characteristics

that converts a continuous sequence of text into discrete units, called tokens, and then analyzes patterns and context to, for example recognize multiple uses for single words. A “self-attention” mechanism weights the importance of different words in a sentence, helping to predict the next most likely word in its response based on the prompt provided. The pretraining database derives from a wide variety of sources such as web pages, books, articles, forums, and other publicly available documents, but is current only up to 2021 as of this writing.

Partly because this pretraining includes large volumes of human-generated text from fiction, contradictory and contentious online discussions, and misinformation, the output of a GPT can include dramatic, personal, shocking, racist, and factually erroneous statements, often stated with infuriating, and misplaced, confidence.² ChatGPT can also generate “AI hallucinations” or “stochastic parroting” – incorrect, fabricated,

or nonsensical output – that can be caused by either limitations and biases in the training data or the failure to fully appreciate context.

To improve performance, accuracy, and appropriateness of responses, human feedback is applied to the algorithm. The features and abilities of these systems are developing dynamically and there is little question that they will become considerably more impressive and reliable in upcoming versions and in competing products.

Humans are biased to imbue computer-simulated interactions with human characteristics, even though they do not arise from human senses, experiences, observations, and reasoning.² The output of GPT tends to lead to anthropomorphizing these systems when they are actually based only on statistical analysis of language. For example, their answers use the first person “I” to indicate their actions and “understanding” to imply that they use reasoning; and their responses are grammatically and syntactically coherent,

giving one the very strong impression they are conversing with a live individual online.

This anthropomorphizing presents the risk of “authority bias,” in which people tend to accept outcomes without question. Another risk is that of “confirmation bias,” where a statement is accepted because it plausibly fits a preexisting expectation. A further risk is simply that of seeing the GPT as a shortcut because of how well and quickly it retrieves information for which a human would have to perform time-consuming research. So, on the one hand, we may resist using this algorithm, and on the other, we may be tempted to use it too uncritically.

Indeed, integrating this software into medical use will require discriminating, thoughtful analysis. While the technology is likely to provide meaningful support to next-generation learners, its implications for radiology training and assessment are significant and should be fully appreciated before the field as a

whole goes all-in on ChatGPT and its technological siblings.

For example, multiple-choice question (MCQ)-based board examinations are long-accepted standards, although their validity and utility have been challenged.^{3,5} Recent experiments have found that ChatGPT can approach a passing score on an examination structured to resemble the United States Medical Licensing Examination (USMLE) but modified to exclude images and graphs.⁶ ChatGPT has also performed surprisingly well on an examination that simulated a portion of the United Kingdom's Fellow of Royal College of Radiology examination.⁷ While these LLMs have not yet overtly passed such tests, these early exercises raise the question as to whether our standard examinations test a sufficiently broad array of skills required to be a competent physician. Augmented Intelligence systems, including such LLMs, are rapidly proliferating and improving, beginning to integrate images and other media, using much larger data sets, and linking to real-time online resources.⁶ Consequently, their ability to convincingly pass professional examinations seems likely in the near future.

Should we allow computer applications to act as physicians? Rather than ponder this absurdity, we may analyze the weaknesses of our current forms of education and certification in the context of AI. Competent physicians can no longer compete with AI in fact-extraction and probabilistic judgments. However, they can perform physical examinations and procedures; detect abnormalities (including rare entities for which no large data sets exist); assemble, interpret, and prioritize information; collaborate; generate conclusions and recommendations; report findings; communicate the importance of information to patients and physicians; show empathy; and demonstrate professionalism,

ethics, and leadership. We question the utility of examinations that fail to test *any* of these skills.

So, if AI algorithms may soon be able to pass some existing professional examinations but remain unable to demonstrate the core skills necessary for clinical competence, are the American Board of Radiology (ABR) Core and Certifying Examinations and Continuing Certification (CC) tests adequate to serve, as the ABR demands, “patients, the public, and the medical profession by certifying that its diplomates have acquired, demonstrated, and maintained a requisite standard of knowledge, skill, understanding, and performance”?

The evidence to answer this question is sparse; however, the validity and utility of MCQ Board examinations were already being questioned prior to the advent of this disruptive technology.^{3,5} Furthermore, standardized testing itself in higher education has been widely criticized,⁸⁻¹⁰ including by an organization (Fairtest.org) devoted to educating the public on problems with standardized testing.

In addition, a stakeholder input survey by the ABR itself has found that “multiple choice questions can adequately (though not optimally) assess knowledge, but the overall process is a poor measure of clinical competence as it pertains to interpretation skills, communication skills, and professionalism.”¹¹ Residency programs monitor a broad set of milestones, and they must affirm that residents are qualified to take their certifying examinations, but they perform no comparable end-of-training assessment. We believe that using an MCQ test as an exclusive “final exam” is obsolete in this era of such increasingly powerful AI tools. In response to its stakeholder survey and other input, the ABR on April 13, 2023, announced that it will convert the Diagnostic Radiology Certifying examination to an online “oral

boards” format in 2028.¹² However, for the moment, the other examinations are left unchanged.

Even before the emergence of this new application of AI, an American College of Radiology membership survey found that only 1.7% of respondents considered the ABR regimen of CC requirements acceptable.⁵ Given these results, many expect better scientific evidence of the examinations’ effectiveness and that they should be more adaptable to the broadly varying practices of radiologists.⁵ The ABR argues that “the oral exam aims to assess higher-level skills that are needed to be an effective diagnostic radiologist and are valued by referring physicians and patients.” However, the ABR has not yet clearly explained how the ABR will adapt to the threats posed by ChatGPT to written/MCQ exams.¹²

Radiology’s value within the healthcare ecosystem is almost entirely dependent upon payers’ willingness to pay (WTP).¹³ Radiologists’ value is not a variable over which referring physicians or patients have much influence, given that they are ancillary stakeholders in any radiology value paradigm and have little control over payers’ WTP in today’s siloed care networks.¹³ Currently, competence as certified by the USMLE and the ABR is recognized by state medical licensure boards, healthcare institutions, courts, and insurance payers as a threshold for WTP. But now that ChatGPT has exposed the vulnerabilities of MCQs for professional assessment, physicians may risk losing their value unless the examinations pivot to a new paradigm.

What alternatives to support WTP could be considered? Modern educational theory points to “authentic testing” as a better means to establishing competence.

Authentic testing can be based on simulations of actual clinical practice. The previous oral board

examination format, imperfect as it was, was the closest radiology had to modern simulation techniques, and we are hopeful that the new oral examination will be restored using principles of authentic assessment. Already, robust simulation-based, authentic-testing assessments have been developed and extensively validated in 68 unique Accreditation Council for Graduate Medical Education programs with over 1700 residents during the past ten years.¹⁵

¹⁶ These are proven efficient and effective at assessing peer competency by subspecialty with eight-hour shift simulation, including normal cases.

As educators know, what students learn is strongly influenced by the knowledge and skills that are tested. Future professional assessment must build upon radiologists' unique human strengths, including those of collaboration, empathy, curiosity, learning without the need for large data sets, and the ability to apply innovative analysis.

Artificial intelligence will increasingly be able to compensate for radiologists' weaknesses by leveraging growing data sets in biology and pathophysiology to provide immediate access to the information they require. However, AI can never fully understand meaning, apply knowledge, or empathize with unique humans in unique situations. It is strategically imperative for physicians to recognize that human uniqueness and tailor their treatment of each patient accordingly. Ultimately, competent physicians of

the future will need to artfully synergize AI with their own experience to serve their patients.

In the meantime, radiology organizations must make the transition to authentic methods of professional assessment and adopt the new AI technologies in order to avoid the obsolescence that threatens to arrive more quickly than we all may expect.

References

- 1) Shen Y, Heacock L, Elias J, et al. ChatGPT and other large language models are double-edged swords. *Radiology*. 2023; 307(2):e230163. <https://doi.org/10.1148/radiol.230163>.
- 2) Kissinger H, Schmidt E, Huttenlocher D. ChatGPT heralds an intellectual revolution. *Wall Street Journal*. Feb. 24, 2023. <https://www.wsj.com/articles/chatgpt-heralds-an-intellectual-revolution-enlightenment-artificial-intelligence-homo-technicus-technology-cognition-morality-philosophy-774331c6>. Accessed 4-19-23.
- 3) Berland LL, Berland NW, Berland MW. ABR psychometric testing: analysis of validity and effects. *J Am Coll Radiol*. 2018;15:905-910. <https://doi.org/10.1016/j.jacr.2018.02.023>.
- 4) Berland LL, Heitkamp DE, Beavers KM, et al. Report of the ACR Task Force on Certification in Radiology: History, Challenges and Opportunities. <https://www.acr.org/Lifelong-Learning-and-CME/ACR-Report-on-Certification-in-Radiology>. Accessed 4-19-23.
- 5) Berland LL, Tarrant MJ, Heitkamp DE, Beavers KM, Lewis MC. Maintenance of certification in radiology: eliciting radiologist preferences using a discrete choice experiment. *J Am Coll Radiol*. 2022;19:1052-1068. <https://doi.org/10.1016/j.jacr.2022.06.012>
- 6) Kung TH, Cheatham M, ChatGPT et al. Performance of ChatGPT on USMLE: potential for AI-assisted medical education using large language models. medRxiv December 21, 2022. doi: <https://www.medrxiv.org/content/10.1101/2022.12.19.22283643v2.full.pdf>. Accessed 4-19-23.
- 7) Elmahdy M, Sebro R. Beyond the AJR: comparison of artificial intelligence candidate and radiologists on mock examinations for the Fellow of Royal College of Radiology Part B. *AJR* 2023 published online. doi:10.2214/AJR.23.29155
- 8) Ravitch D. Lessons learned. In: Ravitch D, ed. *The death and life of the great American school system; how testing and choice are undermining education*. New York, NY: Perseus Books Group; 2010:223-42.
- 9) Wiggins G. A true test: toward more authentic and equitable assessment. *Phi Delta Kappan*. 2011;92:81-93.
- 10) Dalal J, Gunderman RB. Standardized tests: a review. *J Am Coll Radiol* 2011;8:271-4. doi:<https://doi.org/10.1016/j.jacr.2010.08.006>.
- 11) Barr RM. ABR Update. Presentation at Texas Radiological Society, Austin, TX, 2-17-22.
- 12) Transition to New DR Oral Exam. <https://www.theabr.org/news/new-diagnostic-radiology-oral-exam>. Accessed 4-19-23.
- 13) Hardy SM. Value chain: where radiologists should put their focus in threats against income. *Appl Radiol*. 2021;50(4):32-34. <https://appliedradiology.com/articles/value-chain-where-radiologists-should-put-their-focus-in-threats-against-income>.
- 14) United States, Federal Aviation Administration, Department of Transportation. Flight review. 14 *Fed Reg*. 61.56.
- 15) Sistrom CL, Slater RM, Rajderkar DA, Grajo JR, Rees JH, Mancuso AA. Full resolution simulation for evaluation of critical care imaging interpretation; Part 1: fixed effects identify influences of exam, specialty, fatigue and training on resident performance. *Acad Radiol* <https://doi.org/10.1016/j.acra.2019.11.023>.
- 16) Sistrom, CL, Slater RM, Rajderkar DA, Grajo JR, Rees JH, Mancuso AA. Full resolution simulation for evaluation of critical care imaging interpretation-art 2: random effects reveal the interplay between case difficulty, resident competence, and the training environment. *Acad Radiol*. 2019; <https://doi.org/10.1016/j.acra.2019.11.025>.

Informed Consent: A Template for Process Improvement

Evan Ruppell, DO; David Gerson, MD; Steven J. Baccei, MD

Our department recently sought to improve and upgrade our informed consent processes. The goal was to develop a system that allows healthcare professionals to easily locate and deploy standardized, electronic informed consent forms containing the information essential to obtaining informed consent from patients undergoing interventional radiology procedures at our institution.

In this review, we share the challenges we faced and the steps we took, with the goal of helping encourage other healthcare facilities facing similar challenges to adopt standardized, digitally based documentation and facilitate more consistent, and potentially more accurate, informed consent processes.

Taking Inventory

The challenges we faced were daunting. Across our entire enterprise, the radiology department had many different paper and electronic informed consent form templates that 1) were either difficult to locate or nonexistent; 2) lacked standard

wording; and/or 3) lacked some of the required information regarding the risks, benefits, and alternatives for specific procedures.

As a result, we believed our informed consent process could be impaired, potentially leaving our institution open to medicolegal risks associated with failure to provide patients with sufficient information to give their truly informed consent to undergo a given procedure. Standardized, electronic consent forms have been shown to result in an improved informed consent process with greater consistency and lower error rates.¹

As every healthcare professional knows, informed consent is a legally mandated, central part of shared decision making between patients and their healthcare professional. The term “informed consent” itself first appeared in a 1957 California Court of Appeals case, *Salgo v Leland Stanford Junior University Board of Trustees*.

The case involved a patient who had filed suit against his physician for failing to inform the patient beforehand of the risks associated with a procedure that had left the patient permanently paralyzed from the waist down. The Court ruled in the patient’s favor, finding that a physician “subjects himself to liability


if he withholds any facts which are necessary to form the basis of an intelligent consent.”²

Some components of the informed consent process vary by state, but most require the doctor and/or a qualified member of their team to discuss the risks, benefits, and alternatives of a given procedure with each patient. The conversation must be guided by the informed consent document, a signed copy of which serves as the official record of this important physician-patient interaction.³

Consolidating Informed Consent Documentation

We began our quality improvement effort by evaluating the current state of our informed consent processes. We found that hardcopy consent forms were used inconsistently throughout our entire healthcare system; one of our hospitals used hardcopy consent forms for up to 65% of procedures and even added procedure-specific risks by hand in some cases. Almost 90% of templates required some form of alteration, including about one-third of which were missing information; approximately 10% of templates were missing entire sections on risks, benefits, or alternatives.

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[W]e were able to eliminate some templates and consolidate multiple others into one electronic template that can be customized .

We also reviewed all procedures performed in our department during the preceding year. This analysis revealed that certain procedures, such as prostate and pancreatic biopsies, were never performed.

As a result of this comprehensive review, we were able to eliminate some templates and consolidate multiple others into one electronic template that can be customized to generate consent forms with language relating to procedure-specific risks, benefits, and treatment alternatives. Our radiology consent forms now exist as interactive “smart forms” in our electronic health record (EHR) system.

Standardizing Content

The greatest challenge we addressed at this stage related to form content; specifically, whether to include language relating to rare but highly morbid complications on our consent forms, as including such risks may cause undue patient anxiety. In addition, precise mortality risks for some procedures are not available, either because they have not been studied or because they cannot be established. For example, regarding the transjugular intrahepatic portosystemic shunt (TIPS) procedure, it is “impossible ... to separate the risk of death due to the

condition warranting the TIPS”³ from the risk of death due to the procedure itself, as the 30-day mortality rate of TIPS is between 3% and 44%.⁴

Owing in part to the difficulty of such determinations in a variety of procedures, we were unable to find a compilation of mortality rates in literature searches and gathered this information from numerous sources.⁵

Confirmative data came from a recent retrospective cohort study which established a consensus that procedures deemed “high risk” carry a 1% or greater risk of death directly attributable to the procedure itself.⁶ We chose this as our benchmark in determining whether to include risk

of death on our informed consent forms for procedures.

In addition, a 2019 study involving 184 interventional radiology medicolegal cases litigated between 1963 and 2018 found that 73% of cases pertained to the generally higher-risk vascular procedures, with inferior vena cava (IVC) filters alone comprising 12% of cases.⁷ This study also found that a lack of informed consent was relevant in 14% of all cases.

Accordingly, we added risk of death to our templates for lung biopsy, TIPS placement, transarterial chemoembolization (TACE), and IVC filter placement. In addition, owing to the high risks and litigation associated with IVC filter placement, we added language specific to device fracture, embolization, migration, and failure to prevent pulmonary embolism.

As a result of these efforts, our radiologists now overwhelmingly believe the efficiency of our informed consent process has been dramatically improved; hardcopy informed consent forms are now used in only 1% of all cases and procedures.

Some Challenges Remain

Making the changes to our consent templates and forms required the assistance of our radiology information

system (RIS) administrators. We had hoped to introduce keywords to facilitate more efficient searching for specific consent forms. However, our RIS only allows searching by the first word of each procedure. Consequently, we renamed some procedures to improve search accuracy. “Fluid/tissue aspiration,” for example, became “aspiration of fluid/tissue.” We have requested more robust search functionality in future updates to our EHR system.

This undertaking also revealed the value of implementing a periodic, formal review of our informed consent processes, as we believe the lack of a structured program of this type led to many of the issues that prompted our effort to improve our department’s informed consent process. We plan to implement periodic reviews in the near future and recommend this to anyone planning a similar improvement project.

