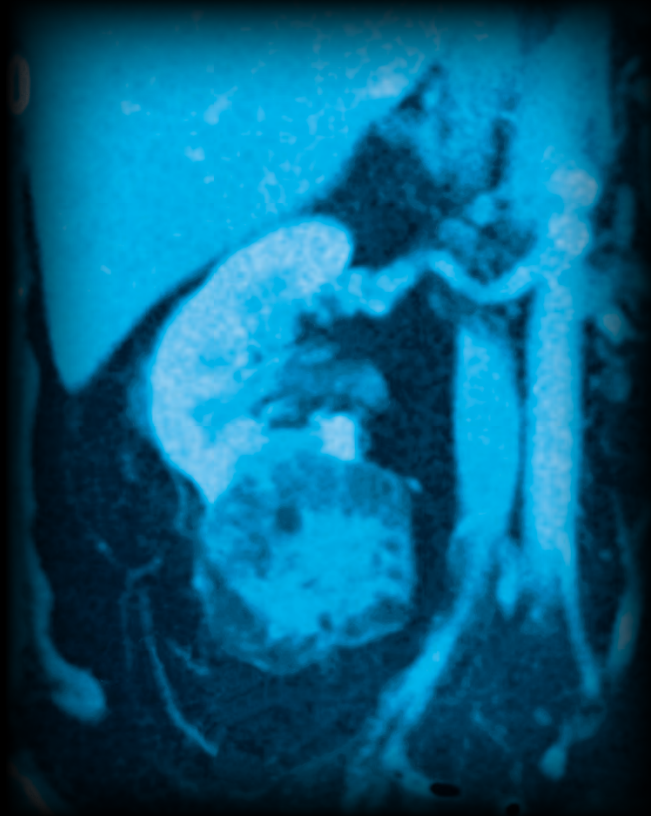


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CME New Trends in
Diagnosis and Imaging
Follow Up of Renal
Angiomyolipomas
Part I: Classic AMLs

The Current Scope of
Artificial Intelligence in
Breast Ultrasound

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Complex

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Radiological Services:
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6 New Trends in Diagnosis and Imaging Follow Up of Renal Angiomyolipomas Part I: Classic AMLs

John P. McGahan, MD; Anthony F. Chen, MD

Angiomyolipomas (AMLs) are comprised of 3 tissue types: vascular, adipose, and muscular, each of which uniquely affects their imaging features and potential impact on clinical outcomes. This review presents a framework for understanding how the pathological features of AMLs translate to imaging features, which can be used for categorization and to differentiate AMLs from malignant renal cell carcinomas, which may have similar appearances.

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Romina Tafreshi, BA; Beatrice Panjwani, MD; Shlomit A. Goldberg-Stein, MD; Mathew Barish, MD; Jocelyn Park MD; Nina S. Vincoff, MD

Breast density reduces the effectiveness of mammography in detecting lesions and is linked to a higher risk of breast cancer. For individuals with dense breasts, supplemental screening options include breast ultrasound, which is cost-effective and widely available, but limited by operator skill and a higher rate of false positives. Artificial intelligence (AI) is being used to improve ultrasound accuracy and consistency in breast cancer screening, and this review article introduces core AI principles for radiologists. It also highlights emerging AI tools for breast ultrasound while exploring clinical challenges and opportunities.

21 Abdominal Manifestations of Tuberous Sclerosis Complex

Muhammad Nabeel Akram, BS; Kai Xue, MD; Kaustubh G. Shiralkar, MD; Steven S. Chua, MD, PhD

Tuberous sclerosis complex (TSC) is a multisystem genetic disorder caused by mutations in tumor suppressor genes. Seizures and intellectual disability are the most common neurological symptoms of TSC, but imaging plays a vital role in identifying associated angiomyolipomas in the kidney, liver, pancreas, and spleen. This review examines the manifestations of TSC, while discussing the role of MRI, CT, and PET/CT in early detection, monitoring, and treatment planning.

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

Continuing Our Digital Transition

Erin Simon Schwartz, MD, FACR, FASPNR

As many of you are aware, 2025 marked *Applied Radiology's* move to being an exclusively digital publication. We very much hope you are enjoying our updated format. For those like me who still want to “page through” the entire journal front to back, that option remains available on our website (<https://appliedradiology.com/>).

Although it may appear to be a final destination, that transition actually reflects only a portion of our ongoing digital journey. Thanks to the very dedicated efforts of our former managing editor, Sharon Breske, and the entire editorial team, we are thrilled to announce our next digital leap, with the rollout of Editorial Manager for *Applied Radiology*.

With Editorial Manager, we have been able to streamline our entire editorial process. Our editorial team will benefit immensely from the capabilities of this platform to organize and track every review article, case report, and column through its entire journey, from initial submission through double-blinded peer review, determination, revision, and ultimately publication.

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We hope all of our contributors, authors, reviewers, and entire editorial team will find this transition to be a significant improvement over our previous processes and we look forward to your feedback.

New Trends in Diagnosis and Imaging Follow Up of Renal Angiomyolipomas Part I: Classic AMLs

Description

Angiomyolipomas (AMLs) are composed of three tissue types: vascular, adipose, and muscular, each of which uniquely affects their imaging features and potential impact on clinical outcomes. The authors provide a framework for understanding how the pathological features of AMLs translate into imaging features, which can be used for categorization and for differentiating AMLs from malignant renal cell carcinomas (RCCs), which may have similar appearances.

Learning Objectives

Upon completing this activity, the reader should be able to

1. Identify imaging features of AMLs.
2. Distinguish AMLs from echogenic RCCs on ultrasound.
3. Manage small (<1 cm) echogenic renal masses detected on ultrasound.

Target Audience

- Radiologists
- Related imaging professionals

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New Trends in Diagnosis and Imaging Follow-Up of Renal Angiomyolipomas—Part I: Classic AMLs

John P. McGahan, MD, FACR; Anthony F. Chen, MD

Introduction

Classification of renal angiomyolipomas (AMLs) may initially seem simplistic. However, there have already been numerous attempts at pathological or imaging-based classification of these tumors, each of which tries to capture the nuances and variation among AML types.

The majority of AMLs are sporadic and asymptomatic and therefore most commonly identified as an incidental finding on imaging. However, AMLs often occur with tuberous sclerosis, a condition where benign tumors may be present in the brain, eye, heart, lungs, and kidneys. While exceedingly rare, AMLs may also be present with pulmonary lymphangioleiomyomatosis (LAM) (Table 1).¹

The following approach attempts to provide a framework for understanding how the pathological features of AMLs translate to imaging features, which can be used for

categorization and to differentiate AMLs from malignant renal cell carcinomas (RCCs), which may have similar appearances.

AML Tissue Types and Imaging

Angiomyolipomas are comprised of 3 tissue types: vascular, adipose, and muscular, each of which uniquely affects their imaging features and potential impact on clinical outcomes—for example, the vascular component of the AML may contribute to spontaneous hemorrhage. In rare instances, AMLs may contain benign epithelial cysts or malignant cells (as in the epithelioid type) (Table 2).

The presence of macroscopic fat is a key imaging feature of classic AMLs. While there are fat-poor or fat-invisible AMLs, where macroscopic fat is not present, that present a greater challenge for imaging diagnosis,¹ as the muscular component of these masses contributes significantly to their imaging features (see Part II of this series), they are rare. In Part I of this 2-part series, we will detail some of the classic features of AMLs that contain macroscopic fat.

Table 1. Etiologies of Renal Angiomyolipomas

OCCURRENCE	
Sporadic	Majority of angiomyolipomas, without associated symptoms
Tuberous sclerosis	Rare
Lymphangioleiomyomatosis	Very rare
Abbreviations: ACR, American College of Radiology; CAR, Canadian Association of Radiologists.	

Table 2. Various Types of Renal Angiomyolipomas

TYPE	FREQUENCY
Classic	>90% with macroscopic fat
Fat-poor	
Hyperattenuating angiomyolipoma	5%
Hypoattenuating angiomyolipoma	Rare
Fat-invisible	Rare
Angiomyolipoma with epithelial cysts	Very rare
Epithelioid angiomyolipoma (potentially malignant)	Very rare

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Figure 1. Renal cell carcinomas are most commonly round in shape (A), while angiomyolipomas (AMLs) have variable shapes including oval (B), angular interface (C), and “overflowing beer” sign in some peripheral AMLs (D).

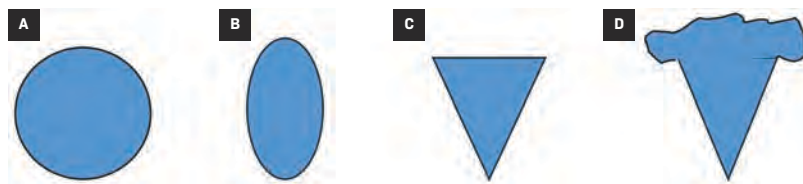


Figure 2. Renal US in an adult with multiple angiomyolipomas, including 2 that are oval (1, 3) and one that is angular with “overflowing beer” sign (2) (arrow).

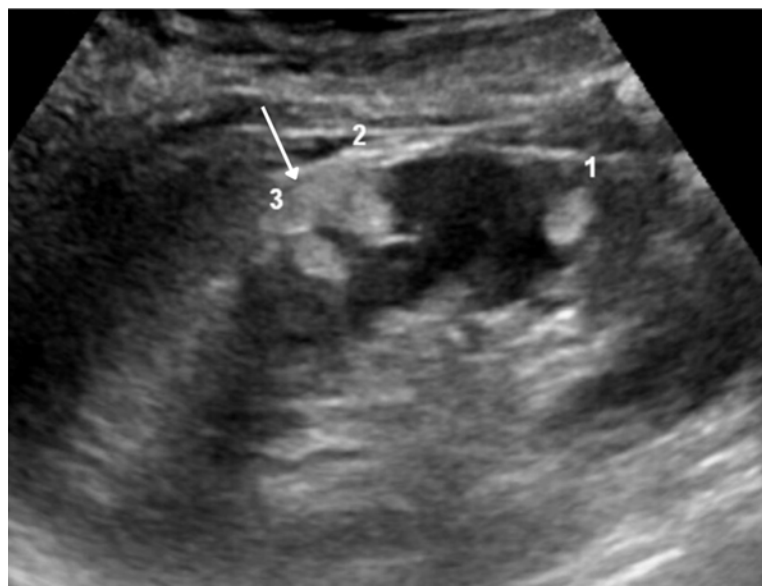
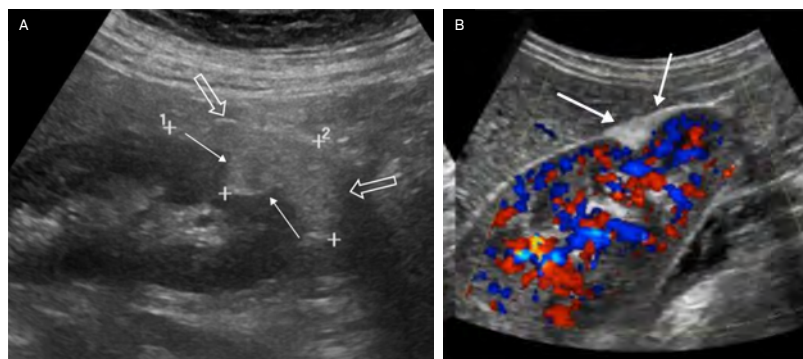


Figure 3. Renal US in an elderly patient with a large angiomyolipoma (AML) demonstrating an angular interface (solid arrows), but in addition the AML overflows the margins of the kidney as the “overflowing beer” sign (open arrows) (A). Renal color Doppler US image in an adult with peripheral AML demonstrating the “overflowing beer” sign (arrows) of the echogenic AML (B).



US Features

It is thought that the macroscopic fat in AMLs contributes to their echogenic imaging features on US. Research has shown that echogenic renal masses are usually AMLs or benign entities such as areas of infarction and/or scarring.² However, an echogenic renal mass may also be an RCC,³ and this overlap creates a diagnostic dilemma. Recent studies have demonstrated characteristics that more reliably differentiate AMLs from RCCs on US, including the shape of the mass, whether it has an angular interface, presence of an “overflowing beer” sign, and an echogenic margin (Figure 1).

Sporadic AMLs may be multifocal, with different shapes (Figure 2), compared with sporadic RCCs. For instance, in separate studies comparing endophytic and peripheral AMLs with RCCs, an oval shape was more common with AMLs than with RCCs, which are almost always round (Figure 2).^{4,5}

Endophytic AMLs were more likely to have an echogenic margin compared with RCCs. An angular interface was identified with peripheral AMLs and rarely with RCCs (Figure 2). Similarly, an “overflowing beer” sign (Figure 3) was only identified with peripheral AMLs and never with RCCs (Table 3). Both studies showed that over 80% of the patients with sporadic AMLs were female.^{4,5} AMLs occurring in the context of syndromes such as tuberous sclerosis are usually multiple and have similar shapes to sporadic AMLs.¹

Researchers using US radiomics, with software that is not yet commercially available, have shown

Figure 4. Benefit of contrast-enhanced US. Renal US demonstrating an echogenic interpolar renal mass with an angular interface, corresponding to an angiomyolipoma (AML) (arrow) (A). Renal US showing a more rounded, lower pole renal mass corresponding to a renal cell carcinoma (RCC) (arrows) (B). Contrast-enhanced US showing renal parenchymal enhancement, but little enhancement within the AML (arrow) (C). Contrast-enhanced US showing that the mass enhances as great or greater than the renal parenchyma, with a slightly enhancing rim, indicating an RCC (arrow) (D). Figure is courtesy of Richard G. Barr, MD, PhD, of Northeast Ohio Medical University.

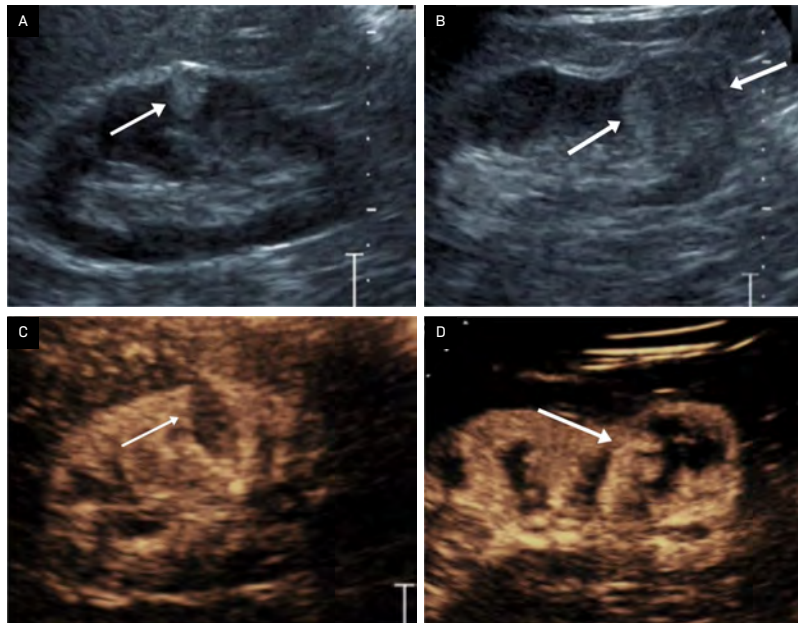


Figure 5. Coronal contrast-enhanced CT of the abdomen shows a right lower pole mass with solid components and macroscopic fat with Hounsfield units < 10 (arrows), consistent with a large, fat-rich angiomyolipoma.



that some AMLs are more echogenic than RCCs.⁶ These authors compared the tumor to cortex echogenicity ratio and 18 other US texture features to differentiate echogenic AMLs from RCCs. They also found that RCCs were larger than AMLs, which may be another distinguishing feature.⁶

Power Doppler US, contrast-enhanced US (CEUS), and microvascular flow imaging are evolving technologies that have been shown to be helpful in diagnosing AMLs. For instance, Barr et al showed that CEUS can be useful in distinguishing echogenic renal masses from other masses (Figure 4).⁷ Cao et al found CEUS features of fast washout and rim enhancement occurring with RCC had a sensitivity of 95% and a specificity of 91% in distinguishing RCCs from AMLs.⁸

Table 3. US Features to Help Distinguish Angiomyolipomas

	RENAL CELL CARCINOMA	RENAL ANGIOMYOLIPOMA
Round	Very common	Present
Oval	Rare	Common
Angular interface	Rare	Present
“Overflowing beer” sign	Almost never	Present
Echogenic margin	Present	Common

Table 4. CT and MRI Features of Classic (Macroscopic Fat) Angiomyolipomas

CT	MRI
Fat attenuation < 10 Hounsfield units	T ₂ W—hyperintense region due to macroscopic fat
No calcifications	Fat sat—signal drop out due to macroscopic fat
Occasional aneurysms	Chemical shift—India Ink artifact on contrast images due to macroscopic fat/water interface

Imaging Follow-Up

There is agreement within much of the medical literature and among most organizations regarding how best to manage incidental echogenic renal masses greater

Figure 6. Classic angiomyolipoma (AML) on MRI. Coronal single-shot fast spin echo T2 image of a left renal peripheral AML (curved arrow), largely isointense to retroperitoneal fat (A). Axial T2 fat-suppressed image showing complete loss of signal intensity consistent with macroscopic fat in an AML (curved arrow) of the left kidney (B). Axial in-phase T1 MRI showing high signal intensity AML (curved arrow) in the left kidney (C). Axial out-of-phase MRI showing the “India ink” artifact as a dark line (arrows) at the interface of the macroscopic fat in the AML with the solid-appearing renal tissue (D).