Conclusion

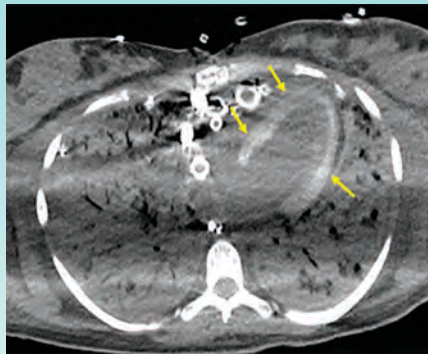
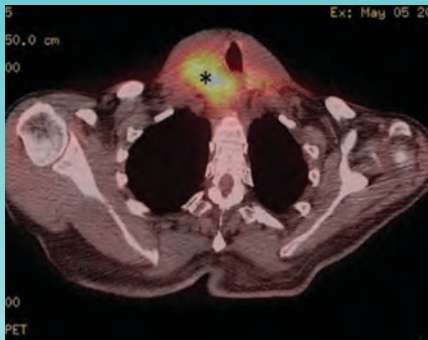
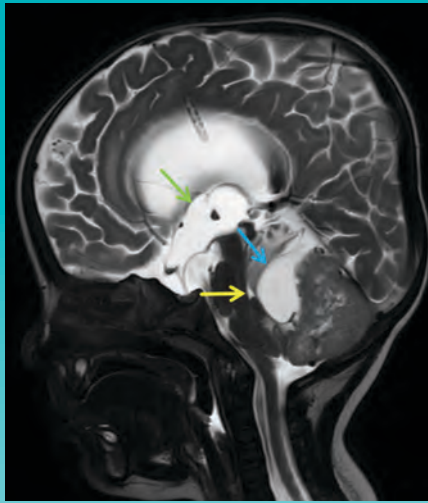
As a result of our quality improvement efforts, vetted, more accurate radiology informed consent documents are now available as interactive documents in our EHR system.

Indeed, we believe our experience demonstrates that a thorough review of the literature and developing departmental consensus around procedural benefits, risks, and

alternatives while transitioning to RIS-based templates and forms can improve the entire informed consent process for healthcare providers and patients.

References

- 1) Spengler EK, Hunsicker LG, Zarei S, Zimmerman MB, Voigt MD. Transjugular intrahepatic portosystemic shunt does not independently increase risk of death in high model for end stage liver disease patients. *Hepatol Commun*. 2017 Jun 7;1(5):460-468. doi: 10.1002/hep4.1053
- 2) Tenenbaum EM. Revitalizing informed consent and protecting patient autonomy : an appeal to abandon objective causation. *Oklahoma Law Rev*. 2012;64:697-758.
- 3) American College of Radiology [Internet]. ACR–SIR–SPR Practice Parameter on Informed Consent for Image-Guided Procedures. [cited 2022 April 1]. Available from: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/informedconsent-image-guided.pdf?la=en>
- 4) Schwarze ML, et al. Development of a list of high-risk operations for patients 65 years and older. *JAMA Surg*. 2015;150(4):325-31. doi: 10.1001/jamasurg.2014.1819.
- 5) West J, Card TR. Reduced mortality rates following elective percutaneous liver biopsies. *Gastroenterology*. 2010;139(4):1230-7. doi: 10.1053/j.gastro.2010.06.015.
- 6) Ascha M, et al. Predictors of mortality after transjugular portosystemic shunt. *World J Hepatol*. 2016 Apr 18;8(11):520-9. doi: 10.4254/wjh.v8.i11.520
- 7) Branach CS, et al. Medical malpractice in image-guided procedures: an analysis of 184 Cases. *J Vasc Interv Radiol*. 2019;30(4):601-606. doi: 10.1016/j.jvir.2018.11.025



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RADIOLOGICAL CASE

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Sepsis-induced Rapid Left Ventricular Calcification

Sherif Mousaw, 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 (50%).

Imaging Findings

Noncontrast chest CT demonstrated ARDS and early diffuse calcifications

Affiliations: University of Alabama at Birmingham, Birmingham, Alabama (Dr Mousaw); University of Ohio Medical Center, Toledo, Ohio (Dr Kattan, Lewis); DrexelUniversity, PA.

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

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 findings 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 = 255%). Follow-up CT chest one month later

Diagnosis

Sepsis-induced dystrophic ventricular calcification

Discussion

Dystrophic calcification of myocardial tissue is not elevated serum calcium. A suggested explanation of mechanism of calcification is the

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Sepsis-induced Rapid Left Ventricular Calcification

Case Summary

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

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Networking for Success

Yasha Parikh Gupta, MD

In business it has been said that your network is your net worth. Startups can fail or flourish depending on the connections their leaders have within the community. This concept has trickled down into our everyday lives, where the right connections can get your child into a preferred school or introduce you to a venture capitalist willing to invest millions into your idea.

Networking, unfortunately, can have a negative connotation. Those without connections see networking as fundamentally unfair, a system where “who you know” matters more than your own accomplishments. Truth be told, networking certainly can give you a leg up in a number of situations. But, in the words of Ice-T, “Don’t hate the player, hate the game.”

You are probably wondering what this has to do with medicine. The entire idea of networking is one reason why medical students who have a program at their institution in their residency field of choice can gain an advantage over those who do not have such a program, given their greater exposure to that field and faculty members in active practice. This is why I encourage students to do rotations away from their institution, especially if they do not have a home program.

A study of medical students wishing to pursue orthopedic surgery, a highly competitive field, found that 57% matched either with their home program or with a program at which they rotated.¹ Similar results have been seen in plastic surgery, findings amplified after the COVID-19 pandemic.² Another paper emphasized that orthopedic surgery

program directors were more likely to rank internal candidates, as the pandemic made gauging student interest more difficult through virtual interviews.³ John Falcone, MD, a surgeon at the University of Pittsburgh Medical Center, defined this phenomenon as “home field advantage.”⁴

Why is this? It all comes back to the value of networking.

Medical centers simply prefer students who have rotated through their department: they *know* you. They know your work ethic, your goals, your drive. They know that when they take you, they are getting a great resident; one who has already proven their mettle. This extends to letters of recommendation. It is true that letters of recommendation can be biased⁵ and often are not reliable predictors of resident success. But a letter from someone the recipient knows makes it easier to trust their recommendation.

The move to the new pass/fail grading system from the original numerical score on the United States Medical Licensing Exam (USMLE) Step 1 examination only adds to the importance of networking. When the National Residency Matching Program (NRMP) surveyed program directors across all specialties, Step 1 was the most important factor in their selection of applicants to interview.⁶ In urology, over 80% of program directors felt that a pass/fail Step 1 removes an important objective measure of the applicant’s qualifications.⁷

What does this mean for you? Again, it highlights the importance of your network. Networking is important at every stage of your career. Getting from

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medical school into residency, getting from residency into fellowship, and even getting from fellowship into your first job—your network will be an invaluable asset throughout your entire career.

How to Build Your Network

It is easier than you may think to build your network of professional contacts and colleagues.

First, you must be visible. Attend institutional events at which faculty will also be present. Also attend local, regional, and national conferences. Meetings of The Radiological Society of North America, American College of Radiology, and the American Roentgen Ray Society are great places to start. Subspecialty conferences such as those of the American Society of Neuroradiology, Society of Breast Imaging, and Society of Thoracic Radiology conferences can be invaluable once you have chosen a radiological subspecialty (even if you have not!).

Be sure to attend lectures and special events to meet as many people as you can to get the full value of networking. Indeed, after-hours events such as “speed-mentoring” and “power hours” can make networking easier. These are nearly always open to trainees; some conferences offer the option to select a mentor when you register, providing an easy way to begin networking even before you step foot in the conference center.

Making use of email and social media is another good way to build your network. Lecturers often include their contact information at the end of their slide presentations. Reach out to those who you think would make great mentors and tell them how much you enjoyed their talk and your interest in pursuing a career in the specialty. Radiology is a very open and welcoming field; challenge yourself to contact five people at the end of each meeting. You are bound to make a meaningful connection with at least one person.

Like most things, the more effort you put into building your network, the more you will get out of it. I have called upon my network when thinking about pursuing a fellowship and more recently, while looking for a position. Something you will commonly hear is that the best jobs are not posted on job boards; that’s because they are usually filled before they make it to that point. Why is that? Networking, of course! In fact, of three jobs I recently considered taking, not one appeared on a job board. I was interviewed because either I reached out to someone else in my network, or they reached out to me.

Your network is truly an invaluable resource that will continue to assist you throughout the many phases of your career. The effort you invest today will continue to pay dividends well into the future.

References

- 1) Chen AF, Secrist ES, Scannell BP, Patt J. Matching in orthopaedic surgery. *J Am Acad Orthop Surg*. 2020; 28(4): 135-144,.
- 2) Hollins AW, Zhang GX, Stoeck JR, et al. Staying close to home: the effects of COVID-19 on the plastic surgery residency match. *Plas Reconstr Surg Glob Open*. 2021; 9(9):e3864.
- 3) Ponterio JM, Levy L, Lakhi NA. Evaluation of the virtual interview format for resident recruitment as a result of COVID-19 restrictions: residency program directors’ perspectives. *Acad Med*. 2022; 97(9):1360-1367.
- 4) Falcone JL. Home-field advantage: The role of selection bias in the General Surgery National Residency Matching Program. *J Surg Ed*. 2013; 70(4), 461-465. doi:10.1016/j.jsurg.2013.03.007
- 5) Grimm LJ, Redmond RA, Campbell JC, Rosette AS. Gender and racial bias in radiology residency letters of recommendation. *JACR*. 2020; 17(1): 64-71. doi:10.1016/j.jacr.2019.08.008
- 6) Results of the 2018 NRMP program director survey. Retrieved March 12, 2023, from <https://www.nrmp.org/wp-content/uploads/2021/07/NRMP-2018-Program-Director-Survey-for-WWW.pdf>.
- 7) Chisholm LP, Drolet BC. USMLE Step 1 scoring changes and the Urology Residency Application Process: program directors’ perspectives. *Urology*. 2020;145:79-82. doi:10.1016/j.urology.2020.08.033

3D Printing: Bridging the Gap Between Radiologists and Surgeons

Kerri Reeves

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

Hand a cardiac surgeon a 3D-printed model of their patient's own heart, or an orthopedic surgeon a 3D-printed model of their patient's own spinal column and watch what happens. Don't be surprised if they respond with nothing less than childlike wonder, says Susan A Churchill, MBA, BSRT(R)(N)(CT).

"We're recreating anatomy in a tangible form, and when you give doctors these prints, they are like kids at Christmastime with a new toy in their hands," says Churchill, supervisor of the Multi-Dimensional Image Processing Laboratory at Duke Radiology, Duke University Health System, Durham, NC. "They stare at it and twist it around, almost gleefully. We're bridging that gap between radiologists and surgeons."

Indeed, thanks to the technological miracle that is 3D printing, radiologists are no longer just converting MRI and CT datasets into multidimensional images that can be turned every which way on a computer screen. They are using the data to generate actual physical models, complete with realistic textures, and colors, for enhanced surgical planning and simulation.

"We take that digital blueprint and turn it into a 3D model that's transportable into the operating room or to the patient's bedside," says Sarah Bastawrous, DO, associate professor of radiology at the University of Washington School of Medicine and VA Puget Sound Health Care System, both in Seattle. "Radiology remains central in the growing field of medical 3D printing to improve the care of patients."

Fides Regina Schwartz, MD, a senior research associate in the department of radiology at Duke, agrees.

"The fact that we now have resolutions of .6 mm with most systems and even a CT scanning system that can provide spatial resolution down to .2 mm slice thickness, that really helps a lot in making the models true to what you'd actually see in the patient," Dr Schwartz says.

Clinical Benefits

Among a growing number of other 3D printing applications, models of the spine are being used to plan surgery for scoliosis and other deformities, says David Ballard, MD, assistant professor of radiology and director of the 3D Printing Lab at the Mallinckrodt Institute of Radiology at the Washington University School of Medicine in St Louis, Missouri. At Duke, Churchill says, models of the pelvis and shoulder are being used to help plan treatment of femoroacetabular impingement and complex fractures, while 3D-printed models of the brain are being used to plan surgery for refractory epilepsy.

The technology is also being used to treat cardiac diseases in children, despite the challenges of obtaining the data needed to print such small heart models for these cases. These include the size of the patients and the patient motion during CT and MRI scans. Fortunately, advances in imaging technology are making it easier

Chest Wall Desmoid Tumor. Complex anatomic model for surgical planning in an adult with a desmoid tumor of the left chest wall. An anatomic model was requested by the cardiothoracic surgeon to visualize the tumor, degree of chest wall and pleural invasion, and existing hardware, prior to tumor resection and chest wall reconstruction. The model shows the relationship of the tumor (in yellow) to the underlying ribs, pleura, and hardware (in blue). The overlying and surrounding chest wall musculature is seen in pink. *Image courtesy of Sarah Bastawrous, DO.*



to capture high-quality imaging data in these patients, says Churchill.

“The quality of the 3D model is only as good as the data used to create it,” she observes. “In gated studies, the ability to take a motion-free image is huge. The advancements in spatial resolution give us better visualization for the detailed anatomy, faster scans, and reduced motion artifacts ... which all improves the output.”

Patient-specific 3D models also facilitate communication as well as patient and family understanding of their condition and proposed treatment(s).

“If the patient can see and hold their model, they understand what they’re dealing with and can really be part of the planning and care,” Churchill says.

In recent years, 3D printer capabilities and modeling materials have both improved while the costs of 3D printing have been falling, says Dr Schwartz. Improved technology and reduced costs have led to widespread use of 3D printing across healthcare,

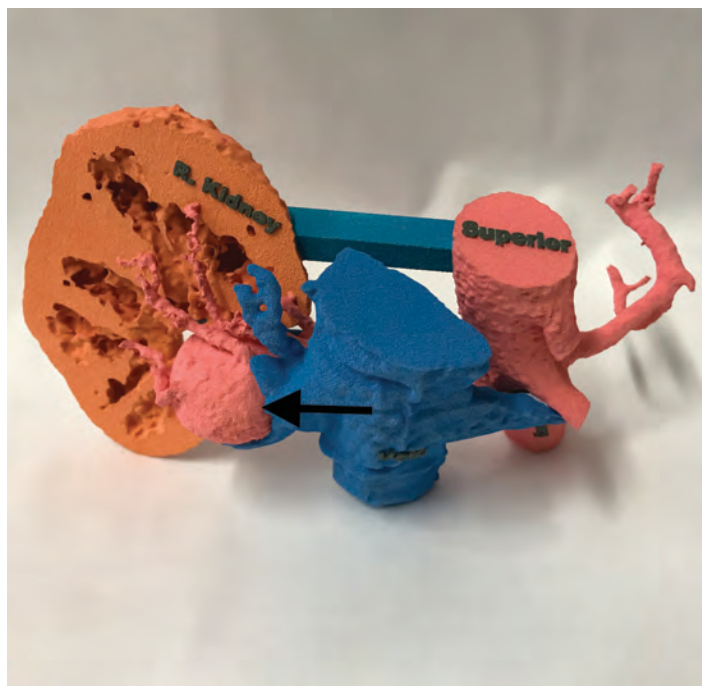
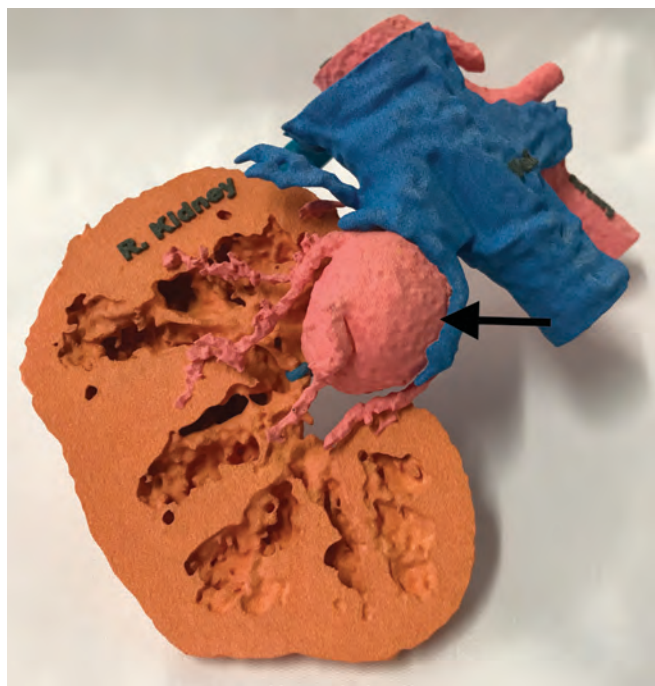
despite challenges such as reimbursement, funding, and regulatory considerations.

Hospital-based 3D printing programs can vary dramatically, from novelty applications to established clinical services with large volume production across many medical domains. As the possibilities for clinical use and research expand, Dr. Bastawrous asserts, “Medical 3D printing will add value to our surgical colleagues and allow for personalized patient care to improve health outcomes and patient satisfaction.”