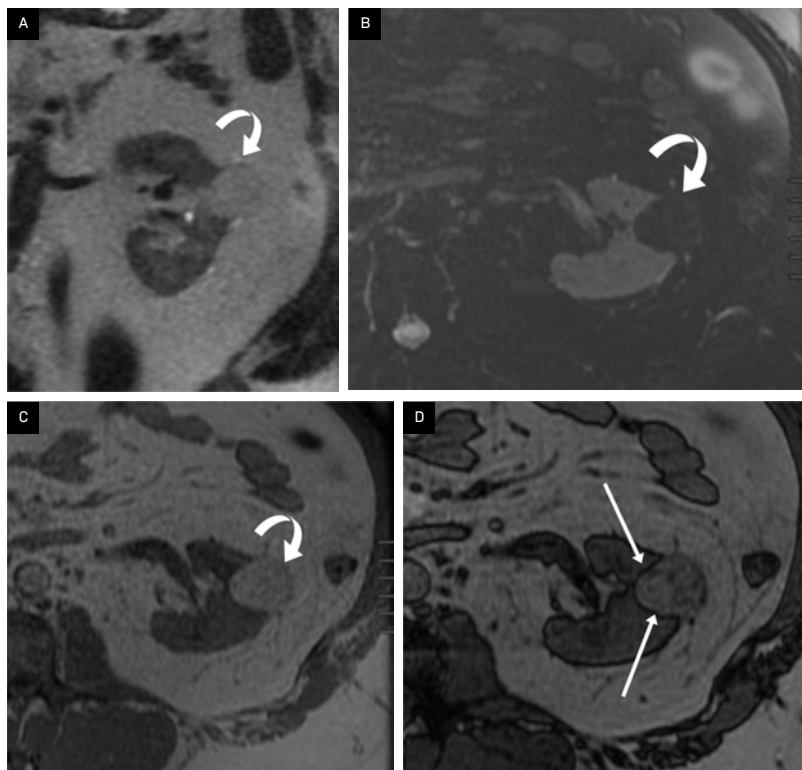
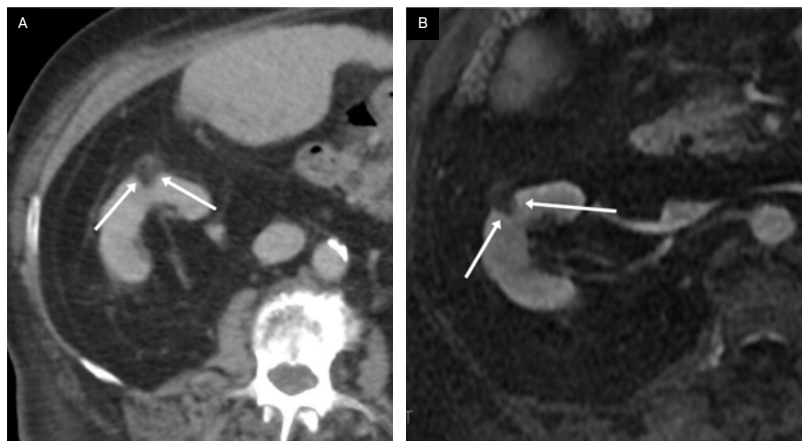


Figure 7. Angular interface on CT/MRI of angiomyolipoma (AML). An elderly patient with a peripheral AML on contrast-enhanced CT (A) and T1 LAVA post-contrast-enhanced MRI (B) showing angular interface (arrows).



than 1 cm in diameter. Thin-section CT should be considered as the next step in imaging evaluation when an echogenic mass is detected, as it can identify

classic AMLs with macroscopic fat having Hounsfield units < 10.⁹ The consensus statements from the Canadian Association of Radiology (CAR) and the American College

Figure 8. An elderly patient with a simple right renal cyst demonstrating an angular interface (curved arrow). Also note smaller peripheral hypodensity with an angular interface (arrow) probably representing an additional small cyst.



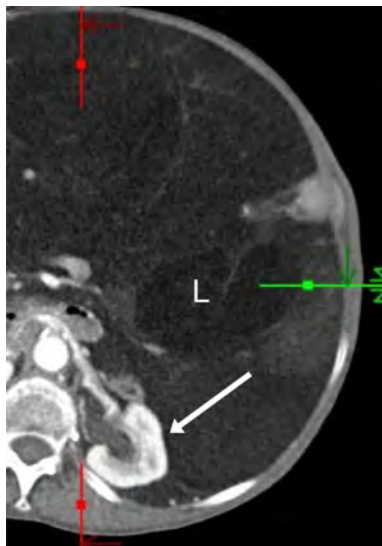
of Radiology (ACR) agree on the recommendations for echogenic masses greater than 1 cm,^{10,11} but disagree on smaller echogenic masses. For example, the ACR's statement indicates that masses smaller than 1 cm in diameter are so rarely malignant that they do not require follow-up,¹⁰ whereas the CAR statement recommends annual US for 5 years.¹¹ Given the more recent studies analyzing the morphological features of these common sub-centimeter renal masses, then the recommendation of the ACR can be followed if features such as an echogenic margin, oval shape, angular interface, or “overflowing beer” sign are present.

CT/MRI: Classic AMLs

Most AMLs occur spontaneously in women and contain macroscopic fat. Renal AMLs are a common occurrence in patients with tuberous sclerosis and can appear in patients with LAM. The features of AMLs occurring with either tuberous sclerosis or LAM are similar to those of the various types of spontaneous AMLs.

Fat-rich AMLs are by far the most common type and are definitively diagnosed on CT and MRI. A classic CT feature of the fat-rich AML is CT

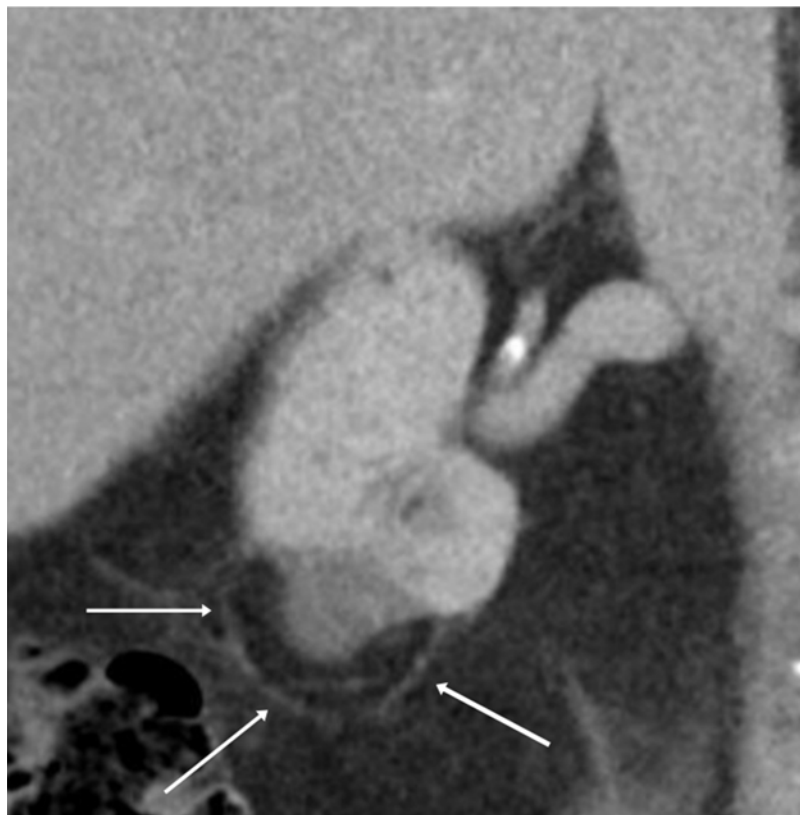
Figure 9. An elderly patient with a large retroperitoneal liposarcoma (L) that is poorly encapsulated and displaces the left kidney (arrow) without a capsular defect.



attenuation of -10 Hounsfield units or less within the macroscopical fatty component (Figure 5).^{11,12} MRI features of fat-rich AMLs include increased signal intensity on T2-weighted MRI images, but this is not pathognomonic of AMLs. However, utilizing fat-suppression techniques allows the region of high signal intensity to be suppressed on these sequences, confirming the presence of macroscopic fat (Figure 6). Likewise with chemical shift imaging, there will be an “India ink” artifact at the fat/water (renal parenchyma) interface in the same region as the high signal intensity on T2-weighted imaging (Figure 6; Table 4).^{13,14}

Morphological features of exophytic renal masses may be useful in distinguishing benign renal masses (cysts and AMLs) from RCCs on MRI.¹⁵ Verma et al showed that the presence of an angular interface of an exophytic mass > 2 cm on T2 MRI was a strong predictor of benignity.¹⁵ This angular

Figure 10. An elderly patient with a 1-year follow-up contrast-enhanced CT after radiofrequency ablation of a clear cell renal cell carcinoma, showing an avascular mass with surrounding encapsulated fat (arrows).



interface may be identified with AMLs (Figure 7) and with simple cysts (Figure 8), making it a helpful feature in determining the benignity of a mass.

Other distinguishing features include intratumoral calcifications and aneurysms. Intratumoral calcifications are rare within AMLs but may be present with RCCs. Conversely, intratumoral aneurysms may occur with classic AMLs but are rare with RCCs.

Less common renal and/or retroperitoneal masses may also have a macroscopic fatty component. For instance, retroperitoneal liposarcomas, when discovered, are typically large, with an average diameter of 21 cm in one series.¹⁶ They less commonly have an associated

renal parenchymal defect than large AMLs, and liposarcomas are more often poorly margined, sometimes displacing the kidney (Figure 9).¹⁶ Patients treated for RCC by radiofrequency ablation may have encapsulated retroperitoneal fat “pseudomass” at the site of ablation (Figure 10), not to be mistaken for a fat-containing neoplasm.¹⁷

Conclusion

Understanding the histology and imaging features of classic AMLs can aid in the distinction of these lesions from other primary renal neoplasms, most commonly RCC. While emerging radiomics and advanced US techniques can provide increasingly

valuable information, CT and MRI remain the mainstay for imaging characterization of these masses.

References

- 1) Skelton WP, Leslie SW. Renal angiomyolipoma. *StatPearls [Internet]*. StatPearls Publishing. 2024.
- 2) Kwong A, Mitchell A, Wang D, McGahan JP. Etiology of small echogenic renal masses. *J Ultrasound Med*. 2022;41(10):2567-2575. doi:10.1002/jum.15946
- 3) Sidhar K, McGahan JP, Early HM, et al. Renal cell carcinomas: sonographic appearance depending on size and histologic type. *J Ultrasound Med*. 2016;35(2):311-320. doi:10.7863/ultra.15.03051
- 4) Chen AF, Getz MLD, McGahan JP, Wilson MD, Larson MC. Predictors of benignity for small endophytic echogenic renal masses. *J Ultrasound Med*. 2025;44(3):483-492. doi:10.1002/jum.16610
- 5) Chen AF, McGahan JP, Wilson MD, et al. Are there ultrasound features to distinguish small (<3 cm) peripheral renal angiomyolipomas from renal cell carcinomas?. *J Ultrasound Med*. 2023;42(9):2083-2094. doi:10.1002/jum.16229
- 6) Habibollahi P, Sultan LR, Bialo D, et al. Hyperechoic renal masses: differentiation of angiomyolipomas from renal cell carcinomas using tumor size and ultrasound radiomics. *Ultrasound Med Biol*. 2022;48(5):887-894. doi:10.1016/j.ultrasmed-bio.2022.01.011
- 7) Barr RG, Peterson C, Hindi A. Evaluation of indeterminate renal masses with contrast-enhanced US: a diagnostic performance study. *Radiology*. 2014;271(1):133-142. doi:10.1148/radiol.13130161
- 8) Cao H, Fang L, Chen L, et al. The value of contrast-enhanced ultrasound in diagnosing small renal cell carcinoma subtypes and angiomyolipoma. *J Ultrasound Med*. 2022;41(6):1415-1423. doi:10.1002/jum.15824
- 9) Simpson E, Patel U. Diagnosis of angiomyolipoma using computed tomography region of interest < or = -10 HU or 4 adjacent pixels < or = -10 HU are recommended as the diagnostic thresholds. *Clin Radiol*. 2006;61(5):410-416. doi:10.1016/j.crad.2005.12.013
- 10) Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. *J Am Coll Radiol*. 2010;7(10):754-773. doi:10.1016/j.jacr.2010.06.013
- 11) Kirkpatrick IDC, Brahm GL, Mnatzakian GN, et al. Recommendations for the management of the incidental renal mass in adults: endorsement and adaptation of the 2017 ACR incidental findings committee white paper by the Canadian association of radiologists incidental findings working group. *Can Assoc Radiol J*. 2019;70(2):125-133. doi:10.1016/j.carj.2019.03.002
- 12) Park BK. Renal angiomyolipoma: radiologic classification and imaging features according to the amount of fat. *AJR Am J Roentgenol*. 2017;209(4):826-835. doi:10.2214/AJR.17.17973
- 13) Jinzaki M, Silverman SG, Akita H, et al. Renal angiomyolipoma: a radiological classification and update on recent developments in diagnosis and management. *Abdom Imaging*. 2014;39(3):588-604. doi:10.1007/s00261-014-0083-3
- 14) Thiravit S, Teerasamit W, Thiravit P. The different faces of renal angiomyolipomas on radiologic imaging: a pictorial review. *Br J Radiol*. 2018;91(1084):20170533. doi:10.1259/bjr.20170533
- 15) Verma SK, Mitchell DG, Yang R, et al. Exophytic renal masses: angular interface with renal parenchyma for distinguishing benign from malignant lesions at MR imaging. *Radiology*. 2010;255(2):501-507. doi:10.1148/radiol.09091109
- 16) Woo S, Kim SY, Cho JY, Kim SH, Lee MS. Exophytic renal angiomyolipoma and perirenal liposarcoma: revisiting the role of CT for differential diagnosis. *Acta Radiol*. 2016;57(2):249-255. doi:10.1177/0284185115574543
- 17) Grewal A, Khara SS, McGahan JP, et al. Utility of intraprocedural contrast-enhanced CT in ablation of renal masses. *AJR Am J Roentgenol*. 2020;214(1):122-128. doi:10.2214/AJR.19.21584

The Current Scope of Artificial Intelligence in Breast US

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Introduction

Breast density limits the sensitivity of mammography to detect breast lesions and is associated with an increased risk of breast cancer.¹ In September 2024, the US Food and Drug Administration (FDA) mandated that all patients undergoing mammography be notified of their breast density.² Options for supplemental screening in patients with dense breasts include breast US, breast MRI and contrast mammography. Of the 3 modalities, US is the most affordable and accessible option and does not require intravenous contrast.

However, breast US is limited by high user dependence and higher

false-positive interpretations.³ As more patients receive mandatory breast density notifications, interest in supplemental screening, including breast US, will likely grow. This may drive an expanding role for artificial intelligence (AI) tools to enhance breast US performance.

This review outlines fundamental AI concepts relevant to radiologists, examines 4 breast US AI tools currently available or in development, and discusses clinical implementation challenges and future directions.

Basics of AI

AI is increasingly capable of performing tasks that traditionally required human intelligence, such as image interpretation, reasoning, and

problem-solving. In radiology, AI offers the potential to enhance diagnostic accuracy and efficiency. Machine learning (ML), a core component of AI, allows systems to learn from imaging data without explicit programming. This learning can be supervised, where labeled datasets are used for model training, or unsupervised, where models identify patterns in unlabeled data. For example, a breast cancer detection and classification model may rely on input features such as lesion shape, margins, and orientation, paired with known outcomes such as “benign” or “malignant.” When new images are introduced, the model can analyze them and predict their classification.

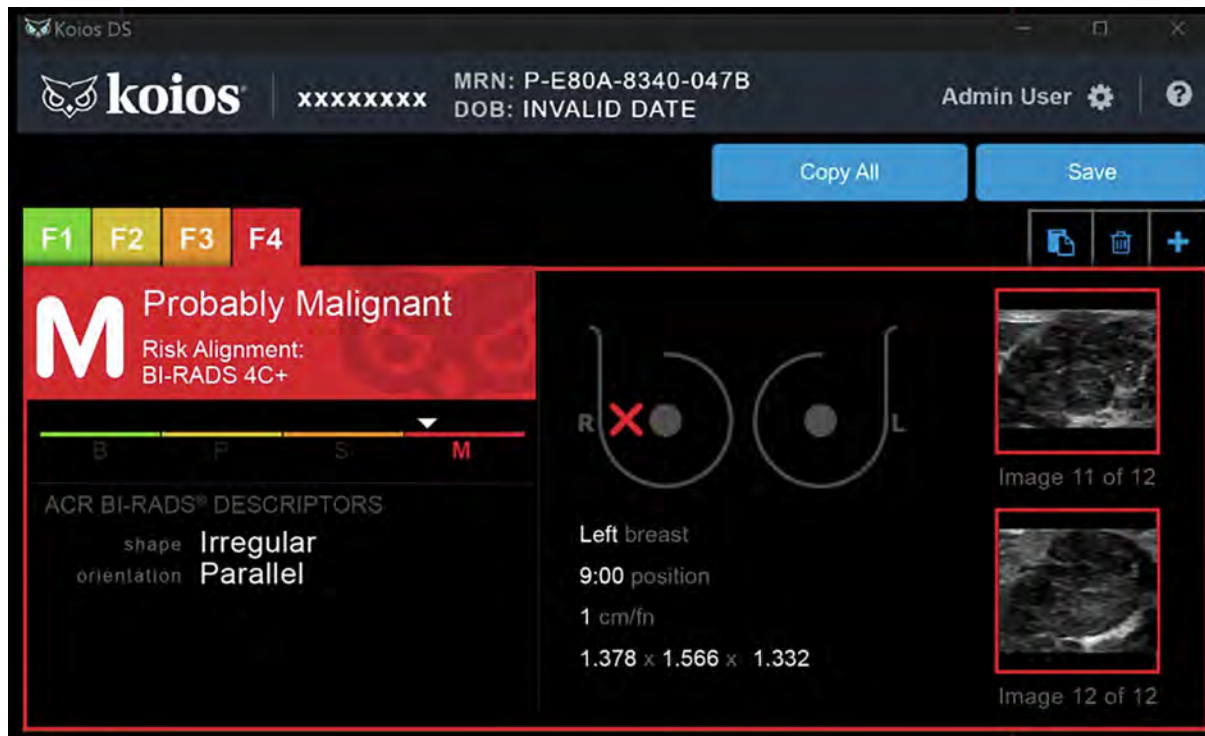
Deep learning (DL), a more advanced subset of ML, uses multilayered neural networks to identify complex patterns in large datasets. This approach powers applications such as image recognition and natural language processing. In the context of cancer detection, DL models can analyze images to identify features indicative of malignancy, assist radiologists in detecting early-stage tumors, and improve diagnostic accuracy by

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Figure 1. BI-RADS 4C+. Koios artificial intelligence Decision Support interface displays the clockface location of the lesion of interest with corresponding measurements. Lesion characteristics such as shape and orientation are used as descriptors for the model to predict this lesion to be probably malignant. Images courtesy of Koios Medical, Inc.



reducing false positives and false negatives.^{4,5}

AI in Breast Imaging

The role of AI in breast imaging has advanced rapidly in recent years. ML and DL models have been applied to mammography to increase the detection of tumors. AI tools in mammography and MRI are also being investigated for their potential to evaluate image data, such as tissue patterns, and assess a patient's risk of developing cancer.^{6,7} AI tools under development have the potential to augment the work of radiologists through read-time reduction, improved detection, and more personalized cancer care delivery, especially when combined with other patient data such as genetic testing.⁷

Current Results of AI Algorithms in Analyzing Breast US Images

AI models applied to breast US have shown promise in improving specificity, sensitivity, efficiency, error rate, and accuracy in lesion detection and diagnosis.⁸ The utility of AI decision support systems (DSS) for lesion characterization and diagnostic accuracy varies depending on lesion characteristics and the specific AI tool. One FDA-cleared AI DSS demonstrated higher accuracy than radiologists in detecting irregularly shaped lesions.⁹ Such tools may benefit less confident readers by reducing false-positive rates.

Beyond lesion analysis, future AI algorithms may facilitate molecular subtyping of breast

cancer, critical for treatment planning. Preliminary ML models have shown potential for determining molecular subtypes from breast US images.¹⁰ Other models are being developed to predict treatment response, lymph node metastasis, and survival/prognosis, offering hope for improved personalized treatment planning.¹⁰

Breast US AI Technologies

Below is a review of several AI tools developed for breast US. Owing to rapid advancements, this review cannot include all breast US AI products on the market or in development.

In addition, the authors do not have specific experience with these products, and their inclusion here should not be interpreted as

Figure 2. Invasive ductal carcinoma (IDC). Craniocaudal mammographic view (A) and breast US (B) demonstrate a left breast mass (arrow) that was retrospectively assessed as “suspicious,” BI-RADS category 4A-4B by Koios artificial intelligence (AI) Decision Support (DS). This mass was reported as “probably benign” by a radiologist. At the 6-month follow-up, left breast craniocaudal mammogram (C) and breast US (D) demonstrate that the mass (arrow) has increased in size. The mass is assessed as “probably malignant,” BI-RADS category 4C+ by Koios AI DS owing to its irregular shape and nonparallel orientation. Biopsy demonstrated triple-negative IDC. Images from Coffey et al.¹⁴ Images courtesy of Koios Medical, Inc.

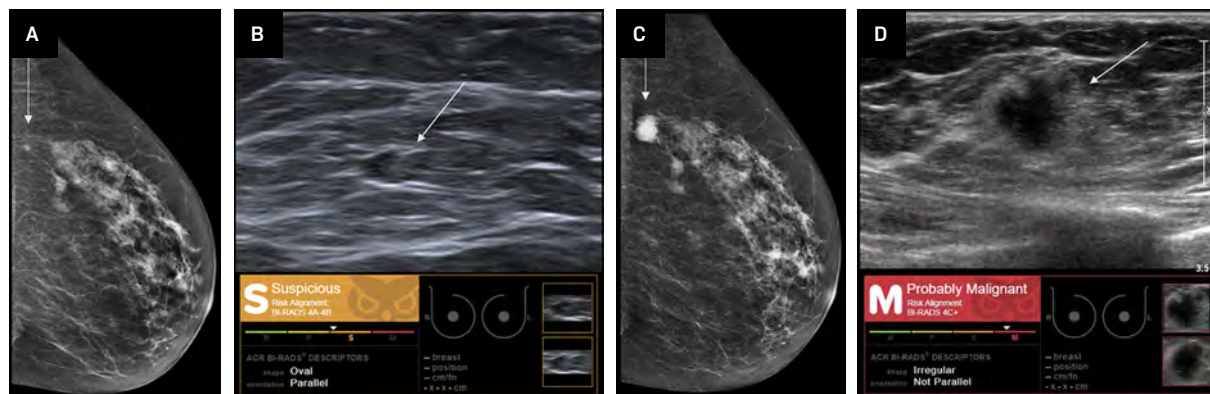
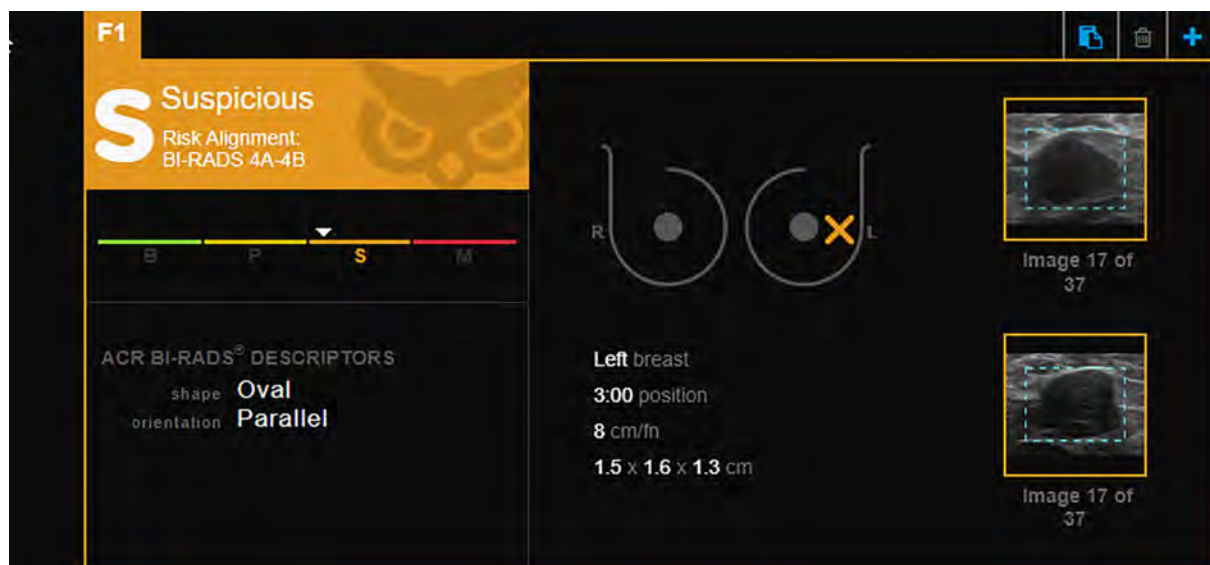


Figure 3. Invasive ductal carcinoma (IDC). Retrospective Koios artificial intelligence Decision Support categoric assessment of lesions previously identified as IDC via breast US-guided biopsy. White triangle marker position indicates the level of confidence in the assignment in the “suspicious” BI-RADS category 4A-4B. Images courtesy of Koios Medical, Inc. and Victoria Mango, MD.



endorsement. At the time of this writing, only Koios Decision Support (DS) has received FDA 510k clearance for US evaluation of lesions or nodules suspicious for breast cancer. Other vendors either have FDA clearance for more limited indications or are awaiting FDA clearance. Users should ensure they understand the approval

status of any AI tool before clinical implementation.

Koios Decision Support

Koios Medical's Decision Support (DS) is an FDA-cleared, AI/ML-based computer-aided diagnosis software device for use in breast diagnostic US. Utilizing DL algorithms, Koios

DS classifies lesions using shape and orientation to assign BI-RADS categories.

In a multicenter, retrospective study, 15 readers (11 radiologists, 2 surgeons, and 2 gynecologists) evaluated 900 breast US lesions (470 benign, 430 malignant) with and without Koios DS. Mean area

Figure 4. BI-RADS 5. See-Mode's interface displays the clockface location of the lesion of interest and displays measurements side by side with the US images. This case was a BI-RADS 5 classification, owing to irregular shape, angular margins, and hypoechoic echo pattern. Images courtesy of See-Mode.

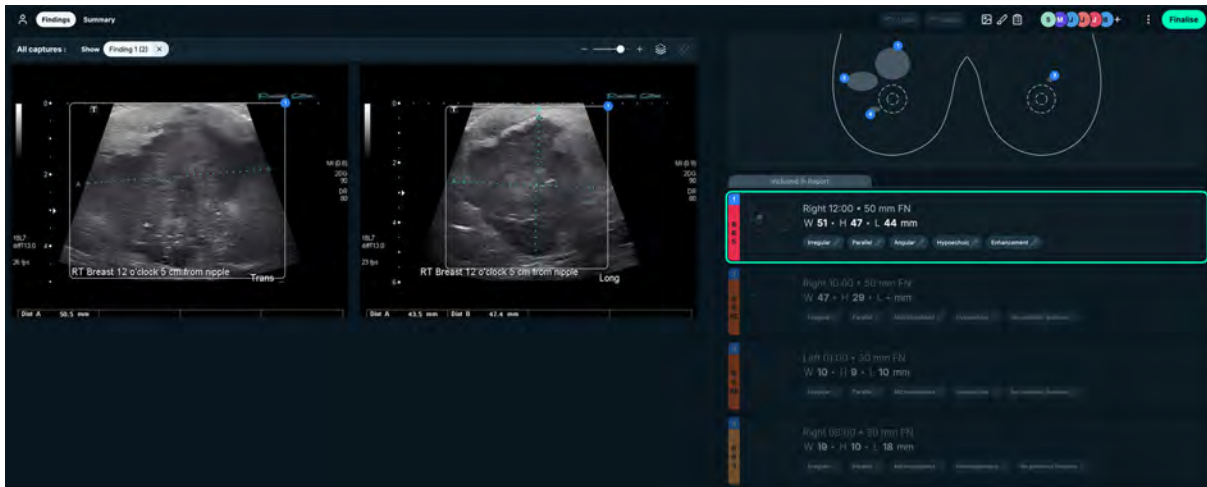
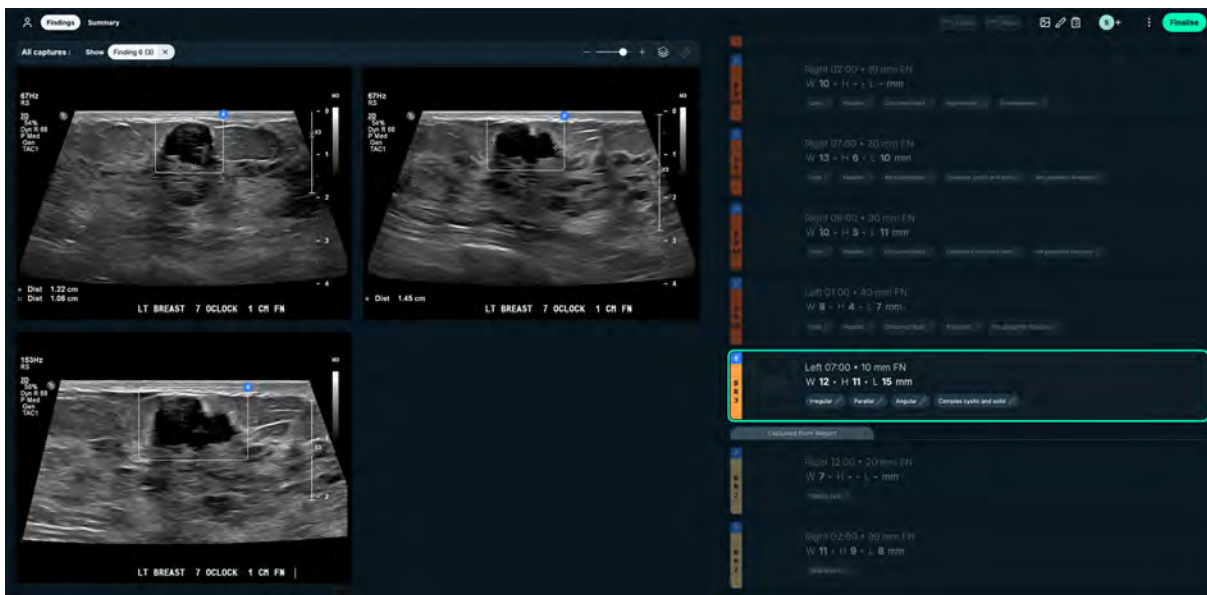


Figure 5. BI-RADS 3. See-Mode's interface displays lesion measurements side by side with the US images. This case was a BI-RADS 3 classification due to irregular shape, angular margins, and complex cystic and solid appearance. Images courtesy of See-Mode.



under curve (AUC) was significantly higher with DS alone (0.88) and US plus DS (0.87) compared with US alone (0.83, $P < .0001$). Interobserver agreement improved from 0.54 to 0.68 with DS, and intra-observer variability decreased from 13.6% to 10.8% ($P = .04$). The effect of DS on sensitivity and specificity, however, varied with reader experience, suggesting that the tool may

not offer significant accuracy improvements for experienced breast radiologists.^{11,12}

A separate retrospective analysis of the Koios AI DS tool in 75 patients (83 lesions) found 100% accuracy in identifying suspicious lesions and recommending biopsy for invasive lobular carcinoma, a diagnosis often challenging owing to subtle imaging features.¹³ Similarly, a

single-site retrospective study of 332 patients found the Koios AI DS system identified up to 97% of triple-negative breast cancers, which can be difficult to detect due to their sometimes benign-appearing imaging features. The model's false-negative rate in this study was comparable to that of breast radiologists. The algorithm uses parameters such as shape, direction, internal composition, and

Figure 6. BI-RADS 2. See-Mode's interface displays lesion measurements side by side with the US images. This case had a simple cyst appearance. Images courtesy of See-Mode.