Workflow and Resource Considerations

Despite 3D printing’s growing value to medical care, healthcare systems face a variety of operational and financial challenges to implementation. For one, the complexity of the 3D printing process demands a dedicated 3D printing lab and specially trained CT and MRI technologists and radiologists.

An adult with a 3.2 cm right renal artery aneurysm. A 3D model was requested to better understand the complexity of the aneurysm sac, anatomic location, as well as the best treatment approach. It was also used in discussing treatment options with the patient. *Image courtesy of Sarah Bastawrous, DO.*



“You can’t just take the images you have in PACS and put them into a 3D printer,” says Dr Schwartz. “The DICOM format doesn’t print in 3D.” Instead, the radiologist or technologist must devise a special protocol for image acquisition and creation of an STL file for printing the 3D model. Many quality control steps are then executed in the segmentation and printing process before the model’s final review by a radiologist, she says, noting that adding 3D printing to already existing daily responsibilities of most technologists and radiologists would be “nearly impossible.”

Dr Ballard agrees, adding that, “you need at least one FTE (full time equivalent) — usually a non-physician — who’s doing the 3D printing and the majority of the segmentation, and a radiologist who often acts as an overseer of accuracy.”

The Costs of 3D Printing

The costs associated with opening and operating a 3D printing lab are significant. While equipment prices have dropped in recent years, they remain considerable. Duke purchased a 3D printer in 2016 for \$350,000, with printing materials priced at about \$600 per package. This year, Duke was quoted \$56,000 for a similar printer, with materials coming in at about \$400, Dr Schwartz says.

Dr Ballard adds that low-end printers range anywhere from \$500 to \$5,000, while mid-tier printers can cost \$5,000 to \$20,000; and high-end printers can reach upwards of \$100,000 to \$300,000.

“A lot of people get excited about the idea of a low-cost 3D printer, but it’s important to know what your surgeons—your end users—want in terms of capabilities and benefits. The less expensive ones may not perform as well,” Dr Ballard says. Other costs that must be taken into account include segmentation software licensing and the time required for technologists to print each model and radiologists to review it.

“If it takes the radiologist one hour per case, that may be too much time if it’s not accounted for, a big cost consideration for starting a 3D printing lab,” Dr Ballard says, noting that 3D printing cannot simply be a “pet project” of two or three radiologists. Instead, it must have the full backing of the institution.

Finally, there is the fact that 3D printing and models are not yet eligible for Medicare reimbursement. “In the vast majority of cases, it’s not reimbursed at all or adequately,” Dr Ballard says. “Just about every 3D printing lab I know of ... operates at a loss.”

However, given the 2019 approval of temporary category III Current Procedural Terminology (CPT) codes for the emerging technology, there is the chance that Medicare eventually will eventually

cover it. In the meantime, Dr Ballard advises institutions to get “creative” when it comes to covering their costs.

At Barnes-Jewish Hospital and St Louis Children's Hospital where he currently practices, Dr Ballard says 3D printing price tiers are based on the length of time, level of difficulty, and other factors associated with generating a given 3D model. These charges are then folded into the diagnosis-related group charge for surgery.

Healthcare systems would also do well to look beyond the direct financial returns on their investment in 3D printing, as it can result in savings associated with faster surgical procedures and shorter patient recovery times.

“When the surgeons have planned it out ahead of time [with 3D printed models], the outcomes are better, the surgery is faster, so they improve turnaround and recovery times and save money,” Duke's Churchill says.

Benefits like these have sparked efforts by major radiological groups to have 3D printing approved for reimbursement. The Radiological Society of North America and the American College of Radiology, for example, have partnered to establish a 3D printing clinical data registry, the goal of which is to provide the data needed to support the technology's transition coverage under Category I CPT codes.

“The anecdotal evidence we see day to day is there, but the biggest challenge is making the time to establish the scientific evidence. This is something we need to improve in the community,” Dr Ballard says.

For her part, Dr Bastawrous remains optimistic that 3D printing will become a mainstay of radiology sooner rather than later. “As more clinical evidence showing the utility and benefits of 3D printing become available, category I (CPT) codes will be adopted, and reimbursement will follow,” she says.

Why Radiologists are Key to Maximizing AI's Potential in Healthcare

Elad Walach

On March 29, 2023, Elon Musk and other tech leaders issued a letter calling for a pause on the “dangerous race” to make artificial intelligence (AI) as advanced as human intelligence. While AI is not new, perceptions and misconceptions are being accelerated thanks to ChatGPT, which has thrust AI into the mainstream spotlight, bringing accessibility, excitement and, in some cases, fear to all kinds of industries.

Two points are worth noting in terms of this letter that generated worldwide attention.

First, dialogue from influential leaders like Musk is concerning because it begins to generalize AI as one thing when the distinction between generative AI, ChatGPT, is significantly different from healthcare AI, which has been on a fundamentally different trajectory for some time. Second, the human versus AI debate is the wrong discussion about AI's value – especially in healthcare. With the massive challenges facing health systems today, hospitals must work smarter, not just harder, and AI provides that opportunity.

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While AI should not be viewed as a savior for healthcare, it is one of the few technologies that helps health systems directly address financial, performance, and resource limitations on day one. For example, a study from Cedars Sinai Medical Center in Los Angeles, California, found clinical AI aiding a reduction in inpatient length of stay (LOS) of 11.9% for patients with intracranial hemorrhage and a 26.3% LOS reduction for those with pulmonary embolism.¹

Radiology's Role in Driving AI Success

Yet results like these are not guaranteed. They are the byproduct of a strategic and scalable approach to AI. Enter radiology — a specialty uniquely positioned to serve as a trusted and needed AI navigator to health systems for two primary reasons.

First, radiologists sit at the center of several crucial patient care milestones with significant downstream impacts. Second, radiologists have long been early adopters and innovators of new approaches to efficient healthcare, including PACS and healthcare AI. In fact, numerous studies have already demonstrated how AI-assisted radiologists benefit from downstream financial

and quality improvements. Consider some of the following impacts:

- 26% decrease in interpretation time for malignant lung nodules.²
- 40% improvement in radiologist read time for low suspicion 3D mammograms.³
- 7-hour decrease in time from imaging to thrombectomy.⁴

To be that valuable resource, however, radiologists need to look beyond the reading room.

If every department implemented AI in a silo — such as radiology AI to radiologists or stroke AI to neuroendovascular surgeons — it would require more information technology (IT) resources and fragment facility-wide return on investment potential. Physicians would encounter obstacles that may delay clinical care, radiologic throughput, and overall efficiency.

If we look at the studies demonstrating AI's positive cross-department benefits, they leverage technology orchestration that brings disparate systems together. In other words, they prove the value in moving from a single AI solution to an enterprise-wide strategic approach that leverages an AI platform, otherwise known as an AI operating system (aiOS).

Radiology is a specialty uniquely positioned to serve as a trusted AI navigator to health systems...

Guiding Facilities from a Point Solution to a Platform

An aiOS is a tool that efficiently coordinates the flow of data between different points within a healthcare network, allowing physicians to optimally use multiple AI-based tools for their own clinical needs in an interoperable fashion while eliminating the need to rework the IT infrastructure for every new integration.

Each time a new solution designed to detect a different pathology is integrated, an aiOS orchestrates the algorithms of the integrated solutions to ensure that they do not conflict, but rather complement, each other when possible.

In a scenario where two solutions can technically detect the same pathology, an operating system can make automated decisions to optimally apply the right algorithm to match the suspected pathology. This principle extends beyond the reading room and well into other segments of direct patient care, as well.

The aiOS can be key to a successful AI strategy because it is NOT purely focused on one department. Indeed, an ideal aiOS is:

- All-encompassing, providing the ability to integrate applications across specialties versus managing separate solutions requiring different platforms.

- Scalable, capable of managing from 1 to 50 solutions at the flip of a switch.
- Seamless, integrating within native workflow and IT infrastructure (PACS, electronic health record, scheduling, etc.).
- Highly measurable, with the ability to show value to myriad stakeholders.

In care coordination scenarios, an aiOS could improve communication between caregivers within a health network with automated alerts, delivering relevant information for timely review by, for example, an interventional radiologist or an endovascular surgeon.

Becoming a Champion

Healthcare AI is no longer in its infancy; it continues to be refined and adapted as lessons are learned and more adept solutions are developed. By addressing the challenges and pitfalls that historically have hampered the adoption of AI, health systems can fully harness the power of AI to bring about meaningful and lasting change in the industry.

Developing a comprehensive AI strategy that includes an enterprise approach, an integrated aiOS and a robust change-management process can be a game-changer for

health systems, driving growth and improving patient care for the short and long term.

Radiology will have a key role to play in leading this evolution.

REFERENCES

- 1) Petry, M., Lansky, C., Chodakiewitz, Y. G., Maya, M. M., & Pressman, B. D. (2022b). Decreased hospital length of stay for ich and pe after adoption of an artificial intelligence-augmented radiological worklist triage system. *Radiol Res Pract.* 2022; 1–7. <https://doi.org/10.1155/2022/2141839>
- 2) Aidoc. (2023). A Medicare Claims-Based Analysis of the impact of ai on readmission rates. [White paper]
- 3) Lo, S. B., Freedman, M. L., Gillis, L., White, C. L., & Mun, S. K. (2018). JOURNAL CLUB: Computer-aided detection of lung nodules on ct with a computerized pulmonary vessel suppressed function. *Am J Roentgenol.* 210(3): 480–488. <https://doi.org/10.2214/ajr.17.18718>
- 4) Van Winkel, S., Rodriguez-Ruiz, A., Appelman, L., Gubern-Mérida, A., Karssemeijer, N., Teuwen, J., Wanders, A. J. T., Sechopoulos, I., & Mann, R. M. (2021). Impact of artificial intelligence support on accuracy and reading time in breast tomosynthesis image interpretation: a multi-reader multi-case study. *Euro Radiol.* 31(11): 8682–8691. <https://doi.org/10.1007/s00330-021-07992-w>
- 5) Gupta, K. (2022) Mechanical Thrombectomy, Artificial Intelligence And The Activation Of A Pulmonary Embolism Response Team. Presented at PERT Consortium. <https://pertconsortium.org/wp-content/uploads/2022/09/Use-of-Artificial-Intelligence-in-the-Activation-of-a-Pulmonary-Embolism-Response-Team.pdf>



Sustainable Global Outreach Through a Holistic Approach to Virtual Learning

Mai Elezaby, MD; Carley Hansen-Prince, MEd, RT (R) (ARRT); Jenna MacLaine, RT(R), CTIC, CAE, BSc

Global healthcare disparities and poor health outcomes in low- and middle-income countries (LMICs) require innovative interventions to bring about health system-wide improvements.¹ A comprehensive approach to upscaling healthcare education is an important way to address these goals.

Indeed, through the macro-level (eg, increasing knowledge of organizational structures, governance, healthcare economics), meso-level (learning innovative strategies for networking, communications and sharing of interdisciplinary knowledge across healthcare systems), and micro-level (increasing medical knowledge, procedural skills and clinical operations for staff at individual sites). The World Health Organization in 2016 called upon the international community to upscale the quantity, quality, and sustainability of healthcare education through innovative teaching and communication strategies.² Yet, as of 2022, significant global shortages of healthcare professionals still existed.³ According to a recent report by Hricak, et al,

radiology equipment and workers are in short supply in LMICs, where upscaling has significant potential to improve patient outcomes.⁴

From the oncology perspective alone, simulations show that scaling up imaging for the 11 leading cancers worldwide in LMICs could avert 2.46 million deaths between 2020 and 2030, while upscaling imaging, treatment, and quality of care could avert 9.5 million deaths, saving 232.30 million life-years.⁴

Leveraging education to upscale imaging services globally and domestically is a primary mission of RAD-AID.⁵ However, the challenges of collaborating with stakeholders around the world highlight the need for a versatile, web-based platform to facilitate communication and content delivery.

To this end, in 2014, RAD-AID began developing its Online Learning Center (OLC). Learning management systems (LMS) and online education platforms greatly facilitate distance-learning; they provide versatility in content creation and deployment, allowing students to progress at their own pace through material tailored to their individual needs.

The robust tools available on many platforms encompass assignments, quizzes with facilitated grading, and

discussion forums allow instructors to monitor students' progress.⁶ Learning management systems can be deployed on smartphones, tablets, and laptop computers, facilitating user access to online education, especially in technology-deprived regions of the world.⁷ Indeed, LMSs represent an invaluable opportunity for RAD-AID volunteers to sustain healthcare education and maintain connections between outreach trips, as well as during times when travel may be limited.

In RAD-AID's case, several online products were considered; ultimately, Moodle™, an open source LMS was chosen based on such factors as its cost, ease of deployment, maintenance, and user accessibility, as well as its global accessibility, versatility, and wide technical support.⁸

Next, content expert groups, drawn from RAD-AID's vast network of 14,000 volunteers and chapters in 92 ACGME-accredited academic and community-based medical centers in the US and Canada, were formed to collect and author educational materials. Collaborations with and generous donations from several radiological societies and other expert groups facilitated course development.

RAD-AID took a holistic approach to its educational mission. It began

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The RAD-AID Online Learning Center currently hosts 39 courses for upwards of 1,500 registered users; user engagement and content relevance to partner countries are monitored continuously in collaboration with local stakeholders.

by educating and affirming the expertise of its multidisciplinary team members and volunteers through the Proficiency in Global Health (PGH) Certificate program. The longitudinal, blended curricular program focuses on project planning and implementation to upscale imaging services according to each country's specific public health concerns and health system's capacity and infrastructure.

The PGH certificate program also covers cultural competency, medical ethics, and communications training to prepare global outreach workers for often unfamiliar practice environments. RAD-AID leaders also created a pipeline for future physicians with a passion for global health in radiology with the Medical Students Global Health Radiology Online certificate.⁹

The OLC curriculum for students, meanwhile, addresses multiple areas of training for all health-care professionals and radiology department staff. For instance, it covers interpretive skills for medical students, radiology residents, and practicing radiologists in all subspecialties, as well as technical instructions for radiologic technologists, radiation therapists, sonographers, physicists, and radiology nurses.

The OLC also covers business development, finance, and even informatics infrastructure. All course materials, moreover, are continuously developed and updat-

ed according to sound educational theories and published curricula.¹⁰ The OLC currently hosts 39 courses for upwards of 1,500 registered users; user engagement and content relevance to partner countries are monitored continuously in collaboration with local stakeholders.

The OLC faced one of its first major tests in the midst of the COVID-19 pandemic, when travel restrictions forced many medical specialty groups and nonprofits to suspend their outreach efforts. The OLC helped onsite educational and clinical collaborations quickly pivot to virtual learning, resulting in exponential growth and utilization of the OLC.

Future Directions

Going forward and keeping in line with RAD-AID's philosophy of continuous assessment and self-improvement, the OLC and its curriculum will be expanded and updated as necessary to achieve the highest possible educational outcomes. Importantly, the robust OLC curricula have made it possible to initiate subspecialty fellowships in breast imaging and interventional radiology, as well as the option for certification in sonography proficiency. These initial successes promote high-quality local health-care workforce development and are setting the stage for additional expansion into other subspecialties and certifications.

References

- 1) Kruk ME, Gage AD, Arsenault C, et al. High-quality health systems in the sustainable development goals era: time for a revolution. *Lancet Global Health*. 2018;6(11):e1196-e1252. doi: 10.1016/S2214-109X(18)30386-3
- 2) World Health Organization. Transforming and scaling up health professionals' education and training: World Health Organization guidelines 2013.
- 3) Global Burden of Disease 2019 Human Resources for Health Collaborators. Measuring the availability of human resources for health and its relationship to universal health coverage: estimates for 204 countries and territories from 1990 to 2019. *The Lancet*. 2022. doi: 10.1016/S0140-6736(22)00532-3
- 4) Hricak H, Abdel-Wahab M, Atun R, et al. Medical imaging and nuclear medicine: a Lancet Oncology Commission. *The Lancet Oncol*. 2021;22(4):e136-e172. doi: [https://doi.org/10.1016/S1470-2045\(20\)30751-8](https://doi.org/10.1016/S1470-2045(20)30751-8)
- 5) Mollura DJ, Soroosh G, Culp MP. 2016 RAD-AID Conference on International Radiology for Developing Countries: Gaps, Growth, and United Nations Sustainable Development Goals. *J Am Coll Radiol*. 2017;14(6):841-847. doi: <https://doi.org/10.1016/j.jacr.2017.01.049>
- 6) Dziuban C, Graham CR, Moskal PD, Norberg A, Sicilia N. Blended learning: the new normal and emerging technologies. *Intl J Educat Tech Higher Ed*. 2018;15:1-16.
- 7) Ghanem S. E-learning in higher education to achieve SDG 4: benefits and challenges. 2020 Second International Sustainability and Resilience Conference: Technology and Innovation in Building Designs(51154) 2020; 1-6.
- 8) Moodle. <https://moodle.org/>. Accessed 2023 March 15.
- 9) England RW, Lugossy A-M, Mollura DJ. Increasing opportunities for trainees to engage in global health radiology: radiology In training. *Radiology*. 2021;300(2):E320-E322. doi: 10.1148/radiol.2021210371
- 10) Culp MP, Stein-Wexler R, Elezaby M, et al, eds. *Radiology in Global Health: Strategies, Implementation, and Applications*. Cham: Springer International Publishing, 2019; p. 141-153.