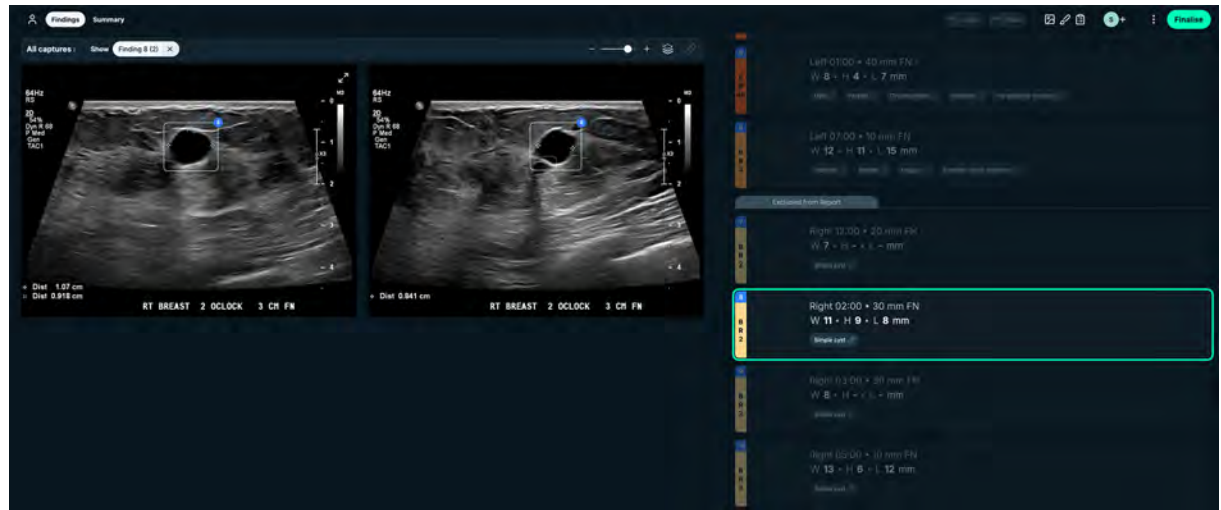
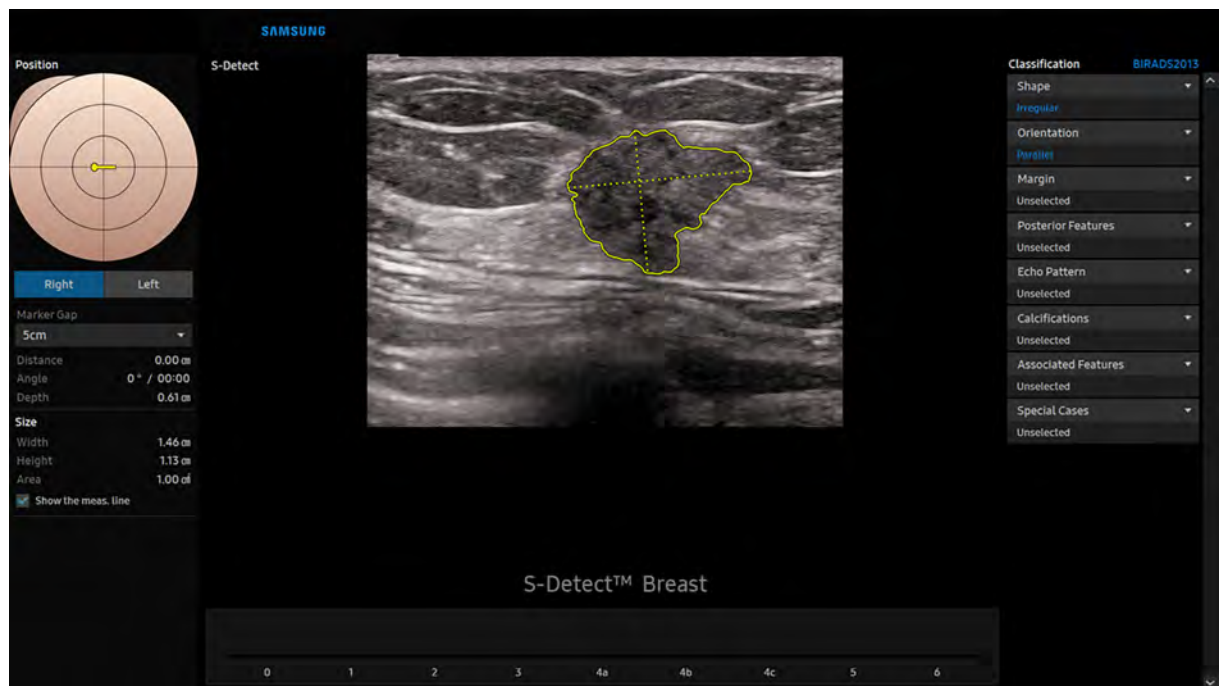


Figure 7. Irregular mass. S-Detect artificial intelligence Decision Support creates a lesion map with position and measurements on the left side of the figure, US image in the center, and selected classification features on the right. This mass was classified as irregular shape and parallel orientation. Images courtesy of Samsung Electronics.



margin circumscription for lesion assessment (Figures 1–3).¹⁴

In another assessment of Koios AI DS, a multicenter retrospective study of 715 breast masses found that none of the BI-RADS-2 assignments made with AI assistance were later identified as malignant. This

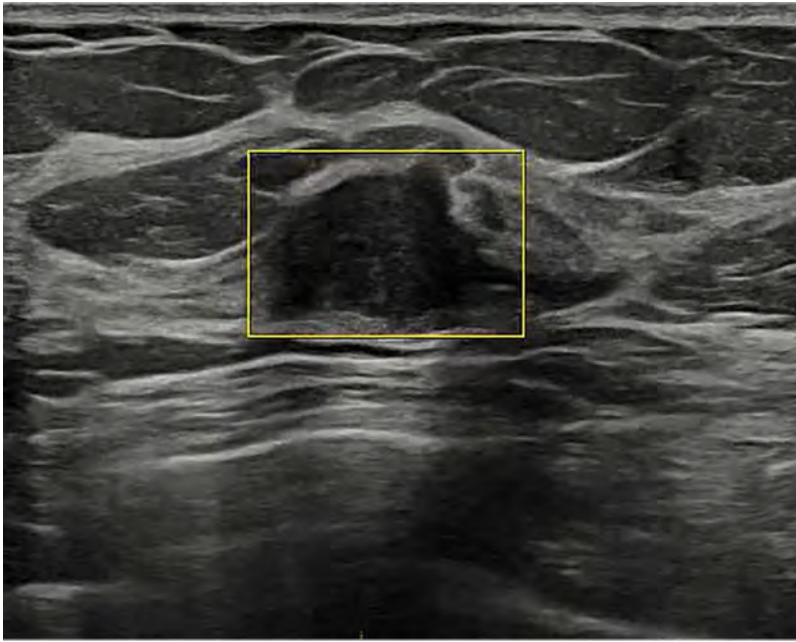
approach contributed to an 11% reduction in benign biopsies within the study population.¹⁵

See-Mode

See-Mode has developed breast US analysis software, currently under FDA review, to analyze

lesion shape, orientation, margins, echogenicity, and posterior features to generate a BI-RADS assessment category. To account for variations in image acquisition and patient characteristics, model training incorporates site-specific and regional data.

Figure 8. Artificial intelligence (AI) lesion detection. S-Detect AI Decision Support has a US Food and Drug Administration-pending feature that detects potentially abnormal findings and displays a yellow box to highlight the finding to the sonologist during live US scanning of the breast. Images courtesy of Samsung Electronics.



The See-Mode software highlights suspected lesions with visual markers such as colored overlays and bounding boxes, along with measurements. A standardized clock face design is also included in the interface for lesion localization (Figures 4–6).

S-Detect

Samsung's S-Detect for Breast is designed to assist radiologists during US imaging. Currently available for use on Samsung US systems, the software analyzes lesion shape, orientation, margins, echogenicity, posterior features, and calcifications to generate a BI-RADS assessment category (Figure 7).

One study compared S-Detect's performance to radiologists with varying experience levels. Analyzing 206 breast masses (118 benign, 88 malignant), S-Detect

Figure 9. BI-RADS 2. Breast Ultrasound Computer-Aided Diagnosis interface showing a navigation bar on the left and an US image with the outlined lesion in the center. The right side displays a map of the probe on the breast (top right) with clock face coordinates below. This mass was categorized as BI-RADS 2, likelihood of malignancy < 0.1%. Image courtesy of TaiHao Medical Inc.

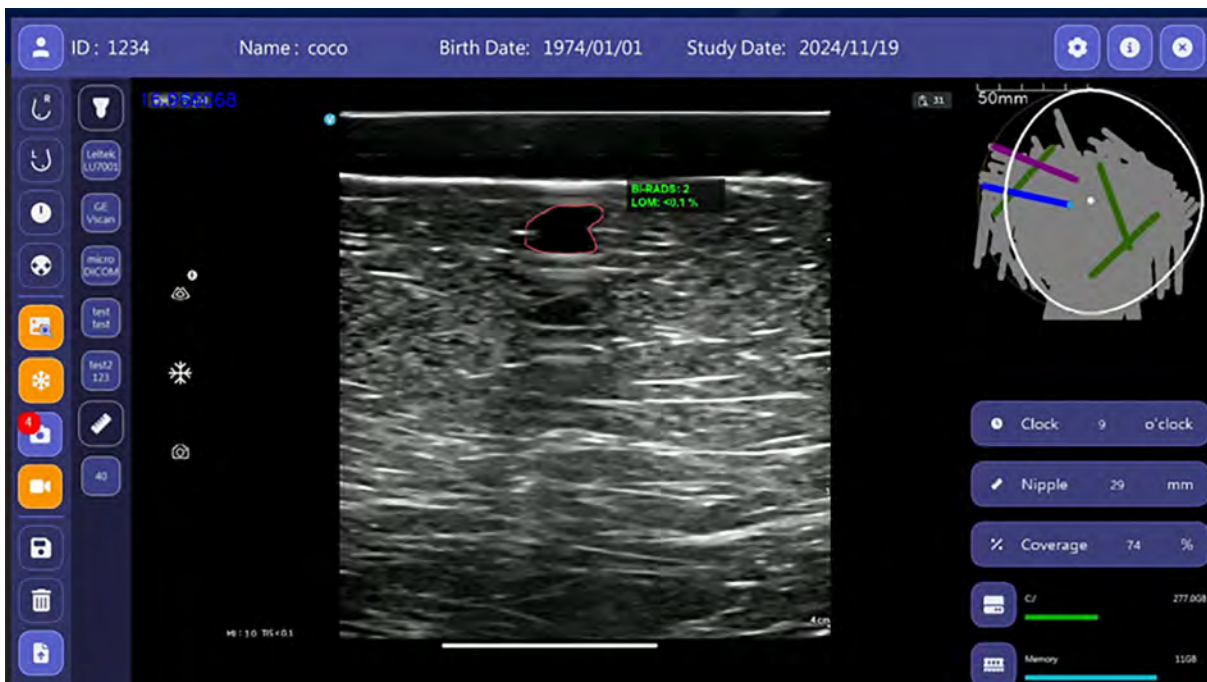


Figure 10. BI-RADS 2. Breast Ultrasound Computer-Aided Diagnosis interface with the US image of the outlined lesion with accompanying measurements in the center. This mass was categorized as BI-RADS 2 based on its oval shape, parallel orientation, and circumscribed margins. Image courtesy of TaiHao Medical Inc.

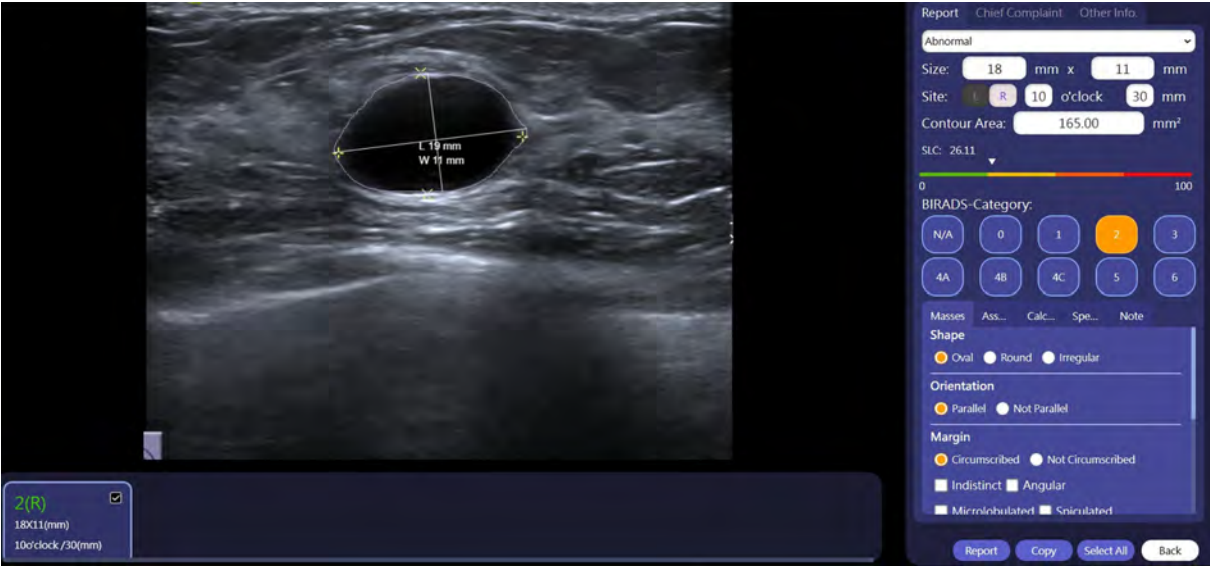
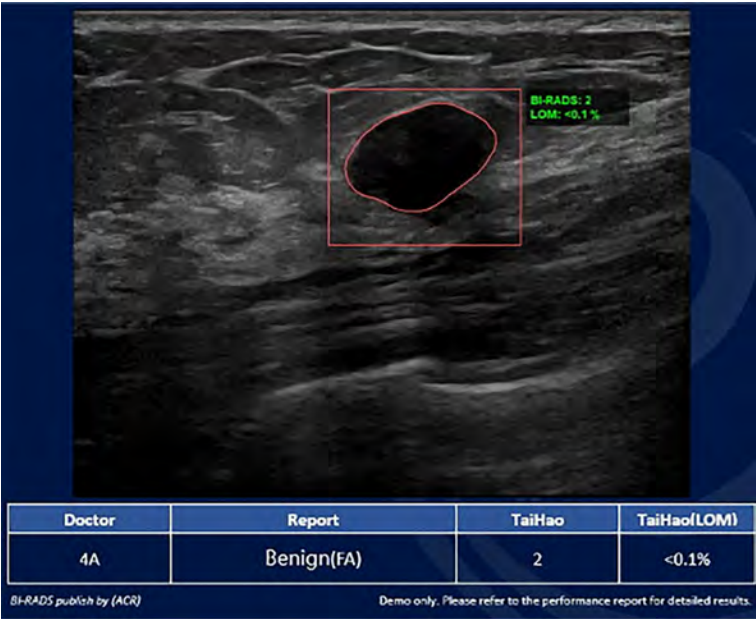


Figure 11. Artificial intelligence/radiologist discrepancy. Breast Ultrasound Computer-Aided Diagnosis (BU-CAD) interface with the US image of the outlined lesion. This mass was categorized as BI-RADS 2, <0.1% likelihood of malignancy (LOM). At the bottom, the radiologist's assignment of BI-RADS 4A and TaiHao's BU-CAD assignment of BI-RADS 2 are displayed. This mass demonstrated benign pathology via fine needle aspiration. Image courtesy of TaiHao Medical Inc.



demonstrated 91.1% sensitivity, 80.1% specificity, and 85.4% overall accuracy. Radiologists using S-Detect showed improved specificity (from 76.2% to 84.4%) and slightly increased accuracy

(from 85.4% to 88.3%), suggesting that S-Detect may enhance diagnostic assessments.¹⁶

S-Detect's "Live Breast Assist" feature (Figure 8), currently under FDA review, uses DL to detect

areas of interest in real time during scanning. This feature supplements the sonologist's lesion detection by automatically highlighting potential abnormalities.

BU-CAD

Breast Ultrasound Computer-Aided Diagnosis (BU-CAD), developed by TaiHao Medical Inc, is designed to analyze 2D and 3D images. The system evaluates lesion shape, orientation, margins, echogenicity, posterior features, and calcifications (Figures 9–11) and generates automated BI-RADS categorizations. A study evaluating BU-CAD using a dataset of 14,624 images from 7516 patients across multiple centers reported a 13.6% increase in specificity without compromising sensitivity, along with lower inter-reader variability.¹⁷

Summary of AI Tools for Breast US

Each of these AI tools offers distinct features to aid in breast lesion detection and diagnosis

Table 1. Chart Summarizing the Capabilities of 4 Currently Available Breast US Artificial Intelligence Tools: Koios, See-Mode, S-Detect, and BU-CAD Systems

	Koios	See-Mode	S-Detect	BU-CAD
Shape	✓	✓	✓	✓
Orientation	✓	✓	✓	✓
Margins		✓	✓	✓
Echogenicity		✓	✓	✓
Calcifications			✓	✓
Posterior Features		✓	✓	✓
AI Lesion Detection			✓	

(Table 1). They vary by the specific morphological features they use to characterize masses, but most characterize findings already identified by the sonologist. While each tool has its strengths, their differences may indicate different suitability for varied clinical and workflow needs.

Limitations, Challenges, and Next Steps

The future of breast US in clinical practice is likely to include AI to enhance lesion analysis and aid cancer detection. There are, however, challenges to overcome before AI earns widespread clinical implementation.

First, AI tools will require appropriate governance and monitoring. Many studies to date are limited to single institutions

and do not reflect large or diverse study samples, potentially limiting local applicability in clinical practices.⁶ Pre-validation in the local environment is needed to ensure local model performance is on par with expectations from prior studies. Training bias exists, and local performance will be affected by training datasets that differ from local datasets.

Following clinical deployment, monitoring of algorithm performance is important; assessments must be performed to detect algorithm drift. Algorithm drift can degrade a radiology model's performance after training due to evolving factors such as patient demographics, imaging equipment/protocols, and the emergence of new diseases or variants.

Second, research is needed to evaluate the impact of breast US

AI across clinical environments and practitioners of varying levels of US expertise. AI-based analysis tools may assist technologists and radiologists with less experience. However, reliance on them could increase false-positive findings.

Importantly, the success of AI tools relies on practitioner and patient acceptance. AI algorithms are so-called “black box” solutions that lack transparency in their decision-making processes, potentially hindering their uptake by radiologists.¹⁸ Patient sentiment should also be considered. In one study, half of the women above screening age viewed AI analysis of their breast images favorably, with the other half viewing it with negative and/or neutral sentiments.¹⁹ Education of all stakeholders regarding the benefits and limitations of AI will be an important factor in the successful integration of these technologies into breast imaging.

Conclusion

The FDA's breast density notification mandate is driving increased demand for supplemental breast cancer screening, including breast US, and creating a critical need for AI tools to support successful and efficient implementation.

For radiologists, effectively integrating AI into practice requires a foundational understanding of the technology's principles. This consists of critically evaluating published performance metrics (eg, sensitivity, specificity, area under the curve) in the context of one's own practice, becoming aware of potential biases in training data (and the resulting limitations of AI models), and

understanding the potential for algorithm drift.

While they vary in their features and functionalities, the tools discussed in this review share the goal of enhancing lesion detection and characterization. By actively engaging with these advancements, radiologists can potentially optimize diagnostic accuracy and workflow efficiency in breast US. Further research, including prospective studies and rigorous clinical validation, is crucial to fully realize the potential of AI in breast US.

References

- 1) Freer PE. Mammographic breast density: impact on breast cancer risk and implications for screening. *Radiographics*. 2015;35(2):302-315. doi:10.1148/rg.352140106
- 2) American Cancer Society. Dense breast tissue. 2024. Accessed March 24, 2024. <https://www.cancer.org/cancer/types/breast-cancer/screening-tests-and-early-detection/mammograms/breast-density-and-your-mammogram-report.html>
- 3) Elmore JG. Imaging surveillance of women with a personal history of breast cancer. *Breast Cancer Screening*. 1st ed. Elsevier. 2016:127-136. doi:10.1016/B978-0-12-802209-2.00012-7
- 4) Bahl M. Artificial intelligence: a primer for breast imaging radiologists. *J Breast Imaging*. 2020;2(4):304-314. doi:10.1093/jbi/wbaa033
- 5) McKinney SM, Sieniek M, Godbole V, et al. International evaluation of an AI system for breast cancer screening. *Nature*. 2020;577(7788):89-94. doi:10.1038/s41586-019-1799-6
- 6) Madani M, Behzadi MM, Nabavi S. The role of deep learning in advancing breast cancer detection using different imaging modalities: a systematic review. *Cancers*. 2022;14(21):5334. doi:10.3390/cancers14215334
- 7) Mendes J, Domingues J, Aidos H, Garcia N, Matela N. AI in breast cancer imaging: a survey of different applications. *J Imaging*. 2022;8(9):228. doi:10.3390/jimaging8090228
- 8) Berg WA, Gur D, Bandos AI, et al. Impact of original and artificially improved artificial intelligence-based computer-aided diagnosis on breast US interpretation. *J Breast Imaging*. 2021;3(3):301-311. doi:10.1093/jbi/wbab013
- 9) Heller SL, Wegener M, Babb JS, Gao Y. Can an artificial intelligence decision aid decrease false-positive breast biopsies? *Ultrasound Q*. 2020;37(1):10-15. doi:10.1097/RUQ.0000000000000550
- 10) Brunetti N, Calabrese M, Martinoli C, Tagliafico AS. Artificial intelligence in breast ultrasound: from diagnosis to prognosis—a rapid review. *Diagnostics*. 2023;13(1):58. doi:10.3390/diagnostics13010058
- 11) Villa-Camacho JC, Baikpour M, Chou S-HS. Artificial intelligence for breast US. *J Breast Imaging*. 2023;5(1):11-20. doi:10.1093/jbi/wbac077
- 12) Mango VL, Sun M, Wynn RT, Ha R. Should we ignore, follow, or biopsy? impact of artificial intelligence decision support on breast ultrasound lesion assessment. *AJR Am J Roentgenol*. 2020;214(6):1445-1452. doi:10.2214/AJR.19.21872
- 13) Amir T, Coffey K, Sevilimedu V, Fardanesh R, Mango VL. A role for breast ultrasound artificial intelligence decision support in the evaluation of small invasive lobular carcinomas. *Clin Imaging*. 2023;101:77-85. doi:10.1016/j.clinimag.2023.05.005
- 14) Coffey K, Aukland B, Amir T, et al. Artificial intelligence decision support for triple-negative breast cancers on ultrasound. *J Breast Imaging*. 2024;6(1):33-44. doi:10.1093/jbi/wbad080
- 15) Guldogan N, Taskin F, Icten GE, et al. Artificial intelligence in BI-RADS categorization of breast lesions on ultrasound: can we omit excessive follow-ups and biopsies? *Acad Radiol*. 2024;31(6):2194-2202. doi:10.1016/j.acra.2023.11.031
- 16) Kim K, Song MK, Kim E-K, Yoon JH. Clinical application of S-detect to breast masses on ultrasonography: a study evaluating the diagnostic performance and agreement with a dedicated breast radiologist. *Ultrasonography*. 2017;36(1):3-9. doi:10.14366/usg.16012
- 17) Lai Y-C, Chen H-H, Hsu J-F, et al. Evaluation of physician performance using a concurrent-read artificial intelligence system to support breast ultrasound interpretation. *Breast*. 2022;65:124-135. doi:10.1016/j.breast.2022.07.009
- 18) Zheng D, He X, Jing J. Overview of artificial intelligence in breast cancer medical imaging. *J Clin Med*. 2023;12(2):419. doi:10.3390/jcm12020419
- 19) Lennox-Chhugani N, Chen Y, Pearson V, Trzcinski B, James J. Women's attitudes to the use of AI image readers: a case study from a national breast screening programme. *BMJ Health Care Inform*. 2021;28(1):e100293. doi:10.1136/bmjhci-2020-100293

Abdominal Manifestations of Tuberous Sclerosis Complex

Muhammad Nabeel Akram, BS; Kai Xue, MD; Kaustubh G. Shiralkar, MD; Steven S. Chua, MD, PhD

Introduction

Tuberous sclerosis complex (TSC) is a multisystem disorder that occurs 1 in 6000 live births.¹ The condition's manifestations are highly variable owing to penetrance, which determines the associated clinical presentation and outcome. Inherited in an autosomal-dominant fashion,² TSC is caused by mutations or loss of function in 2 tumor suppressor genes, tuberous sclerosis complexes 1 and 2 (*TSC1*, *TSC2*). These genes encode hamartin and tuberin, respectively, and together with a third subunit, *TBC1D7*, form a trimeric inhibitor complex that inhibits the mechanistic target of Rapamycin 1 (mTOR1) pathway, which is essential for normal growth.³ The loss of *TSC1* or *TSC2* results in constitutive action of the mTOR1 pathway, which eventually leads to abnormal production of the multisystemic hamartomatous tumors seen in TSC.⁴

Seizures and intellectual disability are the 2 most common clinical presentations of TSC.¹ Dermatological findings are also common and present in 90% of cases.⁵ Imaging can play an important role in identifying affected organs and complications. Most of these studies focus on the neurological impacts of TSC, but imaging for thoracoabdominal manifestations is equally important. A retrospective study of patients in a TSC registry demonstrated that thoracoabdominal manifestations occur more frequently in these patients than in the general population, supporting the need for detailed thoracoabdominal imaging to better define disease extent.⁶ This review details the salient abdominal, pelvic, and chest manifestations of TSC to help facilitate and improve clinical diagnosis, treatment, and outcomes. The imaging features and complications of tuberous sclerosis lesions are summarized in Table 1.

Abdominal/Pelvic Manifestations

Angiomyolipomas

Renal angiomyolipoma (AMLs) are the most common abdominal manifestation of TSC¹; they are considered a subset of the perivascular epithelioid cell (PEComa) group of mesenchymal tumors. PEComas have varying growth potential, ranging from benign/nonaggressive entities such as AMLs, through lesions of uncertain malignant potential, to frankly malignant sarcomas that demonstrate aggressive behavior and metastatic potential.¹⁶ Malignant sarcomas will be discussed later in this review.

Renal AMLs are noted in 55-75% of individuals with TSC.¹³ They are characterized by abnormal blood vessels, immature smooth muscle cells, and fat cells.¹⁷ These entities are generally benign and asymptomatic, but large (typically >4 cm) AMLs and those with pseudoaneurysms >0.5 cm can predispose patients to an increased risk of hemorrhage.^{1,9}

Renal AMLs are classified by subtypes based on their fat content (lipid-rich and lipid-poor), which can be distinguished with imaging.¹⁸

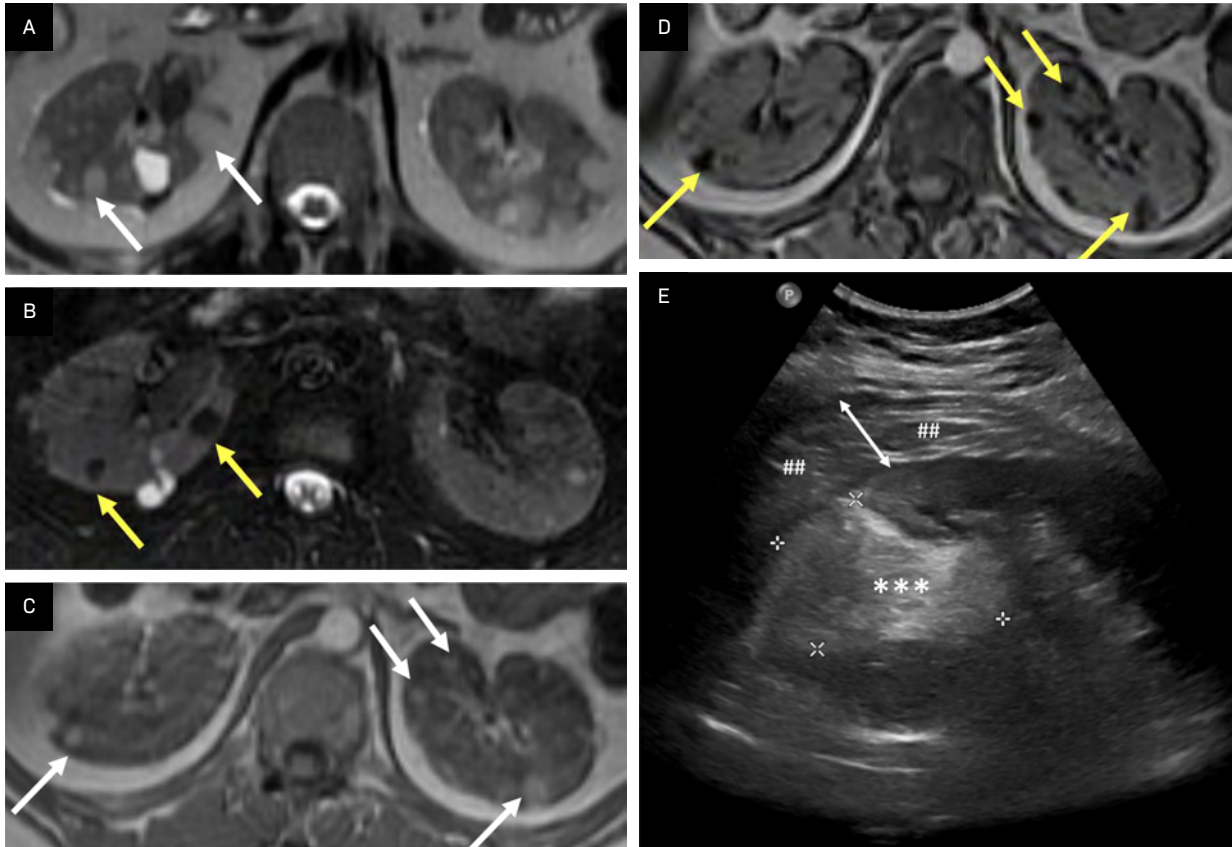
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Table 1. Tuberous Sclerosis Complex Manifestations

ORGAN	LESION	IMAGING FEATURES	COMPLICATIONS
Bone	Osseous lesions	Irregularly circumscribed and sclerotic appearance seen on CT.	Subperitoneal new bone deposition. ¹ Usually asymptomatic. ⁷
Heart	Rhabdomyoma	Variable signal intensities. Usually poorly enhancing.	Impaired ventricular function, valvular dysfunction, and outflow obstruction. ⁸
Kidney	AML (part of PEComa)	Loss of signal in fat-saturated and opposed phase images if typical AML. Lipid-poor AML shows scant fat and variable soft tissues of muscle and vessels with heterogeneous enhancement. T2 hypointense to isointense.	Hemorrhage if size > 4 cm or pseudoaneurysm > 0.5 cm. ^{1,9} Progression of chronic renal disease, renal failure. ¹
Kidney	RCC	T2 hyperintense, heterogeneous to avid enhancement depending on subtype.	Hemorrhage, metastatic disease, venous thrombosis (bland and tumor), arterial involvement. ¹⁰
Kidney	Cysts	Cysts of varying complexities; can be fluid density, proteinaceous/hemorrhagic.	Chronic renal disease, renal failure, increased morbidity, cyst rupture.
Liver	AML (part of PEComa)	Similar to lipid-rich or lipid-poor AMLs in kidney. Lipid-poor hepatic AML can be confused with hepatocellular carcinomas and biopsy may be necessary to confirm.	Potential for rupture and hemorrhage ¹¹ but much less frequent than renal AMLs.
Lung/retroperitoneum	LAM (part of PEComa)	Thin-walled cysts.	Recurrent pneumothoraces and chylous pleural effusions or ascites. ¹²
Lung	MMPH	Ground glass nodules.	Usually stable disease.
Spleen	Hamartoma	Typically T1 hypointense, and T2 hyperintense. Small lesions may be isointense to the splenic parenchyma and seen as contour bulge.	Potential rupture, local mass effect. ¹³
Pancreas	AML (part of PEComa)	Typical pancreatic AML similar to those seen in the kidneys and liver.	May alter pancreatic function. ¹⁴ Rare incidence.
Pancreas	Neuroendocrine tumor (rare)	Hypervascular and avidly enhancing. T2 hyperintense. Functional (hormone secreting) and nonfunctional tumors (non-hormone secreting).	Symptoms vary based on type of hormone secreted and if tumors are functional or not. ¹⁵
Multiorgan	Malignant PEComas	Larger size, heterogeneous enhancement, with areas of necrosis, can metastasize to distant organs and bones.	Metastatic disease, increased morbidity and mortality.
Abbreviations: AML, angiomyolipoma; LAM, lymphangioleiomyomatosis; MMPH, micronodular pneumocyte hyperplasia; PEComa, perivascular epithelioid cell; RCC, renal cell carcinoma.			

Figure 1. Lipid-rich angiomyolipoma (AML). AMLs typically contain macroscopic or bulk fat and can also contain microscopic or intravoxel fat. Intermediate lesions on T2 image (A, arrows) demonstrate loss of signal on T2-fat saturated image (B, arrows), indicating macroscopic fat. Phase imaging with T1 intermediate lesions in the kidneys (C, arrows) demonstrates loss of signal in the opposed phase image, indicating microscopic/intravoxel fat in AMLs (D, arrows). A large, left mid-to-superior renal pole echogenic lesion (E, asterisks and calipers) containing echogenic fat was found to be a ruptured AML with perinephric hematoma (##), whose thickness is delineated by the white double-headed arrow.