Neonatal Thymic Hemorrhage

Jonah A. Wachs; Jade B. Greer, MS; Lavi Nissim, MD; Angela R. Garcia, PhD; Sudhen B. Desai, MD, FSIR

Case Summary

An infant presented with difficulty breathing and feeding. The patient had hyperbilirubinemia and bilious stools since birth and developed acute hypoxic respiratory failure. These signs were related to a large mediastinal mass, severe metabolic lactic acidosis, anemia, acute severe coagulopathy, and hemorrhagic disease of the newborn, all due to vitamin K deficiency.

Laboratory serum analysis demonstrated low hemoglobin and high urine glucose levels. Thrombocytopenia was also present (110 K/ μ L). These were followed-up with x-ray, CT, MRI, and ultrasound to help determine the etiology of the mediastinal mass.

Imaging Findings

Contrast-enhanced chest CT (Figure 1) demonstrated an anterior mediastinal mass measuring 4.3 \times 5.4 cm, exerting pressure on the heart and left brachiocephalic vein with mildly prominent bilateral lymph nodes. Doppler ultrasound of the chest (Figure 2) did not demonstrate blood flow within the lesion.

Contrast MRI of the chest/abdomen (Figure 3) demonstrated the crescent-shaped mediastinal mass measuring 4.1 \times 3.8 \times 1.0 cm anterior to the thymus and heart. A T1 pre-

contrast coronal image of the infant's thoracoabdominal region (not shown) demonstrated mild hyperintensity, but no significant contrast enhancement. T2 images showed hypointense signal.

Diagnosis

Neonatal thymic hemorrhage.

Differential diagnosis of mediastinal mass lesions in neonates includes thymoma, thymic carcinoma, lymphoma/lymphadenopathy, thyroid mass, and germ-cell neoplasm.

Discussion

Thymic hemorrhage is defined by extravasated erythrocytes in the thymic parenchyma. In neonates, this commonly results from diet and vitamin K deficiency but is also possible from trauma.¹ Reported cases of thymic hemorrhage in newborns have presented with respiratory distress, pleural effusion, mediastinal mass lesions, anemia, and vitamin K deficiency.^{2,3}

Vitamin K deficiency is common in newborns, owing to limitations in transplacental passage of vitamin K and only trace amounts of the vitamin present in breast milk. A prolonged deficiency may cause complications such as Vitamin K deficiency bleeding (VKDB),⁴ which is commonly secondary to preexisting bleeding disorders.⁵

A typical dose of vitamin K prophylaxis administered intramuscularly at birth aids in addressing the deficiency. However, out-of-hospital births, concerns among parents about the injection, and anti-vaccination

sentiment can sometimes lead to refusal of prophylaxis, as in this case.⁶

Denial of prophylaxis in this patient potentially resulted in poor Vitamin K-dependent coagulation factors, which subsequently caused coagulopathy and jaundice, two symptoms of VKDB.⁷ On the third day after the neonate's admission to the hospital, the hematology service recommended administration of 2.5 mg of vitamin K supplementation daily. X-ray imaging approximately one month days after admission demonstrated resolution of the mediastinal mass, confirming the diagnosis of thymic hemorrhage mimicking a mass.

The etiology and pathognomonic sequelae of thymic hemorrhage are obscure, but many signs indicate the condition. Respiratory distress in newborns is one initial sign.^{2,3} The most prevalent imaging sign is a mediastinal mass. These lesions are commonly misinterpreted as tumors, owing to their infrequency. Distinguishing a hematoma from a malignancy can be achieved through cross-sectional imaging and short-interval follow-up to ensure lesional resolution.

Lack of k-dependent coagulant proteins from vitamin K deficiency may restrict clotting and cause increased blood loss in atypical regions, including the thymus. Bleeding can also occur intrathoracically, intracranially, and in the abdominal cavity among other locations.⁷

If an infant presents with a large thymic mass due to a potential hemorrhage, determining whether they received vitamin K supplementation at birth is critical as a thymic

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Figure 1. Contrast-enhanced CT scan of the chest demonstrates an anterior mediastinal mass of measuring 4.3 x 5.4 cm. The lesion is displacing the heart and left brachiocephalic vein, but no airway compromise is noted.

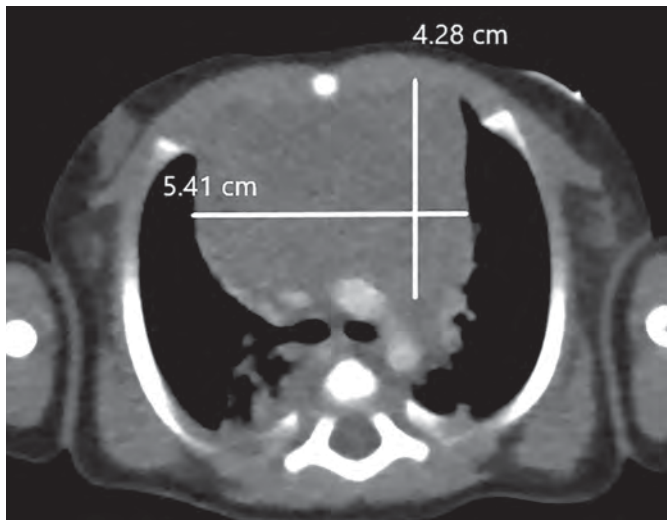


Figure 2. Doppler ultrasound demonstrates lack of flow in the mass.

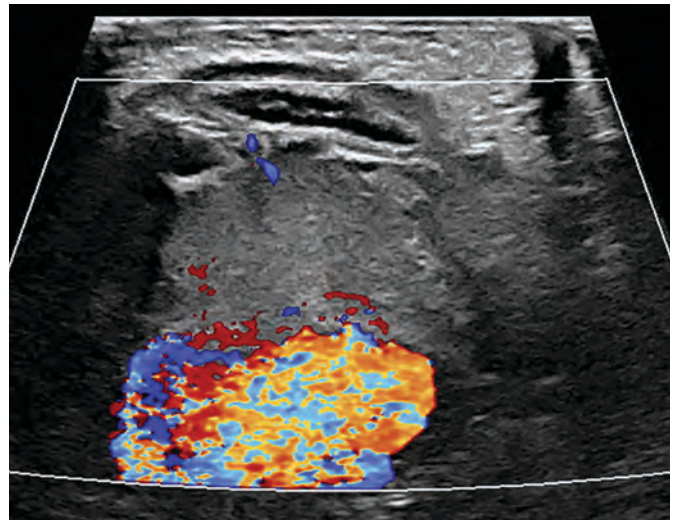
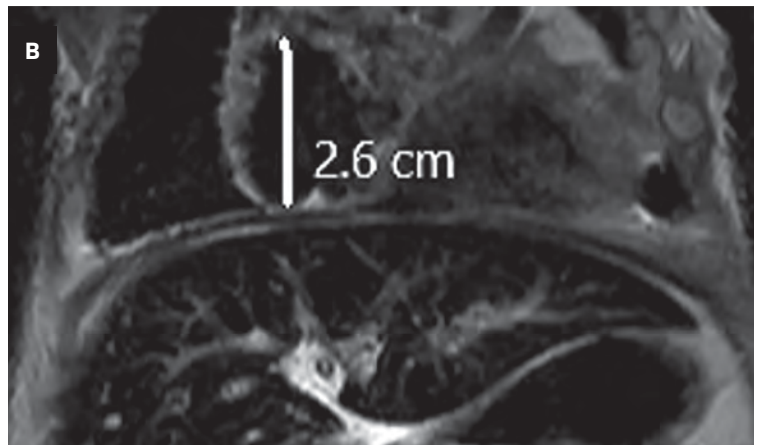
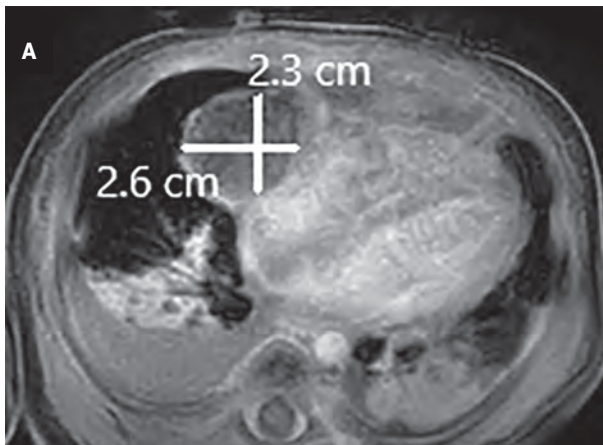


Figure 3. (A) T1 postcontrast axial MRI demonstrates no significant enhancement. (B) Coronal T2 demonstrates hypointense signal.



mass is more likely to be of hemorrhagic etiology if no prophylaxis was administered.

Laboratory results also support the diagnosis under the above circumstances. Low hemoglobin, blood glucose, lymphocyte, and platelet levels, as well as signs of anemia, all demonstrate potential hemorrhage. Thymic bleeding may cause these deficiencies.

Conclusion

Neonatal thymic hemorrhage is an exceedingly rare condition that requires investigation of the etiology. Imaging can help elucidate the etiology of the thymic lesion, particularly

with blood-sensitive MRI sequences in the appropriate clinical setting.

References

- 1) Hobbie K, Elmore S, Kolenda-Roberts HM. Thymus - hemorrhage - nonneoplastic lesion atlas. National Institute of Environmental Health Sciences. <https://ntp.niehs.nih.gov/nnl/immune/thymus/hemorrhage/index.htm>. Published February 3, 2015. Accessed June 15, 2023.
- 2) Walsh SV, Cooke R, Mortimer G, Loftus BG. Massive thymic hemorrhage in a neonate: an entity revisited. *J Pediatr Surg*. 1996;31(9):1315-1317. doi:10.1016/s0022-3468(96)90263-8
- 3) Woolley MM, Isaacs H Jr, Lindesmith G, Vollmer DM, Van Adelsberg S. Spontaneous thymic hemorrhage in the neonate: report of two cases. *J Pediatr Surg*. 1974;9(2):231-233. doi:10.1016/s0022-3468(74)80128-4
- 4) Matsuda I, Nishiyama S, Motohara K, Endo F, Ogata T, Futagoishi Y. Late neonatal vitamin K deficiency associated with subclinical liver dysfunction in human milk-fed infants. *J Pediatr*. 1989;114(4 Pt 1):602-605. doi:10.1016/s0022-3476(89)80704-8
- 5) Ayyan M, Zahid A, Ehsan M, Mehmood Q, Ullah I, Asghar MS. Vitamin K shot in newborn babies: An unprecedented sequelae. *Ann Med Surg (Lond)*. 2022;78:103942. Published 2022 Jun 4. doi:10.1016/j.amsu.2022.103942
- 6) Center For Disease Control and Prevention. Protect babies from life-threatening bleeding - talk to expectant parents about the benefits of the vitamin K shot for newborns. Centers for Disease Control and Prevention. <https://www.cdc.gov/ncbddd/vitamink/vitamin-k-fact-sheet-hcp.html>. Published January 1, 2021. Accessed June 13, 2022.
- 7) Araki S, Shirahata A. Vitamin K deficiency bleeding in infancy. *Nutrients*. 2020;12(3):780. Published 2020 Mar 16. doi:10.3390/nu12030780

Chronic Periaortitis Mimicking Aortic Intramural Hematoma

Adam Kerestes, DO; Thaddeus Yablonsky, MD

Case Summary

An elderly patient with a history of hypertension, hyperlipidemia, and type II diabetes presented initially for gastroenterology evaluation. The patient reported a remote history of jaundice prompting exploratory laparotomy, cholecystectomy, and partial liver resection in another country, with unclear underlying pathology. Records were not available.

To guide further treatment, the gastroenterology service requested abdominal CT with and without contrast. The study demonstrated postsurgical changes in the liver without acute abdominal findings. However, the included portion of the lower chest incidentally revealed a crescentic hyperdensity surrounding the proximal aorta, concerning for intramural hematoma (Figure 1). Computed tomography angiography (CTA) of the chest was subsequently performed.

Imaging Findings

The chest CTA revealed eccentric, lobulated tissue encasing the aorta

from the root through the great vessels extending to the descending aorta. The tissue was hyperdense on noncontrast images, measuring 58-60 Hounsfield units, and contained several calcifications. The findings were concerning for a type A intramural hematoma (IMH, Figure 2).

Diagnosis

Chronic periaortitis.

The patient underwent surgery for presumed type A IMH but instead was found to have rubbery, white tissue encasing the aorta. Biopsy revealed densely fibrotic tissue with plasma cells.

Discussion

Chronic periaortitis (CP) is rare and most commonly described as involving the infrarenal descending aorta and iliac arteries. The spectrum of disease includes idiopathic retroperitoneal fibrosis, as well as inflammatory abdominal aortic aneurysms. However, this process has increasingly been noted to involve the thoracic aorta.

This disorder presents a diagnostic conundrum, as the imaging findings are hard to ignore as a type A IMH. However, the patient denied ever

having symptoms of an acute aortic syndrome. Given the possibility of progression to frank rupture or dissection, the patient was taken to surgery, but instead of an IMH, "a shiny white very firm rubbery tissue that could best be described as resembling cartilage" was encountered as described in the operative report (Figure 3). Biopsies of the periaortic tissue and an aorticopulmonary window lymph node revealed densely fibrotic tissue with chronic inflammation, including plasma cells. Additional special and immunohistochemical stains were performed, the results of which were negative for spirochetes, with only a minor subset positive for IgG4 (<40%), which was considered to be insufficient evidence for IgG4-related disease.

Chronic periaortitis has been postulated to reflect an exaggerated inflammatory response to atherosclerotic plaque antigens.¹ Limited studies exist regarding this condition, however, and its exact etiology remains unconfirmed. Much of the literature is supported by research about other periaortic conditions. A similar autoimmune process affects patients with IgG4-related disease or fibrosing mediastinitis,² which supports an autoimmune etiology. Thoracic involvement has been

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Figure 1. (A) Noncontrast CT through the lower chest demonstrates an eccentric, crescent-shaped hyperdensity (arrow) surrounding the ascending aorta, predominantly along the right edge of the aorta (B, arrow). Axial CT at a higher level demonstrates more lobulated hyperdense tissue along the right ascending aorta.

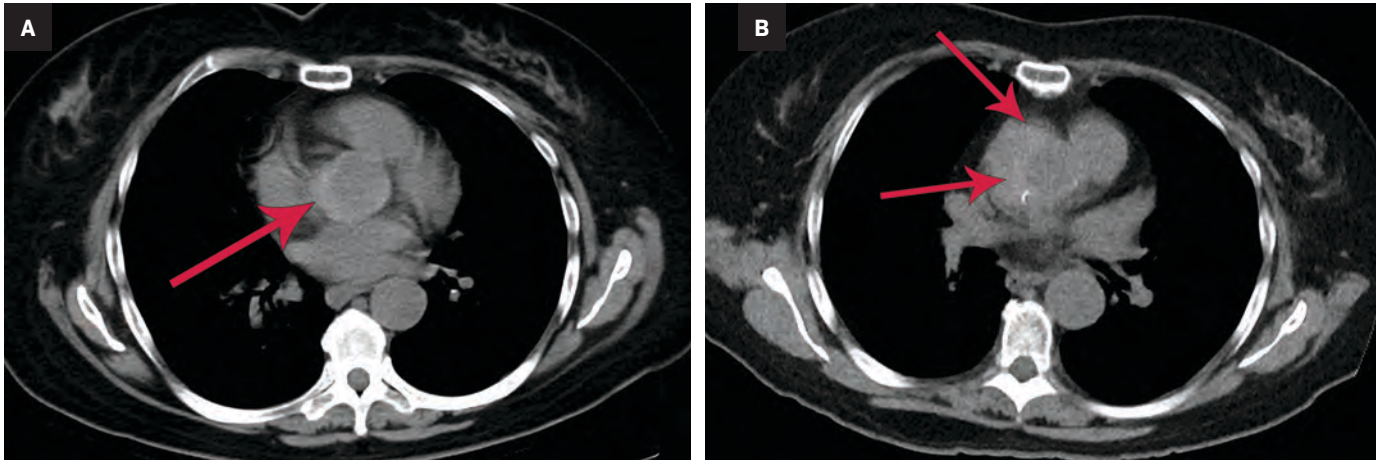


Figure 2. (A) Axial postcontrast arterial phase CT highlights the tissue (arrow) encasing the aorta and demonstrates a calcification laterally within the tissue. (B, C) Coronal postcontrast arterial phase CT demonstrates extent of the periaortic tissue, circumferentially encasing the aorta and extending to surround the great vessels.