MRI can assist in identifying lipid-rich AMLs owing to the presence of macroscopic fat, seen as areas of decreased signal intensity in frequency-selected fat-saturated MRI sequences (Figure 1) and/or the presence of microscopic/intravoxel fat depicted as areas of decreased signal intensity and chemical shift type II artifact in opposed-phase MRI sequences (Figure 1).¹⁸ On US, lipid-rich AMLs manifest as hyperechoic masses in the kidneys (Figure 1); cross-sectional imaging is often utilized to confirm this finding and exclude fat-containing renal cell carcinoma (RCC).¹ On CT, lipid-rich AMLs show macroscopic fatty lesions with attenuation < 10 HU.¹⁸ In addition, heterogeneous

soft-tissue attenuation can also be seen on CT; contrast enhancement varies with vascularity and volume of soft tissue.¹⁸

Lipid-poor AMLs are more complex, with variable soft-tissue composition, including muscular or vascular components with limited or absent fat where no significant loss of signal intensity is seen in the fat-saturated or opposed MRI sequences (Figure 2).¹³ They are typically T2 isointense to renal parenchyma and demonstrate variable contrast enhancement patterns on MRI or CT (Figure 3). Distinguishing lipid-poor AML from RCC can be challenging.¹ The former appears to enhance variably and does not show the wash-in

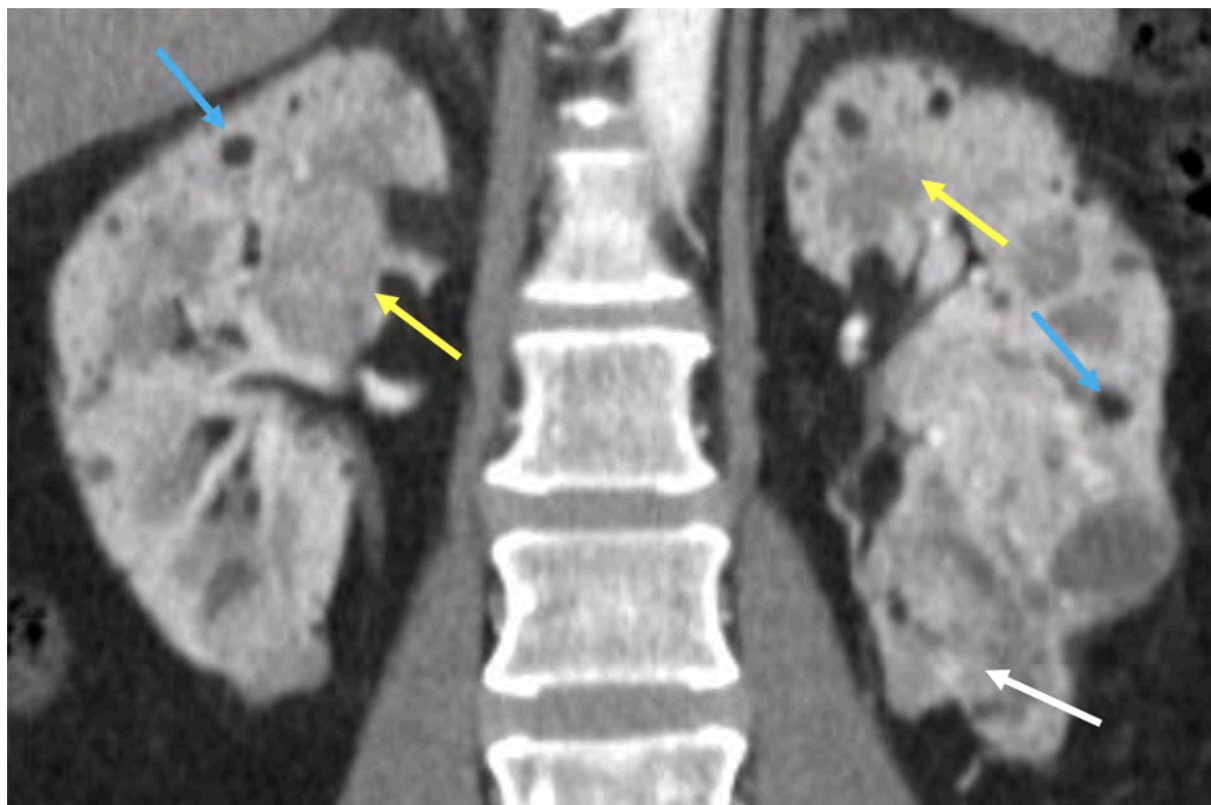
or wash-out characteristics typical of RCCs.¹⁰ Additionally, RCCs may contain microscopic and, rarely, macroscopic fat, thought to result from osseous metaplasia.¹⁹

Although AMLs are usually benign, a rare subtype resulting from the transformation of a benign epithelioid AML via mutation can be malignant. These AMLs can present with locally invasive and aggressive features, as well as distant metastases known as multicentric AMLs of epithelioid morphology.^{13,20-22} These lesions tend to be larger, appear more cellular, have internal necrosis and little fat, and demonstrate heterogeneous enhancement. Distant metastases may resemble RCCs on imaging, favoring a diagnosis of the

Figure 2. Lipid-poor angiomyolipoma (AML). A T2 isointense renal lesion without significant loss of signal in the frequency fat-saturated sequence (T2 FS) suggesting the presence of macroscopic fat (A, arrow), and no loss of signal in the T1 opposed phase sequence suggesting microscopic/intravoxel fat (B, arrow) demonstrates mild arterial enhancement in the T1 fat-saturated, contrast-enhanced image (C, arrow). This lesion can be difficult to distinguish from a renal cell carcinoma.



Figure 3. Variable appearances of renal angiomyolipomas (AMLs) in tuberous sclerosis complex. Predominantly macroscopic fat-containing AMLs show low CT attenuation with macroscopic fat <-10 HU (blue arrows). Lipid-poor AMLs with a more smooth muscle component are higher attenuation (yellow arrows). A more complex AML containing smooth muscle, vascular components, and tiny amounts of fat is seen in the left inferior renal pole (white arrow).



more aggressive epithelioid AML over the typical benign AML.^{14,23}

In addition to the kidneys, AMLs can be found in other abdominal organs, though at a lower incidence. AMLs in the liver, pancreas, spleen,

and/or gastrointestinal tract often coexist with renal AMLs.^{11,24,25} A study of 187 patients with TSC found that only 28 (14%) had hepatic AMLs with renal AMLs²⁶; a large registry study similarly found that 19% of patients

with TSC had liver AMLs.⁶ Hepatic AMLs can demonstrate a macroscopic fat component (Figure 4) but may also be confused with hepatocellular carcinoma if they are lipid-poor. Biopsy is frequently required for

Figure 4. Multiorgan angiomyolipomas (AMLs). Hepatic and pancreatic AMLs appear as regions of T2 hyperintensity in the liver and pancreas in T2. MR image (A, arrows) with loss of signal in the frequency selective fat-saturated T2 MR image (B, arrows).

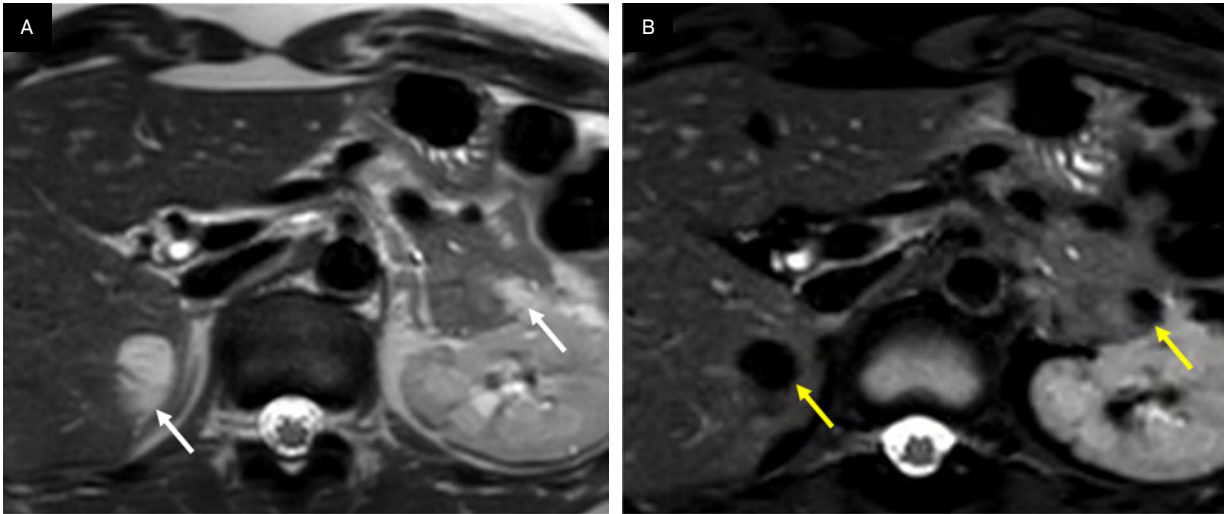
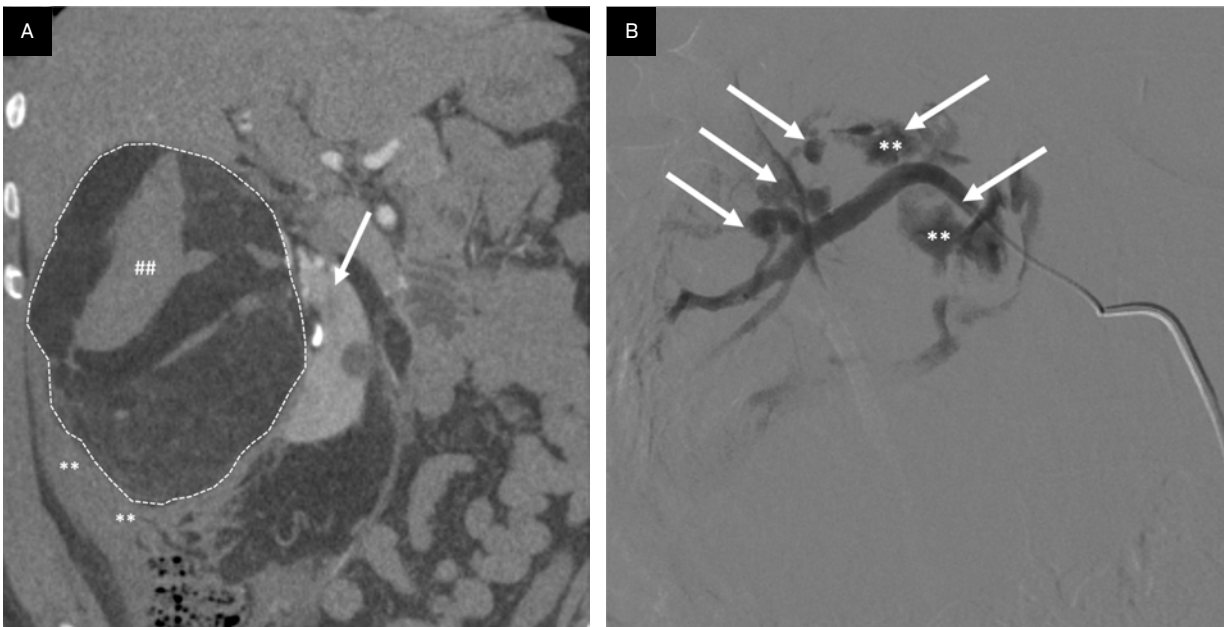


Figure 5. Angiomyolipoma (AML) rupture. AMLs > 4 cm or containing pseudoaneurysms > 0.5 cm have an increased propensity to bleed. (A) Coronal CT reformation through large, ruptured AML with macroscopic fat (dotted white lines outlining lesion) in the right kidney (arrow) with resultant perinephric hematoma (**) and internal hemorrhage (##). (B) Selective catheter arteriogram following AML rupture demonstrating multiple pseudoaneurysms (arrows), 2 with contrast extravasation indicating active hemorrhage (**).



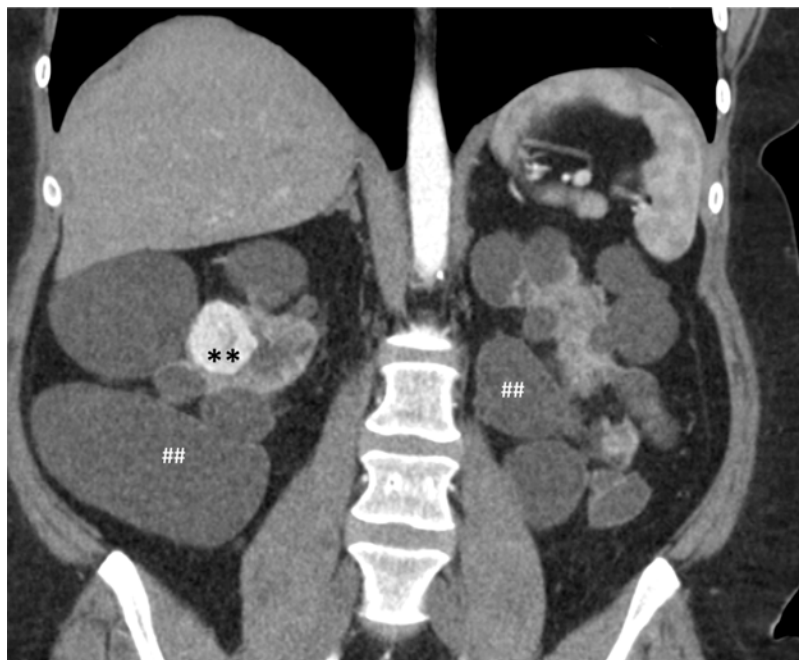
confirmation.²⁴ Hepatic AMLs are not typically stable lesions; they can grow and commonly demonstrate hypervascularity with macroscopic fat on contrast-enhanced imaging.^{13,27} Unlike renal AMLs, hepatic AMLs

rarely rupture, with only 8 such cases reported in the literature.²⁸ These lesions tended to be large, with an average diameter of 8 cm. Hepatic AMLs > 5 cm with more aggressive epithelioid morphology on biopsy

have been shown to benefit from surgical resection.²⁹

AMLs can also occur in the pancreas, where they manifest as macroscopic fatty lesions (Figure 4) and may affect pancreatic function.¹¹

Figure 6. Renal cysts and renal cell carcinoma. Coronal CT reformation in a patient with tuberous sclerosis complex, end-stage renal disease, and associated polycystic kidney disease was found to have an avidly arterially enhancing right renal mass diagnosed as renal cell carcinoma (***) on a background of multiple renal cysts (##).



These AMLs are extremely rare, with only a few cases reported,^{11,30} and are among 1% of pancreatic tumors of mesenchymal origin.³¹ Heywood et al reported a case of a pancreatic AML with hemorrhage that appeared as a heterogeneous lesion on US and a cystic lesion with an irregular, thickened wall on CT.¹¹

As alluded to earlier, large renal AMLs (>4 cm, Figure 5) or those that possess pseudoaneurysms > 0.5 cm can increase the risk for hemorrhage,^{1,9,32} which may be fatal if not detected and promptly treated. Manifestations of shock and hypovolemia in this setting are termed Wunderlich syndrome,^{32,33} which, after status epilepticus, is the second-most frequent complication among patients with TSC.¹³ Prophylactic embolization or resection can help reduce mortality.¹

Renal Cysts

Renal cysts and polycystic kidney disease are common in individuals with TSC (Figure 6)^{17,34,35}; both

were found in approximately 72% of patients in a large registry study.⁶ Renal cysts are typically asymptomatic but can lead to polycystic kidney disease and the development of hypertension and/or renal failure in the setting of TSC.^{17,34,35}

Renal Cell Carcinoma

Renal cell carcinoma is another manifestation that can occur in patients with TSC (Figure 6).^{1,8,13,36-39} These tumors tend to occur in young adults and can be of any subtype (clear cell, papillary, or chromophobe), the most common being clear cell.^{17,38,40} This finding underscores the importance of continuous imaging surveillance in patients with renal lesions, preferably with multiphasic MRI owing to its superior soft-tissue resolution, ability to perform chemical shift sequences and fat saturation, and lack of ionizing radiation. Multiphasic MRI should be performed every 1-3 years as part of a thoracoabdominal imaging

protocol for TSC.⁴¹ Where MRI is contraindicated, multiphasic CT with a renal mass-oriented protocol may be helpful.

Hamartomas

Splenic hamartomas may be encountered in patients with TSC, albeit rarely.¹³ US imaging typically demonstrates solid masses hyperechoic to their surroundings along with increased blood flow on Doppler imaging.¹³ Other common sonographic findings are calcifications and cystic changes. On MRI, splenic hamartomas are usually T1 hypointense and T2 hyperintense to the splenic parenchyma. They can also be hypervascular and diffusely contrast-enhancing, particularly on early postcontrast imaging.¹³

Cardiothoracic and Musculoskeletal Manifestations

Lymphangioleiomyomatosis

One pulmonary manifestation of tuberous sclerosis is lymphangioleiomyomatosis (LAM),⁴²⁻⁴⁴ which is also a member of the PEComa group of tumors.¹⁶ LAM manifests as an abnormal proliferation of smooth muscle cells in the lymphatic system accompanied by cystic changes within the lung parenchyma. This can result in lung parenchymal destruction, dyspnea, and ultimately require lung transplantation.^{12,45} There are 2 forms of LAM: one associated with TSC (TSC/LAM) and a more common sporadic form, both with female predominance.⁴⁶ The TSC/LAM form is the more aggressive of the 2, presents with more severe disease, and is seen in 26-39% of patients with TSC.⁴⁷ One complication of LAM is chylous pleural effusion formation, which disrupts the lymphatic system in the chest.¹ On CT imaging, LAM will manifest as multiple

Figure 7. Other manifestations of tuberous sclerosis complex (TSC). (A) Axial CT showing pulmonary lymphangioleiomyomatosis characterized by thin-walled cysts (white arrows) and micronodular pneumocyte hyperplasia manifested by ground glass nodules (yellow arrows) in a patient with TSC. (B) Coronal T2 MRI showing how lymphangioleiomyomas can develop in the retroperitoneal region as in this T2 hyperintense signal mass (##, arrows) in the left retroperitoneal region abutting the left kidney. (C) T1 fat-saturated postcontrast axial image of the heart demonstrating a nonenhancing rhabdomyoma (white arrow) in the right ventricle. (D). Dixon fat-only MRI sequence with a tumor containing macroscopic fat at the ventricular septum (arrow) TSC appearing as a hyperintense lesion consistent with a cardiac angiomyolipoma. (E) Sagittal CT reformation of the spine in a patient with TSC and multiple sclerotic bony lesions in the vertebral bodies (arrows).

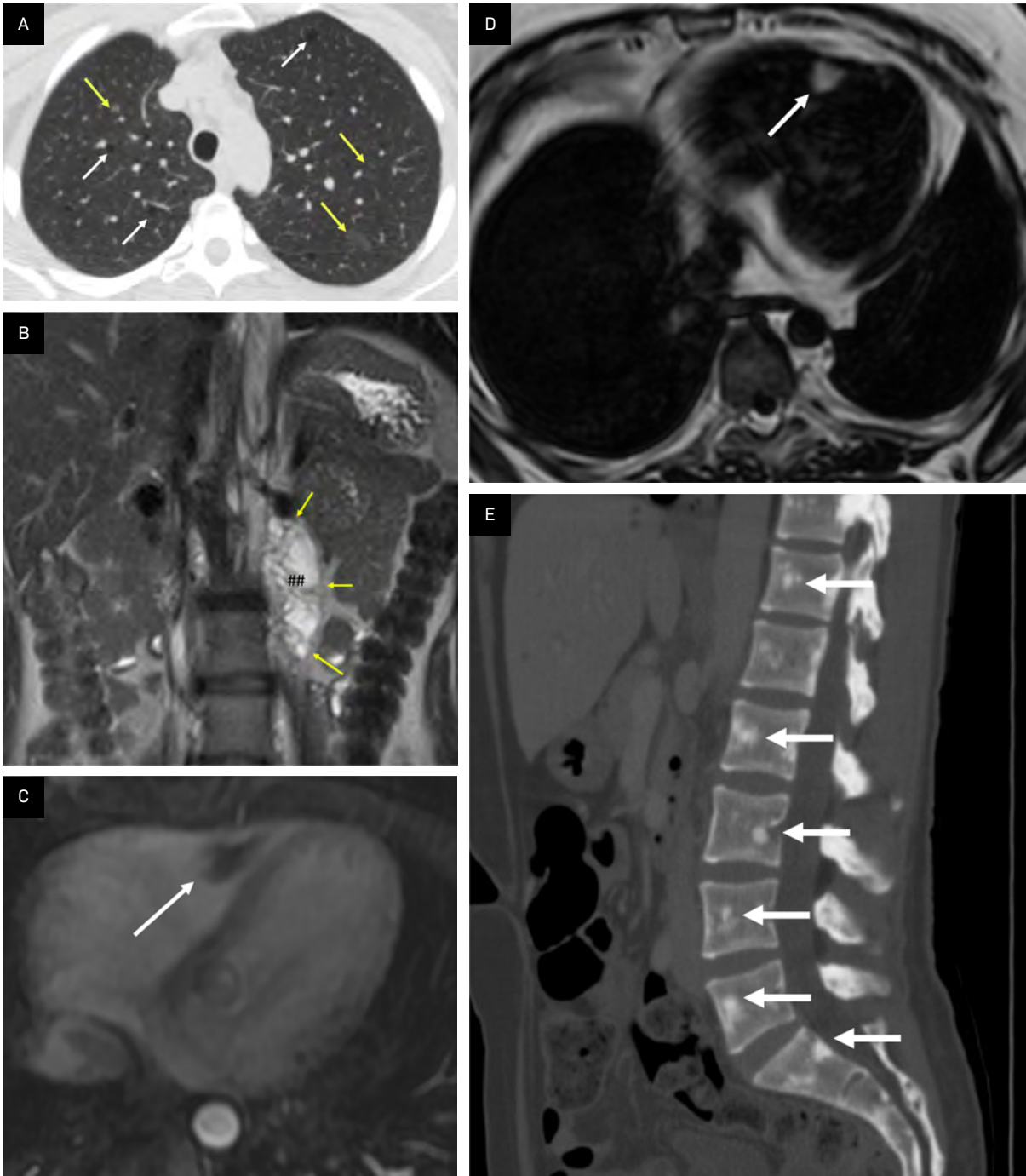


Figure 8. Aggressive malignant perivascular epithelioid cell tumor (PEComa). T1-fat saturated postcontrast MRI demonstrates an expansile and aggressive left pelvic lesion (arrows) eroding the left iliac crest and invading the adjacent left gluteal (G) and left iliopsoas (I) muscles. The tumor is heterogeneously enhanced with areas of internal necrosis (*) and was proven to be a recurrent malignant PEComa in a patient with a previous pulmonary PEComa that was treated and subsequently resected. A satellite lesion in the left iliac bone is also seen (##).



thin-walled cysts (Figure 7).^{44,48}

Reticular opacities may also be seen, which may indicate that edema is obstructing vessels.¹⁷ Pneumothorax is another complication of LAM that may require intervention.^{1,17}

Lymphangiomyomas can also be seen in the retroperitoneal region as T2 hyperintense cystic dilatations involving the lymphatic system and lymphadenopathy.⁴⁹ Complications include mass effect on retroperitoneal organs, chylous ascites, cyst rupture, and abdominal pain.^{7,50}

Micronodular Pneumocyte Hyperplasia

A third, less common, pulmonary manifestation of TSC is multifocal micronodular pneumocyte hyperplasia (MMPH), seen in approximately 18% of patients in a registry study.⁶ The condition is characterized by a well-demarcated nodular proliferation scattered randomly throughout the lungs and manifesting as ground glass nodules on CT (Figure 7).^{49,51} MMPH

can occur concomitantly with or independently from LAM.

Cardiac Manifestations

Cardiac-related conditions are prominent in TSC.^{1,38,43} Approximately 70% of children with cardiac rhabdomyomas have TSC.¹ Rhabdomyomas are benign, striated muscle tumors accompanied by “spider cells.”^{17,42} US typically depicts a well-defined hyperechoic mass along the intraventricular septum.¹³ On MRI, rhabdomyomas show little to no contrast enhancement (Figure 7).

Although less common than rhabdomyomas, AMLs can also be intracardiac and are usually located at the apex or in the ventricular wall.⁵⁰ Noncontrast CT may show fat attenuation (<10 HU) in these lesions. Cardiac AMLs show macroscopic fat and are hyperintense on Dixon fat-only sequences (Figure 7).

Osseous Manifestations

Osseous findings of TSC include sclerotic lesions, bone cysts, and periosteal new bone formation,

the latter occurring particularly in the metacarpal areas.⁵² Sclerotic lesions can be identified in the ribs, vertebral posterior elements, and along the iliac side of the sacroiliac joints (Figure 7).⁵² Rarely, TSC can cause macrodactyly.⁵³ As nonspecific findings, these are nondiagnostic of TSC.⁵²

PEComas

PEComas are rare mesenchymal neoplasms that can be benign or malignant entities with variable biologic features and oncologic outcomes.^{54,55} Both types of lesions are associated with alterations predominantly of the TSC2 gene, while a distinct subset of malignant PEComas can harbor other mutations.^{55,56} Benign lesions of the PEComa family include AML and LAM, while more aggressive entities termed malignant PEComas/sarcomas demonstrate a higher mitotic rate and growth potential. Malignant tumors can be found in patients with TSC and sporadically in patients without TSC.^{13,15,16}

On imaging, malignant PEComas can be differentiated from their benign counterparts based on their typically larger size (>5 cm), infiltrative growth, necrosis, and/or osseous destruction (Figure 8). They can also invade blood vessels and metastasize to other organs and tissues such as the liver, lungs, and bones.^{13,15,57} Owing to their deregulated growth, malignant PEComas can demonstrate fluorodeoxyglucose avidity on PET/CT.⁵⁸ Multiphasic MRI and CT and PET/CT can all be useful in screening for malignant PEComas and assessing treatment efficacy with serial imaging studies.

Patients with TSC with AMLs and non-AML PEComas, as well as some with gastrointestinal polyps, have an overall increased risk for developing

malignancies. AMLs and non-AML PComas are also associated with pancreatic neuroendocrine tumors,⁵⁹ further underscoring the need for imaging surveillance.

Conclusion

Tuberous sclerosis complex has a wide range of manifestations in the abdomen, pelvic, and chest. Renal AMLs are most common, but they can also occur in the liver, pancreas, and spleen. Thoracic manifestations include LAM, MMPH, and cardiac rhabdomyomas and AMLs. Recognizing these lesions can facilitate accurate diagnosis and optimal treatment planning in patients with TSC.

References

- Manoukian SB, Kowal DJ. Comprehensive imaging manifestations of tuberous sclerosis. *AJR Am J Roentgenol*. 2015;204(5):933-943. doi:10.2214/AJR.13.12235
- Rosengren T, Nanhoe S, de Almeida LGD, et al. Mutational analysis of TSC1 and TSC2 in danish patients with tuberous sclerosis complex. *Sci Rep*. 2020;10(1):9909. doi:10.1038/s41598-020-66588-4
- Dibble CC, Elis W, Menon S, et al. TBC1D7 is a third subunit of the TSC1-TSC2 complex upstream of mTORC1. *Mol Cell*. 2012;47(4):535-546. doi:10.1016/j.molcel.2012.06.009
- Orlova KA, Crino PB. The tuberous sclerosis complex. *Ann N Y Acad Sci*. 2010;1184:87-105. doi:10.1111/j.1749-6632.2009.05117.x
- Curatolo P, Bombardieri R, Jozwiak S. Tuberous sclerosis. *Lancet*. 2008;372(9639):657-668. doi:10.1016/S0140-6736(08)61279-9
- Ritter DM, Fessler BK, Ebrahimi-Fakhari D, et al. Prevalence of thoracoabdominal imaging findings in tuberous sclerosis complex. *Orphanet J Rare Dis*. 2022;17(1):124. doi:10.1186/s13023-022-02277-x
- Elia D, Torre O, Cassandro R, Caminati A, Harari S. Ultra-rare cystic disease. *Eur Respir Rev*. 2020;29(157):190163. doi:10.1183/16000617.0163-2019
- Khallouk A, Ahallal Y, Doublali M, et al. Concurrent bilateral renal angiomyolipoma and renal cell carcinoma in a patient with tuberous sclerosis complex. *Rev Urol*. 2009;11(4):216-218.
- Yamakado K, Tanaka N, Nakagawa T, et al. Renal angiomyolipoma: relationships between tumor size, aneurysm formation, and rupture. *Radiology*. 2002;225(1):78-82. doi:10.1148/radiol.2251011477
- Xie P, Yang Z, Yuan Z. Lipid-poor renal angiomyolipoma: differentiation from clear cell renal cell carcinoma using wash-in and washout characteristics on contrast-enhanced computed tomography. *Oncol Lett*. 2016;11(3):2327-2331. doi:10.3892/ol.2016.4214
- Heywood G, Smyrk TC, Donohue JH. Primary angiomyolipoma of the pancreas. *Pancreas*. 2004;28(4):443-445. doi:10.1097/00006676-200405000-00014
- Boehler A, Speich R, Russi EW, Weder W. Lung transplantation for lymphangioleiomyomatosis. *N Engl J Med*. 1996;335(17):1275-1280. doi:10.1056/NEJM199610243351704
- Wang MX, Segaran N, Bhalla S, et al. Tuberous sclerosis: current update. *Radiographics*. 2021;41(7):1992-2010. doi:10.1148/rg.2021210103
- Bharwani N, Christmas TJ, Jameson C, Moat N, Sohaib SA. Epithelioid angiomyolipoma: imaging appearances. *Br J Radiol*. 2009;82(984):e249-52. doi:10.1259/bjr/27259024
- Sobiborowicz A, Czarnecka AM, Szumera-Ciećkiewicz A, Rutkowski P, Świtaj T. Diagnosis and treatment of malignant pcoma tumours. *Oncol Clin Pract*. 2020;16(1):22-33. doi:10.5603/OCP.2020.0003
- Folpe AL, Mentzel T, Lehr H-A, et al. Perivascular epithelioid cell neoplasms of soft tissue and gynecologic origin: a clinicopathologic study of 26 cases and review of the literature. *Am J Surg Pathol*. 2005;29(12):1558-1575. doi:10.1097/01.pas.0000173232.22117.37
- Umeoka S, Koyama T, Miki Y, et al. Pictorial review of tuberous sclerosis in various organs. *Radiographics*. 2008;28(7):e32. doi:10.1148/rg.e32
- Pereira JM, Sirlin CB, Pinto PS, Casola G. CT and MR imaging of extrahepatic fatty masses of the abdomen and pelvis: techniques, diagnosis, differential diagnosis, and pitfalls. *Radiographics*. 2005;25(1):69-85. doi:10.1148/rg.251045074
- Richmond L, Atri M, Sherman C, Sharir S. Renal cell carcinoma containing macroscopic fat on CT mimics an angiomyolipoma due to bone metaplasia without macroscopic calcification. *Br J Radiol*. 2010;83(992):e179-81. doi:10.1259/bjr/46452134
- Pea M, Bonetti F, Martignoni G, et al. Apparent renal cell carcinomas in tuberous sclerosis are heterogeneous: the identification of malignant epithelioid angiomyolipoma. *Am J Surg Pathol*. 1998;22(2):180-187. doi:10.1097/0000478-199802000-00005
- Lin WC, Wang JH, Wei CJ, Pan CC, Chang CY. Malignant renal epithelioid angiomyolipoma with aggressive behavior and distant metastasis. *J Chin Med Assoc*. 2003;66(5):303-306.
- Lai H-Y, Chen C-K, Lee Y-H, et al. Multicentric aggressive angiomyolipomas: a rare form of pcomas. *AJR Am J Roentgenol*. 2006;186(3):837-840. doi:10.2214/AJR.04.1639
- Thiravit S, Teerasamit W, Thiravit P. The different faces of renal angiomyolipomas on radiologic imaging: a pictorial review. *Br J Radiol*. 2018;91(1084):20170533. doi:10.1259/bjr.20170533
- Tsui WM, Colombari R, Portmann BC, et al. Hepatic angiomyolipoma: a clinicopathologic study of 30 cases and delineation of unusual morphologic variants. *Am J Surg Pathol*. 1999;23(1):34-48. doi:10.1097/0000478-199901000-00004
- Thipphavong S, Duigenan S, Schindera ST, Gee MS, Phillips S. Nonneoplastic, benign, and malignant splenic diseases: cross-sectional imaging findings and rare disease entities. *AJR Am J Roentgenol*. 2014;203(2):315-322. doi:10.2214/AJR.13.11777
- Jóźwiak S, Sadowski K, Borkowska J, et al. Liver angiomyolipomas in tuberous sclerosis complex-their incidence and course. *Pediatr Neurol*. 2018;78:20-26. doi:10.1016/j.pediatrneurol.2017.09.012
- Ding G-H, Liu Y, Wu M-C, et al. Diagnosis and treatment of hepatic angiomyolipoma. *J Surg Oncol*. 2011;103(8):807-812. doi:10.1002/jso.21814
- Kim SH, Kang TW, Lim K, et al. A case of ruptured hepatic angiomyolipoma in a young male. *Clin Mol Hepatol*. 2017;23(2):179-183. doi:10.3350/cmh.2016.0027
- Calame P, Tyrode G, Weil Verhoeven D, et al. Clinical characteristics and outcomes of patients with hepatic angiomyolipoma: a literature review. *World J Gastroenterol*. 2021;27(19):2299-2311. doi:10.3748/wjg.v27.i19.2299
- Kim JY, Song JS, Park H, et al. Primary mesenchymal tumors of the pancreas: single-center experience over 16 years. *Pancreas*. 2014;43(6):959-968. doi:10.1097/MPA.0000000000000130
- Kim HH, Park DH. Imaging findings of primary angiomyolipoma of the pancreas: a case report. *J Korean Soc Radiol*. 2017;77(1):9. doi:10.3348/jksr.2017.77.1.9