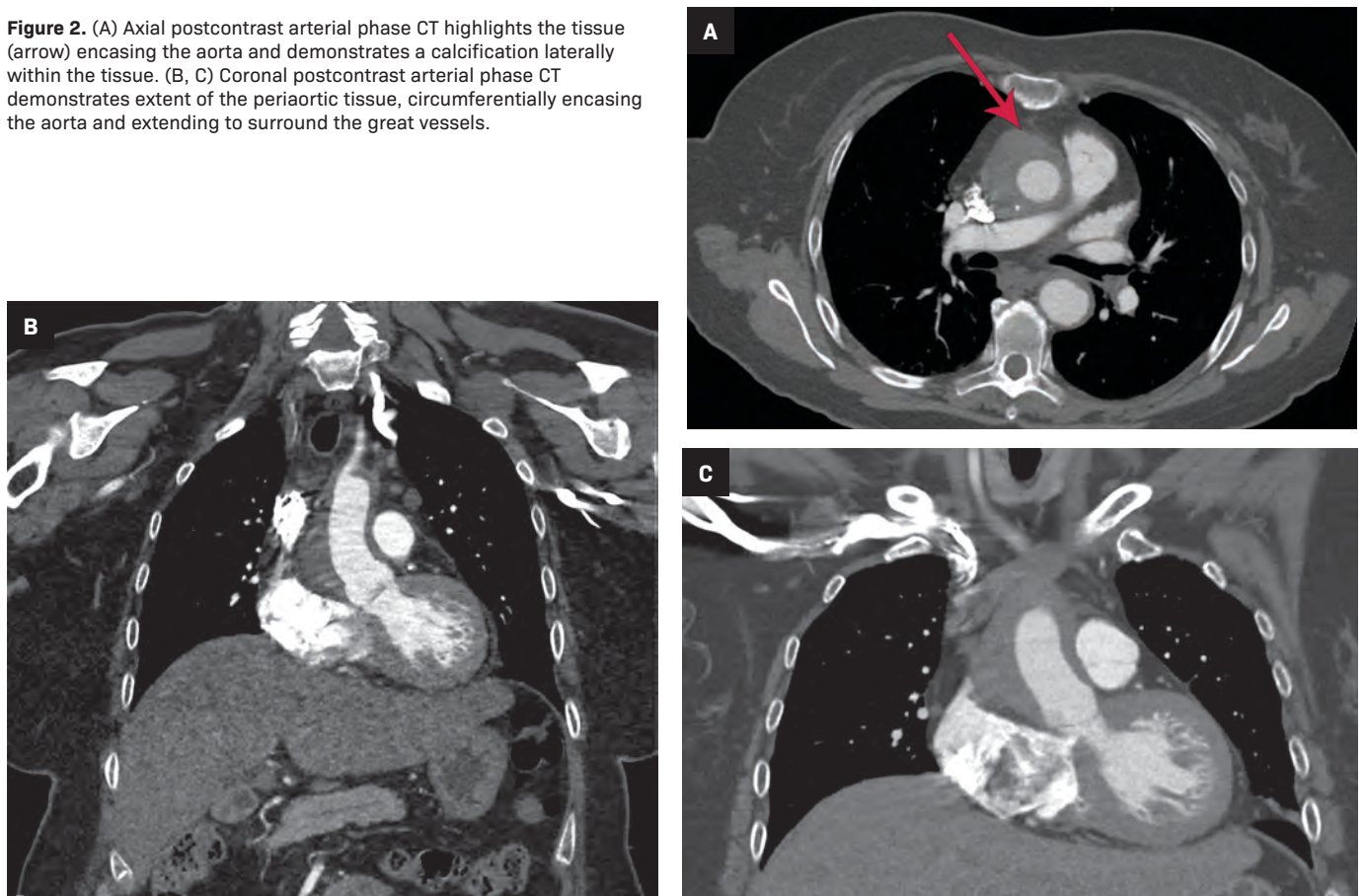
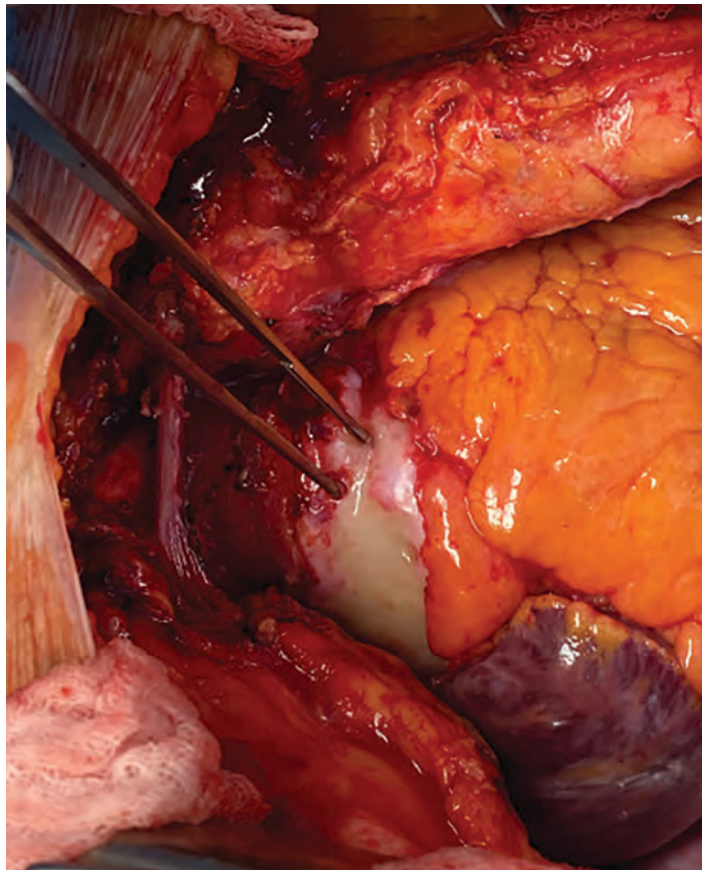


Figure 3. An intraoperative image with the tip of the surgical instrument indicating the abnormal tissue. This was described as rubbery, white tissue resembling cartilage, discordant with the expected finding of intramural hematoma.



described in several studies.^{1,3} In a review by Palmisano, et al, of 153 patients with CP documented by abdominal imaging, 36% were also noted to have thoracic involvement.³

In the same study, the patterns of large thoracic artery involvement mimicked findings seen in other large vessel inflammatory diseases such as giant cell arteritis and temporal arteritis. They compared pathology from patients with inflammatory conditions involving the periaortic abdominal aorta, such as retroperitoneal fibrosis, as well as those with thoracic involvement with or without concurrent abdominal involvement.

Comparison of the two subgroups revealed similar biopsy findings in thoracic and abdominal involvement, namely adventitial inflammation.³ These findings were also present in giant cell and temporal arteritis, suggesting that thoracic

aortic involvement may reflect a large-vessel inflammatory disease³ and be a primary inflammatory or autoimmune disorder.

Mainstays of treatment are inflammation- or immune-modulating medications. Our patient remained asymptomatic, did not show progression on short-term follow-up, and continues to be managed conservatively.

Conclusion

Recognizing the imaging pattern of thoracic aortic intramural hematoma is important, especially in the setting of acute aortic syndrome. Any crescentic hyperdensity surrounding the ascending aorta should prompt further imaging and/or surgical evaluation. This case highlights a rare mimic of this life-threatening condition and demonstrates how

much overlap can exist between certain conditions. Furthermore, this case presents a potential link to other periaortic vascular diseases and may be a topic of future study in radiology and rheumatology.

References

- 1) Vaglio A, Pipitone N, Salvarani C. Chronic periaortitis: a large-vessel vasculitis? *Current Opinion in Rheumatology*. 2011;23(1): 1-6.
- 2) Palmisano A, Maritati F, Vaglio A. Chronic periaortitis: an update. *Curr Rheumatol Rep*. 2018; 20(12): 80.
- 3) Palmisano A, Urban ML, Corradi D, et al. Chronic periaortitis with thoracic aorta and epiaortic artery involvement: a systemic large vessel vasculitis? *Rheumatology (Oxford)*. 2015; 54(11): 2004-2009.
- 4) Jois RN, Gaffney K, Marshall T, Scott DGI. Chronic periaortitis. *Rheumatology*. 2004; 43, (11): 1441-1446.
- 5) Pipitone N, Ghinai A, Versari A, Vaglio A, Palmisano A, Salvarani C. Chronic periaortitis. *Circulation*. 2008; 118(11).

Aneurysmal Bone Cyst

Richard Wang, MD; Karen Yuan, MD; Saad Nini, MD; Gaurav Saigal, MD

Case Summary

A teenager presented with a history of an enlarging, painful mass in his right lower leg and increasing pain with ambulation during the past few months. On physical examination, there was tenderness to palpation of the right lateral lower leg.

Imaging Findings

Radiography (Figure 1) demonstrated a large, expansile mass in the distal fibula with internal septations. There was extensive destruction of the distal diaphysis, metaphysis, physis, and epiphysis with marked cortical thinning and periosteal reaction at both the proximal and distal aspects of the mass.

MRI (Figure 2) redemonstrated an expansile and markedly septated mass containing fluid-fluid levels with surrounding soft-tissue edema. Post-gadolinium imaging showed extensive peripheral and linear septal enhancement with scattered areas of more nodular septal enhancement.

Catheter angiography performed during preoperative embolization (Figure 3) showed the mass to be hypervascular, primarily supplied by the peroneal artery, with feeding

branches from the anterior tibial and posterior tibial arteries.

Diagnosis

Aneurysmal bone cyst.

Differential diagnosis includes telangiectatic osteosarcoma, chondroblastoma, giant cell tumor, metastatic disease, and multiple myeloma.

Discussion

Aneurysmal bone cysts (ABCs) are rare, highly vascularized, expansile benign lytic lesions. They most frequently occur at the metaphysis of the long bones within the first two decades of life and constitute 1-2% of primary bone tumors.¹ Once believed to be non-neoplastic reactive lesions, ABCs have recently been shown to have gene rearrangements, and 70% are considered true neoplasms.² They can also be associated with preexisting bony lesions, as they share characteristics such as histology and location but without underlying genetic mutations.³ ABCs can thus be considered either primary neoplasms or secondary to a preexisting bone tumor.

Radiography demonstrates an expansile, septated, lucent lesion with cortical thinning. They can have irregular margins with periosteal reaction, mimicking more aggressive

malignant lesions.⁴ Cross-sectional imaging with CT or MRI reveals internal fluid-fluid levels, along with improved visualization of septations and cortex.

Magnetic resonance imaging plays a uniquely important role, as the modality can depict the involvement of adjacent soft tissues, presence of solid components, and extent of surrounding edema, which is frequently underestimated on radiographs and CT scans. The presence of enhancing solid components on MRI raise concern for an associated malignant lesion; however, solid variants of ABC have been described.⁵

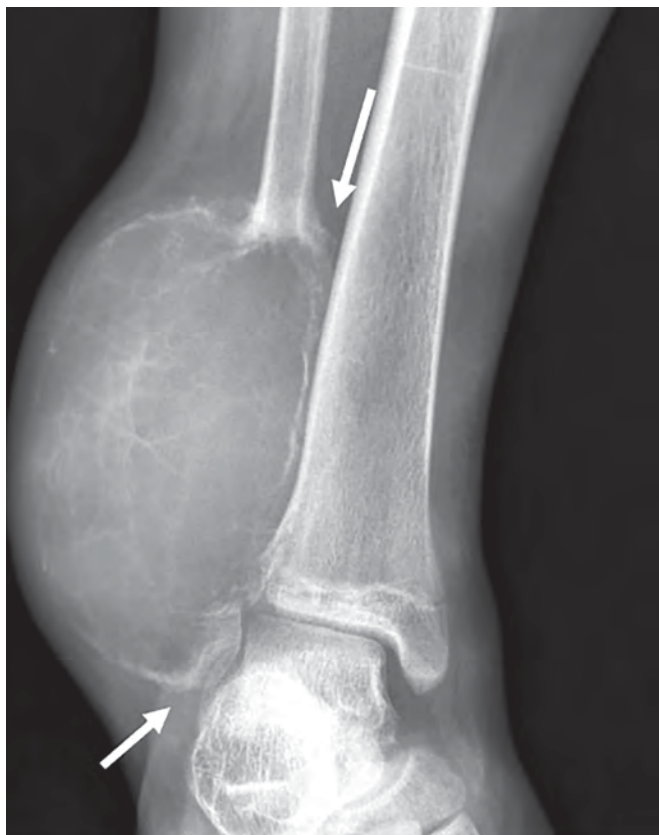
Triple-phase bone scan can be helpful in cases of suspected malignancy to evaluate for osteoblastic activity outside the primary site. Otherwise, for primary ABC, a bone scan will show nonspecific increased radiotracer activity, which reflects osteoblastic activity, hyperemia, and/or new bone formation.⁶

Catheter angiography can be useful vascular mapping and potentially embolization. Overall, imaging plays an important role evaluating expansile lytic lesions like ABCs. However, biopsy and histologic evaluation are required for definitive diagnosis.

Treatment depends on lesion size and region of involvement. Options include curettage with or without bone graft and en bloc resection.

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Figure 1. Radiograph demonstrates an expansile, lytic mass at the distal fibula with periosteal reaction (white arrows) at the proximal aspect of the mass and at the residual lateral malleolus.



Curettage is the standard of care, but it has a variable recurrence rate.⁷ En bloc resection is associated with lower rates of recurrence but also with higher morbidity; thus, it is primarily reserved for cases where it will not compromise function.⁷ Since ABCs are highly vascular structures, preoperative selective arterial embolization with catheter angiography can minimize the risk of intraoperative hemorrhaging of larger lesions, as well as serve as an alternative treatment for those that are difficult to access surgically.⁸

The differential diagnosis for ABC includes telangiectatic osteosarcoma (TOS), chondroblastoma, giant cell tumor, metastatic disease, and multiple myeloma. As a rare, aggressive malignant tumor, TOS tends to show thickened, nodular internal septations with wide zones of transition. They frequently infiltrate adjacent soft tissue and contain solid enhancing components on MRI.⁹

Figure 2. (A) Axial STIR MRI demonstrates a large mass of the distal fibula with multiple fluid-fluid levels (black arrows) and perilesional soft-tissue edema (white arrow). (B) Axial T1, fat-suppressed post-gadolinium imaging demonstrates extensive peripheral and septal enhancement (dashed white arrows) with scattered areas of thickened, nodular, enhancing septations (dashed black arrows).

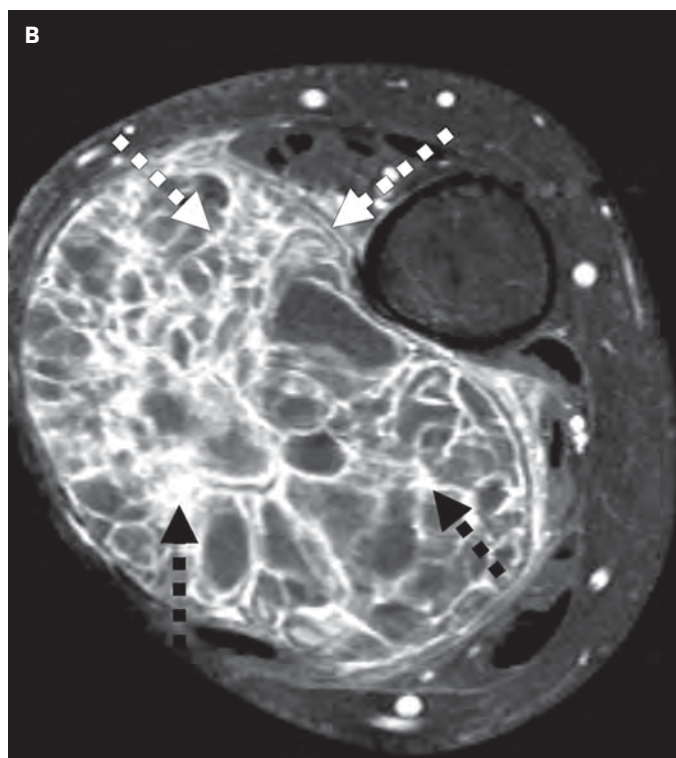
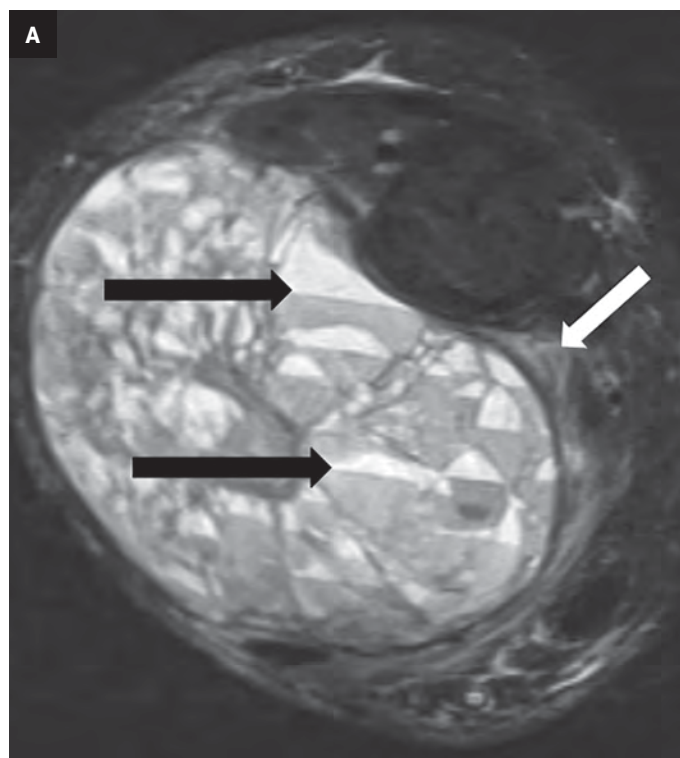
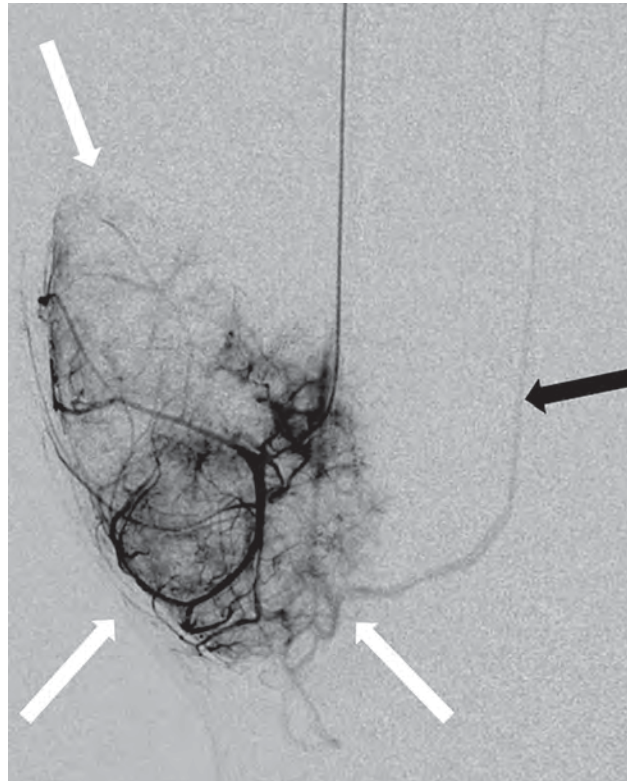


Figure 3. Digital subtraction catheter angiography performed during preoperative embolization demonstrates a hypervascular expansile tumor (white arrows) primarily supplied by the peroneal artery with feeding branches from the anterior and posterior tibial arteries (black arrow).



Chondroblastomas are benign lesions that usually do not feature a soft-tissue component and often present with intact cortical bone. They typically arise from the epiphysis or apophysis of long bones in young patients. Giant cell tumors are benign bony neoplasms that occur at the epiphysis of long bones after growth plate closure. These lesions can show locally aggressive features such as wide zones of transition, cortical thinning, and soft-tissue extension.¹⁰ Despite being considered benign, they can metastasize, most often to the lungs.¹⁰ Metastatic disease and multiple myeloma commonly present with multiple lytic lesions that can be expansile. These should be included in the differential diagnosis for patients over age 40, with the most common expansile metastatic lesions arising from thyroid carcinoma and renal cell carcinoma.

Conclusion

Aneurysmal bone cysts are rare, hypervascular, expansile, benign lytic

lesions often presenting within the first two decades of life. The differential diagnosis includes telangiectatic osteosarcomas, giant cell tumors, chondroblastomas, metastatic disease, and multiple myeloma. Prognosis and management differ among these lesions, and their imaging features often overlap. Imaging plays an important role in assessing their size, location, aggressiveness, degree of soft-tissue extension, and presence of solid components to help guide optimal management.

References

- 1) Zehetgruber H, Bittner B, Gruber D, et al. Prevalence of aneurysmal and solitary bone cysts in young patients. *Clin Orthop Related Res.* 2005;439:136-143. doi:10.1097/01.blo.0000173256.85016.c4
- 2) Oliveira AM, Perez-Atayde AR, Inwards CY, et al. USP6 and CDH11 oncogenes identify the neoplastic cell in primary aneurysmal bone cysts and are absent in so-called secondary aneurysmal bone cysts. *Am J Pathol.* 2004;165(5):1773-1780. doi:10.1016/S0002-9440(10)63432-3
- 3) Cottalorda J, Kohler R, Sales de Gauzy J, et al. Epidemiology of aneurysmal bone cyst in children: a multicenter study and literature review. *J Pediatr Orthop B.* 2004;13(6):389-394.
- 4) Cottalorda J, Bourelle S. Modern concepts of primary aneurysmal bone cyst. *Arch Ortho Trauma Surg.* 2007;127(2):105-114. doi:10.1007/s00402-006-0223-5
- 5) Ghosh A, Singh A, Yadav R, Khan SA, Kumar VS, Gamanagatti S. Solid variant ABC of long tubular bones: A diagnostic conundrum for the radiologist. *Indian J Radiol Imaging.* 2019;29(3):271-276. doi:10.4103/ijri.IJRI_160_19
- 6) Agrawal A, Purandare N, Shah S, Rangarajan V. Metastatic mimics on bone scan: "All that glitters is not metastatic." *Indian J Nucl Med.* 2016;31(3):185-190. doi:10.4103/0972-3919.183605
- 7) Park HY, Yang SK, Sheppard WL, et al. Current management of aneurysmal bone cysts. *Curr Rev Musculoskelet Med.* 2016;9(4):435-444. doi:10.1007/s12178-016-9371-6
- 8) Papagelopoulos PJ, Choudhury SN, Frassica FJ, Bond JR, Unni KK, Sim FH. Treatment of aneurysmal bone cysts of the pelvis and sacrum. *J Bone Joint Surg Am.* 2001;83(11):1674-1681. doi:10.2106/00004623-200111000-00009
- 9) Liu J jian, Liu S, Wang J guang, et al. Telangiectatic osteosarcoma: a review of literature. *OncoTargets and Therapy.* 2013;6:593.
- 10) Montgomery C, Couch C, Emory CL, Nicholas R. Giant cell tumor of bone: review of current literature, evaluation, and treatment options. *J Knee Surg.* 2019;32(4):331-336. doi:10.1055/s-0038-1675815

Melorheostosis and Osteopoikilosis

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Case Summary

A previously healthy adult with no medical history presented to the emergency department following pelvic and lower limb trauma.

Imaging findings

X-rays of the pelvis and left lower limb showed multiple micronodular, high-intensity, homogeneous densities varying in size up to 10 mm. These densities involved the acetabula, bilateral ilio-pubic and ischio-pubic rami, proximal and distal epiphyseal metaphyses of the left femur and tibia, as well as the calcaneus and tarsal bones (Figure 1). The images also revealed homogeneous thickening on the inner cortical surfaces at the distal diaphysis of the left femur and proximal and middle diaphyses of the left fibula (Figure 2), with a “dripping candle wax” appearance.

Diagnosis

Melorheostosis and osteopoikilosis. The differential diagnosis for melorheostosis includes myositis

ossificans, osteoma, focal scleroderma, parosteal osteosarcoma, Caffey disease, sclerotic metastases, and hypertrophic osteoarthropathy.

The differential diagnosis for osteopoikilosis (OP) includes incidental bone islands (enostoses), other sclerosing bone dysplasias, sclerotic metastases, osteosarcoma, lymphoma, osteoid osteoma, chronic multifocal sclerosing osteomyelitis, calcium and phosphate metabolism abnormalities, Erdheim-Chester disease, previous instrumentation or fracture, and Paget disease.

Discussion

Melorheostosis, also known as Leri disease, ranks among the rarest, strangest, and least understood medical disorders.¹ Although this sclerosing bone disorder was initially described in 1922, fewer than 500 reports can be found in the literature.¹ Melorheostosis should be relatively easy to diagnose because it is characterized by sclerotic cortical bone distributed in segments.

However, a variety of radiographic patterns have been reported, and only about one-third of cases show the typical “dripping candle wax” appearance of the cortex.¹ Both the periosteal and endosteal bone surfaces have thick, atypical, and eccentric hyperostosis, and it can affect a single bone or a group of contiguous bones.¹

Generally, the medial or lateral side of the bone is affected, and the boundary between the affected and healthy bone is usually extremely distinct.¹

Concomitant dystrophy/dysplasia issues can be particularly challenging in the syndrome of mixed sclerosing bone, as melorheostosis often coexists with different types of bone sclerosis.¹ At least four distinct forms of this disorder have been identified, depending on the relative predominance of melorheostosis, osteopoikilosis, osteopathia striata, and osteosclerosis.¹

Osteopoikilosis, also known as osteopathia condensans disseminata, or “spotted bone disease,” was initially recognized as an asymptomatic condition in 1915 by Albers-Schönberg. The condition is characterized by the formation of round/oval sclerotic lesions, symmetrically distributed in the epiphyses and metaphyses of the long bones and pelvis that range from 2 to 10 mm in size.² This condition is defined by an anomaly in bone maturation during endochondral ossification.² It first manifests in childhood and carries on throughout adulthood.² An autosomal dominant hereditary condition, OP is brought on by a loss-of-function mutation in the LEMD3 gene.² Typically, radiographs are sufficient to diagnose OP.²

Most of the time OP is asymptomatic, but in 15–20% of patients

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Figure 1. AP Pelvis radiographs and multiple radiographs of the left lower extremity show multiple micronodular, high-intensity, homogeneous opacities, varying in size up to 10 mm, involving the (A) acetabula, bilateral ilio-pubic and ischio-pubic rami, proximal and distal (B) ephyphyses and metaphyses of the left femur and tibia (C, D), calcaneus and tarsal bones with juxta-articular disposition, without cortical disruption or adjacent periosteal reaction.

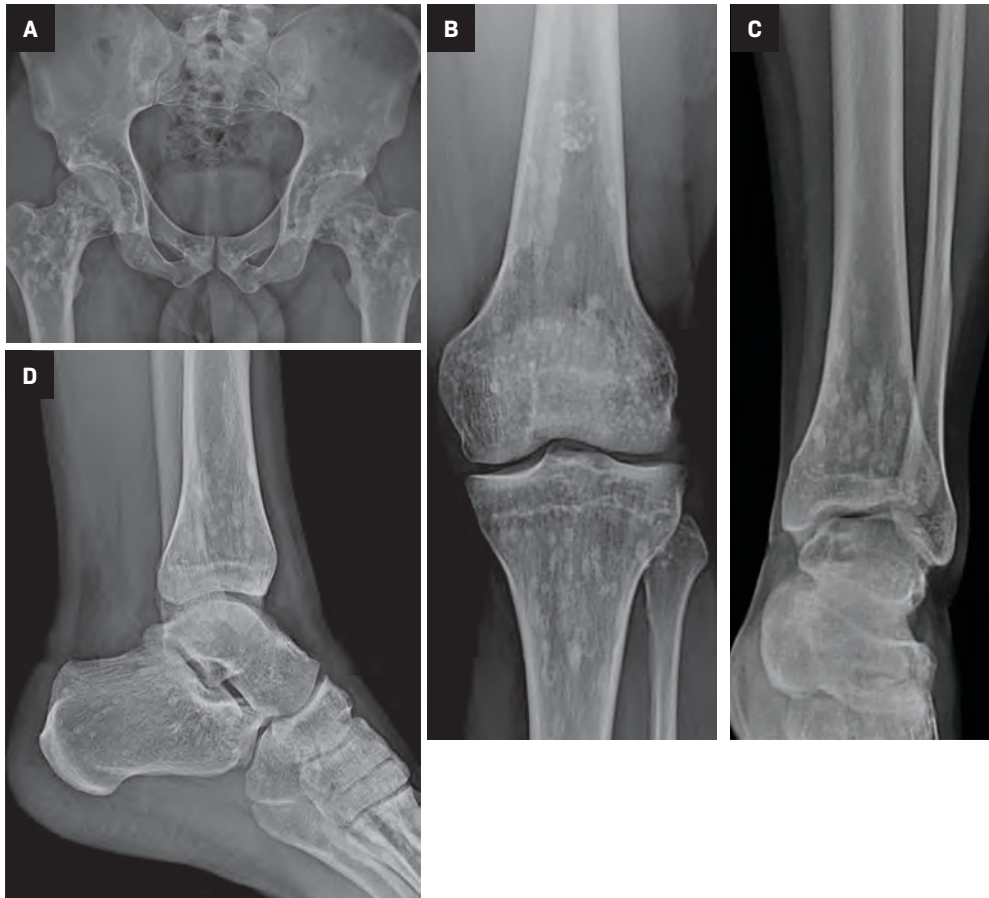


Figure 2. Lateral left knee radiograph demonstrates cortical homogeneous thickening (arrows) on the inner surface at the level of the distal diaphysis of the femur and proximal and middle diaphysis of the fibula, with a “dripping candle wax” appearance, without disruption of the adjacent cortical bone, suggestive of melorheostosis.



it manifests as pain and/or joint effusion, without deformity or dysfunction at the involved site(s).² The cause of the symptoms and signs is unknown.² Similar to the lesions seen in Buschke-Ollendorff syndrome, OP is occasionally accompanied by diffuse white skin lesions (dermatofibrosis lenticularis) and may also be linked to conditions like melorheostosis, keloid propensity, spinal stenosis, dwarfism, tuberous sclerosis, and scleroderma.²

Overlap syndromes are mixed sclerosing bone dysplasias that share characteristics with several different bone dysplasias.³ Dysplasias with hereditary and nonhereditary components can occur simultaneously; the

combination of osteopoikilosis and melorheostosis is the most prevalent overlap syndrome.³ In general, no medical or surgical treatment is necessary for these two bone conditions.

Conclusion

Osteopoikilosis and melorheostosis are rare, but their radiological appearance is quite pathognomonic, and radiologists should be aware of the characteristic findings in these disorders to diagnose them accurately. Patient demographics and presentation are important; most patients begin developing the lesions in early childhood and are asymptomatic. They may also be part of sclerotic

mixed bone disorders associated with other pathologies, making them more challenging to characterize.

References

- 1) Wordsworth P, Chan M. Melorheostosis and osteopoikilosis: a review of clinical features and pathogenesis. *Calcif Tissue Int.* 2019; 104: 530–543. <https://doi.org/10.1007/s00223-019-00543-y>
- 2) Gaudio A, Xourafa A, Rapisarda R, et al. Familiar osteopoikilosis: case report with differential diagnosis and review of the literature. *Clin Case Rep.* 2021;9: 922–926. <https://doi.org/10.1002/ccr3.3611>
- 3) Boulet C, Madani H, Lenchik L, et al. Sclerosing bone dysplasias: genetic, clinical and radiology update of hereditary and non-hereditary disorders. *Brit J Radiol.* 2016; 89(1062), 20150349. <https://doi.org/10.1259/bjr.20150349>

Rectourethral Fistula

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Case Summary

An elderly man with a history of prostate cancer presented to the emergency department with complaints of urethral passage of flatus and feculent material of one week's duration. The patient had undergone open radical prostatectomy and salvage radiation therapy, which was complicated by recalcitrant radiation cystitis status post-cystectomy 10 days before imaging, and ileal conduit formation. The patient was hemodynamically stable; however, leukocytosis was present.

Imaging Findings

Abdominal and pelvic CT with intravenous and rectal contrast revealed a rectourethral fistula (RUF, Figures 1,2).

Diagnosis

Rectourethral fistula

Discussion

A rectourethral fistula (RUF) is defined as a connection between the lower urinary tract and the distal rectum.¹ The condition is rare and can be classified as congenital or acquired. Congenital RUFs are the

more common form of anorectal malformations found in boys,² while acquired RUFs often occur in adulthood as a result of prostate surgery, radiation, trauma, or inflammation. RUF formation can have grave consequences; thus, accurate and prompt diagnosis is imperative.

The diagnosis of a RUF requires a high clinical suspicion and corroborating imaging. Clinical presentation often includes signs and symptoms such as fecaluria, pneumaturia, hematuria, urinary tract infection, abdominal pain, and fever.³ Fecaluria suggests a larger fistula and a poor prognosis.¹ Prior radiation and cryotherapy additionally contribute to poor prognosis, as both may result in microvascular injuries and mucosal damage.

Fluoroscopy, CT-cysto-urethrography, MRI, cystoscopy and/or rectoscopy can be used to diagnose RUF.³ The clinical presentation must be considered when selecting a modality, as each has its own strengths and weaknesses. Cross-sectional imaging offers better evaluation of contextual anatomy and complications. Computed tomography can identify fistulas; the modality is also beneficial in evaluating inflammation and identifying extraluminal disease processes, including abscesses and tumors. Magnetic resonance imaging offers a more detailed view of anatomy and pathology, often making it more appropriate in cases of complex or recurrent fistulas⁴.

Their rarity and variability of their clinical presentation complicate diagnosis and treatment of RUFs. As a result, intervention varies. Patients can undergo conservative or surgical

treatment. Conservative interventions include fecal diversion and/or urinary diversion, which are suitable for non-irradiated RUFs.⁵ However, conservative management often fails, and patients require surgical repair. A variety of surgical approaches are available, including perineal, transanal, transsacral, transsphincteric, and abdominal pull-through.⁶ In this case, surgical intervention was deferred, owing to other recent surgery.

The patient continued to experience symptoms related to the rectourethral fistula, subsequently developed multiple pelvic abscesses, and required surgical repair.

Conclusion

Prostate cancer is the most common cancer among men in the United States.⁷ RUFs are a rare complication associated with prostate cancer treatment. Presentation may include fecaluria, pneumaturia, hematuria, urinary tract infection, abdominal pain, and fever. Fluoroscopy, CT-cysto-urethrography, MRI, cystoscopy and/or rectoscopy can be utilized to diagnose and guide treatment approaches to RUF, which include conservative management and surgical intervention.

References

- 1) Chen S, Gao R, Li H, Wang K. Management of acquired rectourethral fistulas in adults. *Asian J Urol.* (2018); 5(3): 149–154. <https://doi.org/10.1016/j.ajur.2018.01.003>
- 2) Wang C, Diao M, Li L, et al. Laparoscopic dissection and division of distal fistula in boys with rectourethral fistula. *J Surg Res.* 2017; 211: 147–153. <https://doi.org/10.1016/j.jss.2016.11.059>

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Figure 1. Axial CT abdomen and pelvis with intravenous and rectal contrast reveals a fistulous communication between the thickened rectum (thick white arrow), the prostatic surgical bed (arrowhead), and the membranous urethra (dotted black arrow). Rectally administered contrast is seen entering the prostatic bed (thin white arrow) which exited from the urethra (not shown).



Figure 2. Sagittal reformatted CT abdomen and pelvis with intravenous and rectal contrast demonstrating the fistulous communication (thick white arrow) between the thickened rectum (thin white arrow), the prostatic surgical bed (arrowhead) and the membranous urethra (white dotted arrow). Rectally administered contrast is seen entering the membranous urethra (thin black arrow)



3) Ghandour R, Vaillant JC, Genser L. Recto-urethral fistula after radical prostatectomy. *J Gastrointest Surg.* 2022. <https://doi-org.libproxy.temple.edu/10.1007/s11605-022-05449-z>

4) Sharma A, Yadav P, Sahu M, et al. Current imaging techniques for evaluation of fistula in ano: a review. *Egypt J Radiol Nucl Med.* 2020;51:130. <https://doi.org/10.1186/s43055-020-00252-9>

5) Hechenbleikner EM, Buckley JC, Wick EC. Acquired rectourethral fistulas in adults. *Dis Colon Rectum.* 2013;56(3): 374-383. doi: 10.1097/DCR.0b013e318274dc87

6) Dafnis G, Wang YH, Borck L. Transsphincteric repair of rectourethral fistulas following laparoscopic radical prostatectomy. *Intl J Urol.* 2004; 11(11), 1047-1049. <https://doi.org/10.1111/j.1442-2042.2004.00928.x>

Schistosoma Bladder Infection

Andrew A. Wigger; Alexander J. Towbin MD; Daniel Morgan; Richard B. Towbin, MD

Case Summary

A child was referred to the nephrology clinic with several years' history of microscopic hematuria and a single episode of sterile pyuria. The patient reported no other associated symptoms and appeared well overall. Of note, the patient had visited a country in Africa, where they played and bathed in rivers. Their cousins also developed microscopic hematuria, which resolved after being administered an unknown medication.

Urinalysis was remarkable for proteinuria and significant blood but negative for leukocyte esterase and nitrites. Although the white blood cell count was normal, eosinophils were elevated at 23.7%. There were no ova or parasites in the stool. Serology was positive for *Schistosoma* IgG.

Imaging Findings

Bladder (Figure 1) and renal (not shown) ultrasound revealed a moderately distended urinary bladder with asymmetric, lobular, wall thickening

at the fundus and left lateral wall. The urine contained moderate echogenic debris. There was no increased vascularity within the bladder wall. The kidneys were normal.

Diagnosis

Schistosoma bladder infection.

The differential diagnoses for microscopic hematuria and asymmetric bladder wall thickening in a child includes rhabdomyosarcoma and other bladder or urinary tract infections.

Discussion

Schistosomiasis is a parasitic disease caused by blood flukes. At least five known species infect humans, the three most common being *Schistosoma haematobium*, *S japonicum*, and *S mansoni*. The location of disease is determined by the species that infects the patient. For example, *S haematobium* usually infects the urinary system, while *S japonicum* and *S mansoni* migrate and infect areas in the gastrointestinal tract.¹

The schistosoma blood flukes have a unique life cycle requiring two hosts to reproduce and survive. Blood fluke eggs are spread by feces or urine from mammals into a freshwater source. The eggs produce the miracidia form, which can infect freshwater snails.¹ Once inside the

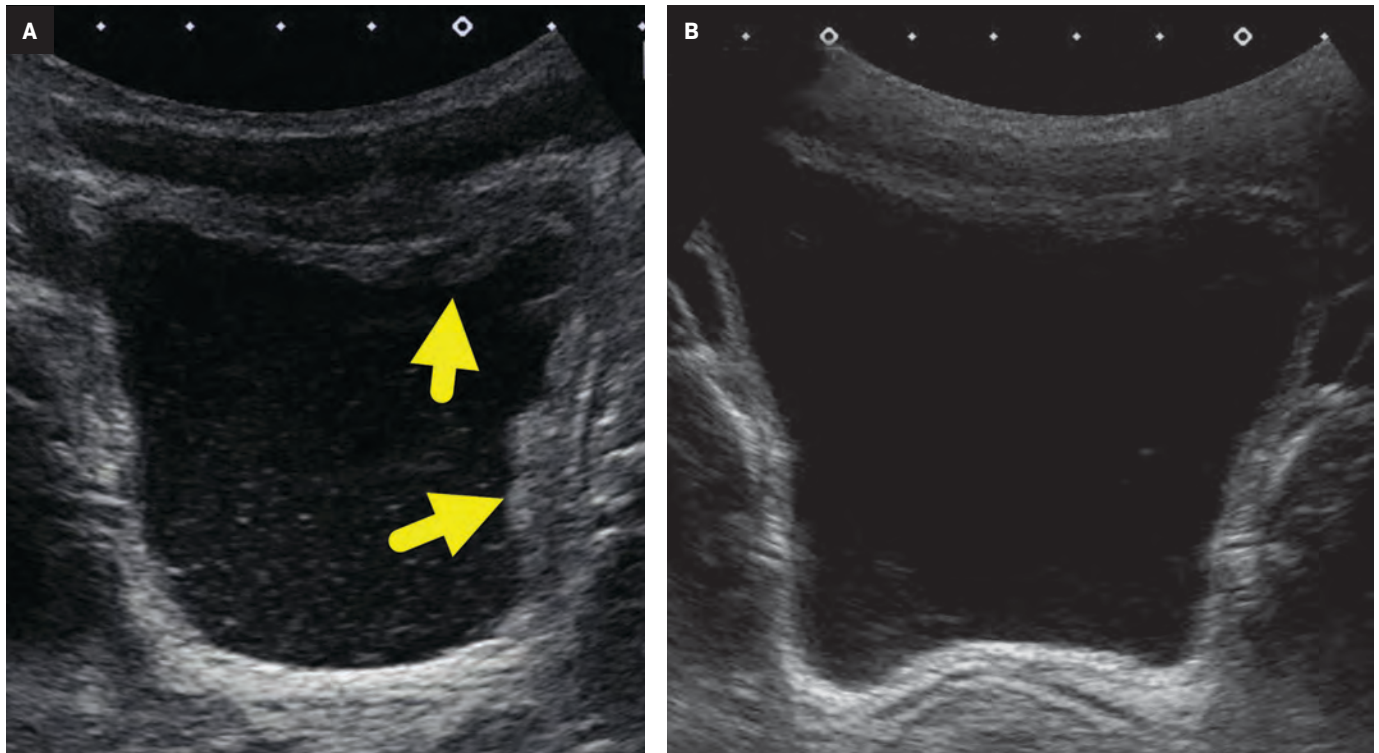
snail, the miracidia undergo asexual reproduction into cercariae larvae.¹ After the larvae leave the snail, the cercariae can directly penetrate mammal skin, then enter the bloodstream and migrate to the portal system of the liver, where they enter their sexual reproduction phase.¹ At this point, *S haematobium* migrates to the venous plexus of the bladder, while *S japonicum* and *mansoni* migrate to the venules in the small and large intestine.²

Schistosomiasis is a tropical and subtropical disease affecting those who live in areas with poor sanitation. The different subtypes are endemic in different parts of the world: *S mansoni* is found throughout Africa, South America, and the Caribbean; *S haematobium* is found throughout Africa and the Middle East; and *S Japonicum* resides in Southeast Asia. Despite the worldwide distribution and transmission of schistosoma, 85% of cases of schistosomiasis are linked to Africa.^{2,3} The parasite is not native to the United States; patients diagnosed in the US will have a recent travel history, typically to an endemic region.

It is estimated that 230 to 250 million people contract schistosomiasis annually, with infection ultimately resulting in 280,000 deaths per year.¹ Children are at increased risk for infection owing to higher rates of

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Figure 1. (A) Bladder US in a child with microscopic hematuria shows asymmetric, lobular thickening affecting the left lateral and anterior bladder walls (arrows). Echogenic debris is present in the urine. (B) Ultrasound performed 5 weeks later after praziquantel therapy shows normal thickness of the bladder wall and anechoic urine.



swimming and bathing in contaminated water sources. According to Colley, et al,⁴ the prevalence of infection is highest in those 10-14 years of age (~55%), with rates decreasing into adulthood.

Schistosoma can induce acute and chronic schistosomiasis. In both forms the symptoms and complications are caused by the host immune response provoking a granulomatous inflammatory reaction against the schistosome eggs.⁴ The acute form, also called Katayama fever, usually occurs weeks to months after the initial infection, when eggs are produced.

Presenting symptoms include fever, urticarial rash, myalgias, malaise, and abdominal pain lasting 2-10 weeks. Patients not treated then enter the chronic form of the disease where the immune response to the eggs is not as severe.

Patients infected chronically with one of the intestinal species of schistosoma may present with

intermittent abdominal pain, diarrhea, and hematochezia. Periportal fibrosis and complications related to portal hypertension may occur if the immune response is not downregulated. Patients with a chronic infection caused by *S haematobium* most commonly present with hematuria, dysuria, urinary frequency, and suprapubic discomfort.

If the patient's immune response is not downregulated, urinary tract fibrosis may occur, resulting in hydronephrosis and an increased risk of superimposed bacterial urinary tract infections. Early treatment is essential, as chronic bladder inflammation can lead to squamous metaplasia and squamous cell carcinoma.⁴

The diagnostic test of choice is microscopy for schistosome eggs in urine or stool. A bladder or rectal biopsy can be performed to examine for eggs, if not present in the urine or stool specimens. However, eggs are not produced for weeks to

months following initial infection. Serology to detect antibodies against schistosoma can be used to screen for infection. However, patients from endemic areas are likely to have antibodies and thus, this test is not able to determine whether an infection is active.⁵

Praziquantel is the drug of choice for the treatment of schistosomiasis. It is thought praziquantel affects the parasite's calcium channels. This causes adult worms to contract and detach from vein walls.⁵ The host immune system can recognize the worm antigens better after detachment.⁶ Patients have a good prognosis when treated early in the course of infection.⁷

The World Health Organization recommends annual or biannual prophylaxis with praziquantel for children and adults living in endemic areas to help suppress egg production.^{3,4} Other preventative measures include water sanitation programs

and the elimination of intermediate snail hosts. A vaccine does not currently exist.⁴

Our patient was treated with a course of praziquantel. A bladder ultrasound performed after therapy showed resolution of the wall thickening.

Conclusion

Several species of schistosoma exist that can infect humans and cause differing complications. All species can cause the acute form of the disease. However, *S mansoni* and *S japonicum* usually cause complications in the gastrointestinal system, while *S haematobium* affects the urinary system. Schistosomiasis should be considered when patients residing in or

having recently traveling to endemic regions have typical presentations.

Multiple modalities exist for diagnosis, including microscopy, biopsy, and serology. Bladder and kidney ultrasounds are essential to determine bladder damage caused by *S haematobium* and to rule out other causes of microscopic hematuria. Prognosis is good with early treatment, and praziquantel remains the drug of choice. Preventative efforts include mass chemoprophylaxis of endemic populations and water sanitation.

References

- 1) Nelwan ML. Schistosomiasis: life cycle, diagnosis, and control. *Current Therapeutic Research*. 2019;91. doi:10.1016/j.curtheres.2019.06.001
- 2) Centers for Disease Control and Prevention. Schistosomiasis. <https://www.cdc.gov/parasites/schistosomiasis.html>. Published August 14, 2019. Accessed July 18, 2022.
- 3) Schistosomiasis. World Health Organization. <https://www.who.int/news-room/fact-sheets/detail/schistosomiasis>. Accessed July 18, 2022.
- 4) Colley DG, Bustinduy AL, Secor WE, King CH. Human schistosomiasis. *Lancet* (London, England). <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4672382/>. Published June 28, 2014. Accessed July 18, 2022.
- 5) Gray DJ, Ross AG, Li YS, McManus DP. Diagnosis and management of schistosomiasis. *BMJ*. 2011;342:d2651. Published 2011 May 17. doi:10.1136/bmj.d2651
- 6) Brindley PJ, Sher A. Immunological involvement in the efficacy of praziquantel. *Exp Parasitol*. 1990;71(2):245-248. doi:10.1016/0014-4894(90)90028-b
- 7) Verjee MA. Schistosomiasis: still a cause of significant morbidity and mortality. *Res Rep Trop Med*. 2019;10:153-163. Published 2019 December 31. doi:10.2147/RRTM.S204345

Interventions for Spinal Muscular Atrophy

Janki Desai; Richard B. Towbin, MD; Carrie M. Schaefer, MD; Alexander J. Towbin, MD

Case Summary

An adult with type 1 spinal muscular atrophy, with initial onset of symptoms at 5 months of age, including delayed milestones and the inability to sit independently. The diagnosis was confirmed by genetic testing. The patient had limited motor skills and had difficulties with activities necessary for independent daily living. Additionally, the patient was ventilator dependent. Spinal fixation from C4-S1 was performed for severe levoscoliosis.

Nusinersin (Spinraza, Biogen, Inc, Cambridge, Massachusetts) is an antisense oligonucleotide inhibitor that increases the amount of SMN protein, needed for normal nerve and muscle function.¹ Intrathecal (IT) nusinersen was instituted at 17 years of age. Since beginning the IT therapy, hand movement and voice quality have improved, resulting in an improved quality of life.

Imaging Findings

There are no pathognomonic imaging findings diagnostic of spinal muscular atrophy. However, over time patients may develop scoliosis because of the imbalance between the flexor and extensor muscles of the

trunk, typically leading to a C-shaped curvature of the spine (Figure 1). If the scoliosis is severe or progressive, spinal fusion is often necessary, as in this patient. The severity of the curvature, the vertebral rotation, and spinal fixation may make traditional approaches for IT medication administration challenging for radiologists performing these procedures.

Diagnosis

Spinal muscular atrophy (SMA). The clinical differential diagnosis is extensive and includes many conditions that present with severe hypotonia, including congenital muscular and neuropathic disorders.¹

Discussion

Spinal muscular atrophy is an inherited, autosomal recessive, neuromuscular disorder most often caused by a homozygous deletion or mutation of the *SMN1* gene on chromosome 5q13 with absent *exon 7*, resulting in absent or deficient levels of survival motor neuron (SMN) protein. A second and nearly identical gene, *SMN2*, produces low levels of functional SMN protein, however this fails to compensate for the loss of *SMN1*.² SMN facilitates the assembly of spliceosomal small nuclear ribonucleoprotein (snRNP) particles, which are thought to function in motor neuron growth and neuromuscular maturation.³ Over time, SMA results in the degeneration of anterior

horn cells in the spinal cord with associated destruction of alpha motor units in lower motor neurons.

SMA presents with varying clinical phenotypes and is classified into five main subtypes based on severity and age of onset. All are characterized by progressive muscle weakness, reduced tone, and atrophy. However, cognition is not affected. Type 0 is congenital SMA, which presents early in neonatal life as severe hypotonia, early respiratory failure, and severe weakness, with death occurring at birth or within the first month of life. Type 1, also known as Werdnig-Hoffman disease, presents in the first 6 months of life with limited head control, hypotonia, areflexia, weakness of intercostal muscles, swallowing difficulties, and tongue fasciculations.

Type 2, Dubowitz disease, is of intermediate severity, presenting at 6-18 months of age. Children with SMA 2 are able to sit but have hypotonia, areflexia, progressive scoliosis, and restrictive lung disease. Mortality is most commonly due to respiratory compromise, but 70% of patients survive until age 25.

Type 3, Kugelberg-Welander disease, is mild SMA, presenting after 18 months of age with more progressive proximal weakness in the legs than in the arms. Type 3 patients are ambulatory and typically do not have restrictive lung disease. Additionally, their life expectancy is not affected.

Finally, type 4 is adult-onset SMA. It has the mildest phenotype and presents

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Figure 1. Scout image of CT of the spine demonstrating the presence of a severe levoconvex rotary scoliosis of the thoracolumbar spine with posterior spinal construct.

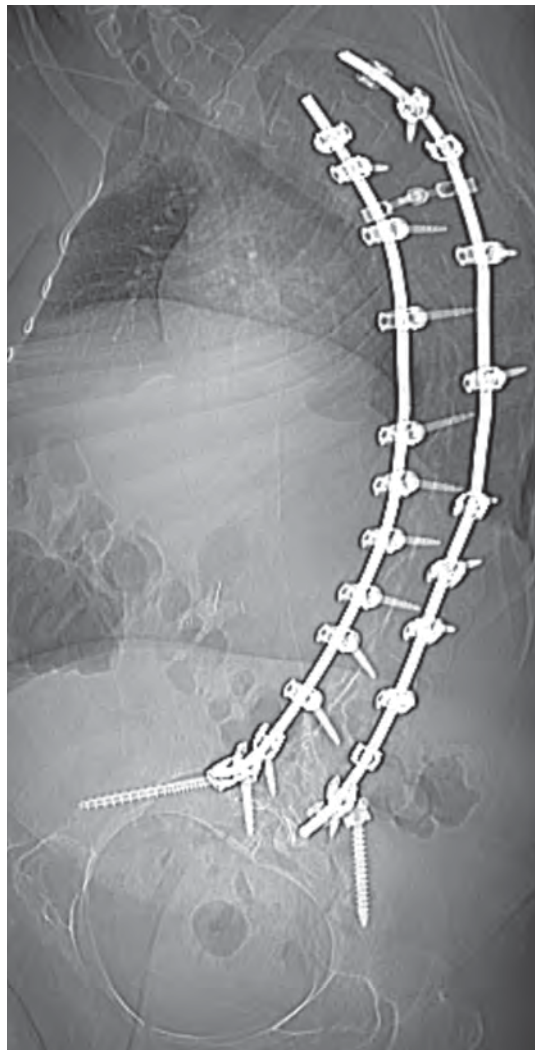
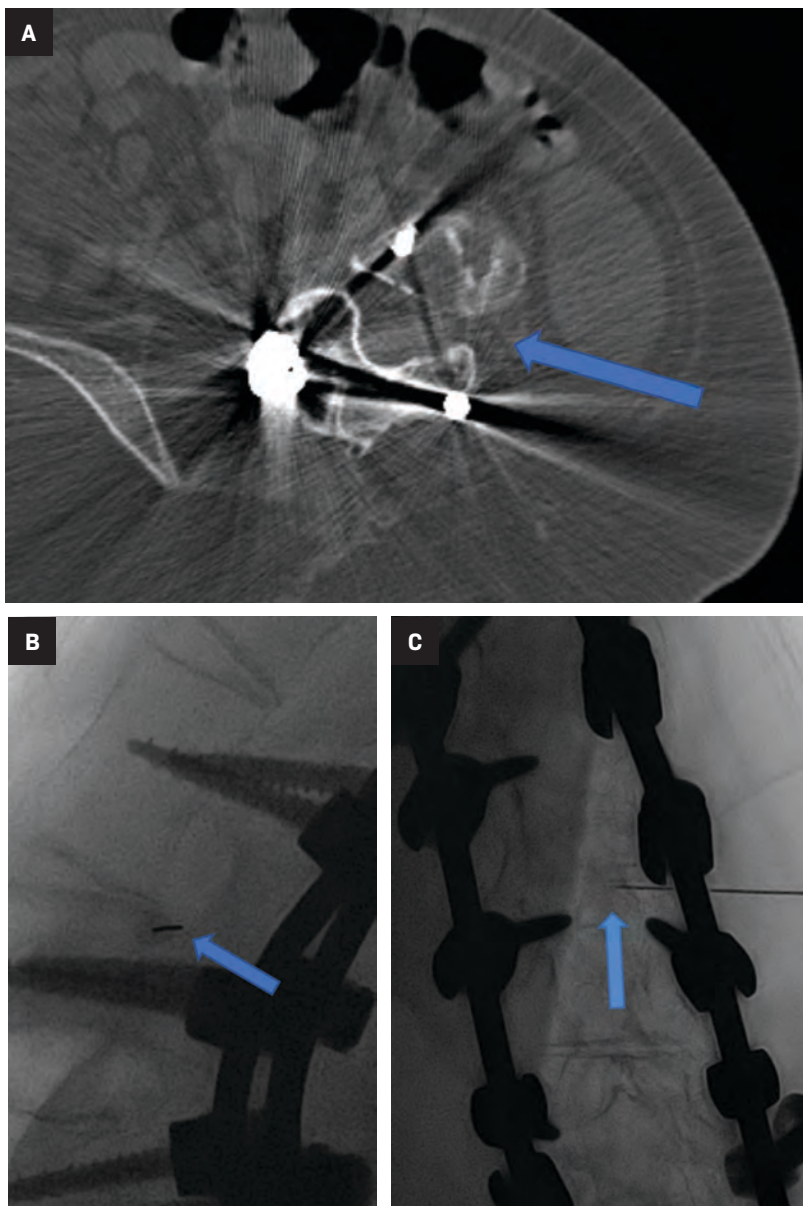


Figure 2. (A) CT axial image of the lumbar spine demonstrating planned left transforaminal access (blue arrow) for intrathecal nusinersen administration. (B) Lateral fluoroscopic view of the lumbar spine with the spinal needle (blue arrow) entering the inferior-most aspect of the neural foramen to avoid the neurovascular structures typically traversing the upper 2/3 of the foramen. (C) Frontal fluoroscopic image demonstrating the spinal needle tip (blue arrow) near the midline of the thecal sac.



in patients older than 21 years, with progressive, mild proximal weakness typically not impairing ambulation or affecting life expectancy.⁴

If clinical history and physical exam findings raise the suspicion for SMA, the diagnosis can be confirmed by molecular genetic testing to detect homozygous exon 7 deletion in the *SMN1* gene, which is 100%

specific for diagnosis. Around 5% of patients with SMA are compound heterozygotes with a single *SMN1* deletion and a frameshift, nonsense, or missense mutation in the other *SMN1* copy. *SMN2* differs from *SMN1* by a single nucleotide that disrupts a splice enhancer in exon 7, producing an unstable protein that is unable to compensate for the loss of *SMN1*.

However, approximately 10-20% fully functional, full-length transcripts are generated from *SMN2*.

There are zero to eight *SMN2* copies in the genome, which is inversely correlated with disease severity. A higher number of *SMN2* copies is often able to produce a milder type 2 or type 3 phenotype of SMA. In the normal population, the *SMN2* copy number

varies from zero to three, with 15% of normal individuals having no *SMN2*. An analysis of 625 unrelated Spanish patients with SMA showed that the majority of individuals with type 1 SMA had one or two *SMN2* copies; most of those with type 2 SMA had three gene copies; and those with type 3 had three or four *SMN2* copies.⁵

Therapeutic approaches are multi-fold, including splicing modification of *SMN2* via antisense oligonucleotides (ASO), small molecules which modulate *SMN2* gene splicing, and *SMN1* gene replacement therapy. Nusinersen, the first molecular drug to treat SMA, is an intrathecally administered ASO which promotes inclusion of exon 7 in mRNA transcripts of *SMN2*, resulting in translation of a higher level of fully functional SMN protein in liver, kidney, skeletal muscle, and central nervous system tissues. SMA patients have experienced significant improvement in motor function and extension in life expectancy after receiving nusinersen.⁷

Intrathecal access in patients with SMA may be challenging based on whether patients have simple or complex spinal anatomy (neuromuscular scoliosis, spinal fusion, and/or instrumentation, Figure 2). Several approaches can be used to facilitate drug injection into the subarachnoid space. In children with uncomplicated spines, a midline lumbar puncture is performed. In those with complex spines, lumbar transforaminal or C1-2 approaches may be required. Although either approach can deliver IT therapy, it is believed that the lumbar approach provides a higher drug concentration to the target lower motor neurons.

The authors prefer the transforaminal approach, as it is reported to be safer and technically easier than the C1-2 approach.^{8,9} Multiple reviews have shown that the complex anatomy commonly present in patients with SMA usually requires preprocedural imaging for careful planning, as well

as intraprocedural guidance to access the subarachnoid space via a transforaminal approach.^{8,9}

A newer, orally administered small molecule called risdiplam (Evrysdi, Genentech) has also been developed to treat SMA. This drug modulates *SMN2* gene splicing by binding two pre-mRNA splice sites in exon 7, increasing levels of full-length SMN mRNA and protein. Risdiplam crosses the blood-brain barrier, achieving systemic distribution with suitable half-life and predictable pharmacokinetics.¹⁰

Onasemnogene abeparvovec (Zolgensma, Novartis) is an *SMN1* gene replacement therapy, which uses a non-replicating, adeno-associated virus capsid carrying *SMN1* complementary recombinant DNA to efficiently deliver wild-type *SMN1* to motor neuron cells. The drug cannot reverse any pre-existing damage to motor neurons and is currently approved for children under age 2 years.¹¹ To achieve the best results it is important to give the drug early in the disease course before there is injury to the motor neurons.

Conclusion

Spinal muscular atrophy is an inherited neuromuscular disorder characterized by progressive muscle weakness. It has varying clinical severity ranging from mild proximal muscle weakness to death from restrictive lung disease. The diagnosis is confirmed by genetic testing. Treatment includes the *SMN2* splicing modulator nusinersen, facilitated by interventional radiologists. This may be challenging to administer intrathecally as patients develop scoliosis over time, making midline or paramedian lumbar punctures more challenging. Patients with complex spinal anatomy may benefit from pre- and intraprocedural imaging to allow for a transforaminal approach to the thecal sac.

References

- 1) Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [Updated 2020 Dec 3]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2021. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK1352/>
- 2) Kolb SJ, Kissel JT. Spinal muscular atrophy. *Neurol Clin*. 2015 Nov;33(4):831-46. doi: 10.1016/j.ncl.2015.07.004. PMID: 26515624; PMCID: PMC4628728.
- 3) Fan L, Simard LR. Survival motor neuron (SMN) protein: role in neurite outgrowth and neuromuscular maturation during neuronal differentiation and development. *Hum Mol Gen*. 2002; 11(14) 1605-1614. <https://doi.org/10.1093/hmg/11.14.1605>
- 4) Burr P, Reddivari AKR. Spinal Muscle Atrophy. 2021 Jan 29. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan. PMID: 32809522.
- 5) Calucho M, Bernal S, Alías L, et al. Correlation between SMA type and *SMN2* copy number revisited: An analysis of 625 unrelated Spanish patients and a compilation of 2834 reported cases. *Neuromuscul Disord*. 2018;28(3):208-215. doi:10.1016/j.nmd.2018.01.003
- 6) Rouzier C, Chaussonnet A, Paquis-Flucklinger V. Molecular diagnosis and genetic counseling for spinal muscular atrophy (SMA). *Arch Pediatr*. 2020 Dec;27(7S):7S9-7S14. doi: 10.1016/S0929-693X(20)30270-0. PMID: 33357600.
- 7) Paton DM. Nusinersen: antisense oligonucleotide to increase SMN protein production in spinal muscular atrophy. *Drugs Today (Barc)*. 2017;53(6):327-337. doi: 10.1358/dot.2017.53.6.2652413. PMID: 28799578.
- 8) Mousa MA, Aria DJ, Schaefer CM, Kaye, RD, Abruzzo TA, Bernes, SM, Willard SD, Riemann MC, Towbin, RB. A comprehensive institutional overview of intrathecal nusinersen injections for spinal muscular atrophy. *Pediatr Radiol*. 2018;48(12):1797-1805. doi:10.1007/s00247-018-4206-9
- 9) Towbin R, Schaefer C, Kaye R, Abruzzo T, Aria DJ. The complex spine in children with spinal muscular atrophy: the transforaminal approach—a transformative technique. *AJNR Am J Neuroradiol*. 2019; 40(8):1422-1426. doi: 10.3174/ajnr.A6131. Epub 2019 Jul 11. PMID: 31296522; PMCID: PMC7048480.
- 10) Ratni H, Ebeling M, Baird J, et al. Discovery of risdiplam, a selective survival of motor neuron-2 (SMN2) gene splicing modifier for the treatment of spinal muscular atrophy (SMA). *J Med Chem*. 2018; 61(15):6501-6517. doi: 10.1021/acs.jmedchem.8b00741. Epub 2018 Jul 25. PMID: 30044619.
- 11) Messina S, Sframeli M. New treatments in spinal muscular atrophy: positive results and new challenges. *J Clin Med*. 2020;9(7):2222. doi: 10.3390/jcm9072222. PMID: 32668756; PMCID: PMC7408870.

*"The Beatles took LSD and wrote Sgt Pepper—
Anna Nicole Smith took legal drugs and couldn't
remember the number for nine-one-one."*

—Bill Maher

*"An enormous amount of direct advertising from
pharmaceutical companies are offering a kind of
instantaneous solution to problems."*

—Leon Kass

"Ask Your Doctor"

C Douglas Phillips, MD, FACR

I get ideas for this column in various and sundry fashions. This one hit me broadside a few weeks ago. Who can guess what will light you up? Provide motivation? Not I.

Over the past year, I've spent a fair amount of time listening to the news. Now, that's not so much a dramatic revelation, with the veritable \$@*storm of events lately. I'll bet you all do from time to time, trying to stay informed as citizens and humans, or maybe just out of a morbid curiosity to see today's train wrecks. I will NOT talk about my sources for this news, because that's how you start fistfights.

When I listen to news on the radio in the car (I do infrequently), you get the commercials. Some are for doctors, clinics, and lawyers, but the ones that get me started are the ones for prescription drugs that we need to be on. **STAT**. How do I know I need to be on these drugs? Well, for starters, they are "doctor prescribed" or "widely available" and "perhaps for you." Hmmm. Perhaps, yes. And, yes, obviously, I do have some personal favorites.

I want to be on the drug (you likely know it) from the commercial where the woman taking it is petting a horse, and then in the next scene using a power saw. She seems so happy about it, you know? I want to take that drug, pet the horse, and use a power saw. Seems best to be in that order for some reason. I want to be on the drug that allows all the people using it to participate in beach volleyball, and then sit by the campfire.

"Some side effects, including infection, cardiac arrhythmias, sudden death, and hallucinations may occur." Nope. I just want to play me some volleyball, pet a horse, sit by the fire, and then use a power saw. I'll pay extra to avoid that other stuff, if you please.

There are ads for "male enhancement" drugs that used to require a visit to your doctor. Nope. Now, they have toll-free numbers and docs on the phone who will clear you and write a script simply by you answering a few questions. Overnight delivery in a "confidential package." Wow, what kind of Circle of Hell job is that? A medical degree to talk to people on the phone and prescribe "male enhancement" tabs? Any idea how well this job pays? Is this a potential retirement gig?

And, obviously, doctors and lawyers advertise as well. Lawyers a whole lot more. I don't have a joke here. I'll just leave that and walk away. But doctors and clinics are advertising. Oh yes, and radiologists and imaging centers. "Ask your doctor if an MRI might be right for you." Damned straight. Ask them if you might need a whole-body study while you're at it. Maybe your shoulder hurts, but next week it might be your knee or your spleen, so let's take a quick peeky-loo.

I'd be better with this if I thought there was some greater purpose served, other than the opportunity for profit. Okay. No, I wouldn't.

Keep doing that good work. Mahalo.



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