- 32) Zhang JQ, Fielding JR, Zou KH. Etiology of spontaneous perirenal hemorrhage: a meta-analysis. *J Urol.* 2002;167(4):1593-1596. doi:10.1097/00005392-200204000-00006
- 33) Moratalla MB. Wunderlich's syndrome due to spontaneous rupture of large bilateral angiomyolipomas. *Emerg Med J.* 2009;26(1):72. doi:10.1136/emj.2008.062091
- 34) Sampson JR, Maheshwar MM, Aspinwall R, et al. Renal cystic disease in tuberous sclerosis: role of the polycystic kidney disease 1 gene. *Am J Hum Genet.* 1997;61(4):843-851. doi:10.1086/514888
- 35) Dixon BP, Hulbert JC, Bissler JJ. Tuberous sclerosis complex renal disease. *Nephron Exp Nephrol.* 2011;138(3):e15-e20. doi:10.1016/S0022-5347(17)43234-4
- 36) Bernstein J, Robbins TO. Renal involvement in tuberous sclerosis. *Ann N Y Acad Sci.* 1991;615:36-49. doi:10.1111/j.1749-6632.1991.tb37746.x
- 37) Bjornsson J, Short MP, Kwiatkowski DJ, Henske EP. Tuberous sclerosis-associated renal cell carcinoma. clinical, pathological, and genetic features. *Am J Pathol.* 1996;149(4):1201-1208.
- 38) Crino PB, Nathanson KL, Henske EP. The tuberous sclerosis complex. *N Engl J Med.* 2006;355(13):1345-1356. doi:10.1056/NEJMr055323
- 39) Stillwell TJ, Gomez MR, Kelalis PP. Renal lesions in tuberous sclerosis. *J Urol.* 1987;138(3):477-481. doi:10.1016/s0022-5347(17)43234-4
- 40) von Ranke FM, Faria IM, Zanetti G, et al. Imaging of tuberous sclerosis complex: a pictorial review. *Radiol Bras.* 2017;50(1):48-54. doi:10.1590/0100-3984.2016.0020
- 41) Northrup H, Aronow ME, Bebin EM, et al. Updated international tuberous sclerosis complex diagnostic criteria and surveillance and management recommendations. *Pediatr Neurol.* 2021;123:50-66. doi:10.1016/j.pediatrneurol.2021.07.011
- 42) Hinton RB, Prakash A, Romp RL, et al. Cardiovascular manifestations of tuberous sclerosis complex and summary of the revised diagnostic criteria and surveillance and management recommendations from the international tuberous sclerosis consensus group. *J Am Heart Assoc.* 2014;3(6):e001493. doi:10.1161/JAHA.114.001493
- 43) Gupta N, Henske EP. Pulmonary manifestations in tuberous sclerosis complex. *Am J Med Genet C Semin Med Genet.* 2018;178(3):326-337. doi:10.1002/ajmg.c.31638
- 44) Harari S, Torre O, Moss J. Lymphangioleiomyomatosis: what do we know and what are we looking for? *Eur Respir Rev.* 2011;20(119):34-44. doi:10.1183/09059180.00011010
- 45) McCarthy C, Gupta N, Johnson SR, Yu JJ, McCormack FX. Lymphangioleiomyomatosis: pathogenesis, clinical features, diagnosis, and management. *Lancet Respir Med.* 2021;9(11):1313-1327. doi:10.1016/S2213-2600(21)00228-9
- 46) Avila NA, Dwyer AJ, Rabel A, Moss J. Sporadic lymphangioleiomyomatosis and tuberous sclerosis complex with lymphangioleiomyomatosis: comparison of CT features. *Radiology.* 2007;242(1):277-285. doi:10.1148/radiol.2421051767
- 47) Costello LC, Hartman TE, Ryu JH. High frequency of pulmonary lymphangioleiomyomatosis in women with tuberous sclerosis complex. *Mayo Clin Proc.* 2000;75(6):591-594. doi:10.4065/75.6.591
- 48) Johnson SR, Cordier JF, Lazor R, et al. European respiratory society guidelines for the diagnosis and management of lymphangioleiomyomatosis. *Eur Respir J.* 2010;35(1):14-26. doi:10.1183/09031936.00076209
- 49) Rebaine Y, Nasser M, Girerd B, Leroux C, Cottin V. Tuberous sclerosis complex for the pulmonologist. *Eur Respir Rev.* 2021;30(161):200348. doi:10.1183/16000617.0348-2020
- 50) Lenfant C, Dragean CA. Retroperitoneal lymphatic malformations as first presentation of lymphangioleiomyomatosis. *J Belg Soc Radiol.* 2021;105(1):32. doi:10.5334/jbsr.2468
- 51) Pannu BS, Apala DR, Kotecha A, Boland JM, Iyer VN. Multifocal Micronodular Pneumocyte Hyperplasia (MMPH) in a patient with tuberous sclerosis-evidence for long term stability. *Respir Med Case Rep.* 2017;20:113-115. doi:10.1016/j.rmcr.2017.01.010
- 52) Boronat S, Barber I, Thiele EA. Sclerotic bone lesions in tuberous sclerosis complex: a genotype-phenotype study. *Am J Med Genet A.* 2017;173(7):1891-1895. doi:10.1002/ajmg.a.38260
- 53) Tung HE, Shih SL. Tuberous sclerosis with rare presentation of macrodactyly. *Pediatr Radiol.* 2009;39(8):878. doi:10.1007/s00247-009-1195-8
- 54) Thway K, Fisher C. PEComa: morphology and genetics of a complex tumor family. *Ann Diagn Pathol.* 2015;19(5):359-368. doi:10.1016/j.anndiagpath.2015.06.003
- 55) Gadducci A, Zannoni GF. Perivascular epithelioid cell tumors (pecoma) of the female genital tract: a challenging question for gynaecologic oncologist and pathologist. *Gynecol Oncol Rep.* 2020;33:100603. doi:10.1016/j.gore.2020.100603
- 56) Agaram NP, Sung Y-S, Zhang L, et al. Dichotomy of genetic abnormalities in pecomas with therapeutic implications. *Am J Surg Pathol.* 2015;39(6):813-825. doi:10.1097/PAS.0000000000000389
- 57) Benson C, Vitfell-Rasmussen J, Maruzzo M, et al. A retrospective study of patients with malignant pecoma receiving treatment with sirolimus or temsirolimus: the royal marsden hospital experience. *Anticancer Res.* 2014;34(7):3663-3668.
- 58) Sun L, Sun X, Li Y, Xing L. The role of (18)F-FDG PET/CT imaging in patient with malignant pecoma treated with mtor inhibitor. *Onco Targets Ther.* 2015;8:1967-1970. doi:10.2147/OTT.S85444
- 59) Mowrey K, Northrup H, Rougeau P, et al. Frequency, progression, and current management: report of 16 new cases of nonfunctional pancreatic neuroendocrine tumors in tuberous sclerosis complex and comparison with previous reports. *Front Neurol.* 2021;12:627672. doi:10.3389/fneur.2021.627672

VR Eases Patient Anxiety in Diagnostic and Interventional Radiology

Kerri Reeves

Kerri Reeves is a contributing writer based in Ambler, Pennsylvania.

Innovative applications of digital therapeutics are changing healthcare delivery in numerous ways, from streamlining provider diagnoses to improving patient care experiences. In the pediatric setting, virtual reality (VR) is being leveraged to make radiology procedures less daunting for patients, and, in some cases, reduce or altogether eliminate procedural sedation.

“There are use cases where the benefits [of VR] are profound. In IR [interventional radiology], a lot of the cases [create] this... level of stimulation that is sometimes more anxiety provoking than it is painful. ... You can get kids—and adults—through these procedures with just a good distraction technology like virtual reality,” says Samuel Rodriguez, MD, pediatric anesthesiologist at Stanford Children’s Hospital and clinical professor of anesthesia at Stanford School of Medicine in Palo Alto, California.

“The research has been clear that virtual reality technologies belong in the medical setting as a way to improve patient experiences by reducing pain and anxiety associated with procedural services,” says Joseph Miller, MD, MSHA, MS, CIRCC, associate professor of radiology, interventional radiology, at Children’s Hospital Los Angeles (CHLA).

Both California-based institutions are pioneering clinical programs that use VR before and during IR-based procedures to reduce sedation or, when feasible, completely replace it. The category III CPT codes for VR procedural dissociation (0771T-0774T), approved in 2023 by the American Medical Association, enable use of

“computer-generated VR audiovisual environments to modify a patient’s perception of pain.”

Building on VR’s existing applications in medical imaging modalities such as MRI, PET/CT, and radiography, this nonpharmacological intervention in IR offers new opportunities to improve patient care experiences.

Interventional-Specific Applications

At CHLA in the IR suite, VR is being used as an alternative to sedation in patients undergoing procedures such as lumbar puncture, tunneled catheter placement/removal, peripherally inserted central catheter placement, arthrography, thyroid fine needle aspiration, thoracentesis/paracentesis, and soft tissue fluid aspiration/biopsy, according to Dr Miller.

“We recognized that we had a significant population of patients who needed something more than simple anxiolysis, but less than general anesthesia, and [found] that virtual reality dissociation could fill that gap,” Dr Miller says.

For some sick patients who require lumbar punctures at Stanford Children’s, agrees Dr Rodriguez, VR offers a solid replacement for anesthesia.

Typically, “we use VR to avoid side effects from anesthesia,” such as nausea and vomiting, says Rodriguez. “Sometimes there are dangers of giving the anesthetic to very sick kids, so we [try to] spare them some of the risk by doing [the procedure] while awake, playing a video game with VR” as a distraction.

In the pediatric setting, VR is being leveraged to make radiology procedures less daunting for patients possibly reducing or eliminating procedural sedation.



Another example is anterior mediastinal mass biopsy owing to the risk of respiratory or cardiovascular collapse, Dr Rodriguez explains.

“The mass is in such a bad area ... the front part of the mediastinum ... that giving the sedation is dangerous—more dangerous than the procedure itself. In the past, we’d have to do it with the [child] totally awake getting needles stuck into their chest over and over,” he explains. “Now we have a situation where they can be playing a video game or watching a movie with a VR headset to relieve a lot of the anxiety and stress and some of the pain around having a procedure like that.”

Use of nontraditional, technology-based tools such as VR requires less preparation and results in faster recovery compared with pharmacological interventions. In cases where VR replaces sedation or general anesthesia, fasting is not required, and the families can usually leave the hospital soon after the procedure without the typical sedation side effects, such as drowsiness, dizziness, and confusion, that require a postprocedural monitoring unit and qualified personnel.

“The response has been very positive, and [soon], we’ll likely offer VR for higher-volume procedures such as simple sclerotherapies for venolymphatic malformations,” Dr Miller says. “It also frees up our anesthesia resources for other patients.”

Technology and Support

Stanford Children’s VR use extends beyond its IR suite, part of broader research under the Chariot Program—founded and co-directed by Dr Rodriguez—which applies technologies, including augmented reality, interactive video games, and VR to treat pediatric pain and stress. The program enables departments to call for VR consults and help successfully complete hospital procedures like blood draws or peripheral intravenous catheter insertions, as well as outpatient services such as physical therapy delivery. Interfacing with headsets, tablets, and projectors, Stanford Medicine’s custom-built VR software creates unique passthrough or completely immersive experiences.

“Our research assistants and coordinators work closely with physicians, child life specialists, radiology technologists, PTs, and volunteers They all give input [so we can] provide custom software to adapt to the needs of [various] clinical situations,” says Dr Rodriguez, who helps distribute the software at no cost to interested institutions through the organization Invincikids.

As with many new applications gaining clinical ground, philanthropy plays a role in VR’s wider adoption. At CHLA, the nonprofit Child’s Play

Global Research Updates on VR in Radiology

Researchers across the globe are studying the impact of VR on adult radiology patients. One study examines the benefits of using VR and 360° environments—utilizing 360° panoramic images and nonimmersive technology to provide patients with virtual access to medical facilities and information before coronary CT angiography (CCTA)—to quell anxiety.¹ It shows that visual familiarity and education enhance patients' preparedness and understanding of CCTA, improving their experience during the procedure.

"[The researchers] designed a novel, 360° virtual counselling environment for CCTA patients, which was well accepted...and reported to improve [the patient's] knowledge about the procedure, increase the patient's senses of security and self-efficacy, and reduce anxiety," the authors report.¹

A *Journal of Vascular and Interventional Radiology* study examined VR's effect on pain reduction during interventional radiology procedures.² Seeking an effective nonpharmacological method of sedation, Philadelphia-based researchers from Temple University Hospital and The Lewis Katz School of Medicine analyzed the analgesic and anxiolytic effects of a VR experience in the setting. They found that "digital sedation" yielded statistically significant reductions in anxiety, heart rate, and systolic blood pressure among participants, with no adverse effects.

Similarly, French researchers evaluated the tolerance and feasibility of using VR headsets with patients during interventional radiology procedures, finding that "the use of VR technology as a complement to traditional therapy for procedures under local anesthesia is feasible and safe in interventional radiology and can be beneficial for pain and anxiety management."³

Charity, which delivers therapeutic games and technology to pediatric hospitals, supported the creation of a dedicated VR technologist position to facilitate effective use of VR in clinical practice.

"Just as a clinician shouldn't have to split their attention between performing a procedure and personally administering medications VR dissociation has worked best for us when someone ... ensures the quality of the patient's VR experience," explains Dr Miller, noting the technologist works collaboratively with child life specialists. "It's not just a tablet playing a video to distract them. Like a sedation nurse, a VR tech monitors the patient and observes their interactions with the virtual world to make sure they are comfortable and dissociated."

At CHLA, VR technologist Phoenix Hunt, who has a BFA in immersive reality, tests the hardware and software and manages the patients' active use of the solutions based on user age, clinical procedure type, and level of anxiety to optimize VR's relaxing effects.

"It's critical to see firsthand what the patient experiences in the headset so I can anticipate [their] reactions and provide better care," says Hunt.

CHLA's IR department is working to establish clinical practice protocols internally before offering VR dissociation services to the wider hospital.

"It is a challenge ... to scale [it] beyond just a division within a hospital. Very few places have programs like ours that span multiple departments and specialties," Dr Rodriguez says.

"It's difficult to just buy a headset off the shelf and implement VR dissociation in your practice—not because of any lack in the technology, but because of a lack of experience in utilizing it in the various circumstances of a modern clinical practice," Dr Miller says.

"VR will not be a part of every medical procedure," he concludes. "But for the kinds of procedures that are most common in both diagnostic and interventional radiology practices, the clear benefits of this technology should ensure a healthy role for VR dissociation in the future."

References

- 1) Paalimäki-Paakki K, Virtanen M, Henner A, et al. Effects of a 360° virtual counselling environment on patient anxiety and CCTA process time: a randomised controlled trial. *Radiography*. 2023;29 Suppl 1:S13-S23. doi:10.1016/j.radi.2022.09.013
- 2) Schaake R, Leopold I, Sandberg A, et al. Virtual reality for the management of pain and anxiety for IR procedures: a prospective, randomized, pilot study on digital sedation. *J Vasc Interv Radiol*. 2024;35(6):825-833. doi:10.1016/j.jvir.2024.03.004
- 3) Grange L, Grange R, Bertholon S, et al. Virtual reality for interventional radiology patients: a preliminary study. *Support Care Cancer*. 2024;32(7):416. doi:10.1007/s00520-024-08621-0

Advancing Global Radiological Services: An Academic Medical Center Offers 5 Core Strategies

Joseph Weygand, PhD; Charles R. Thomas Jr., MD

It is estimated that between one-half and two-thirds of the world's population lack access to basic imaging services,¹ reflecting one of the most marked disparities in global healthcare. Nowhere is this more evident than in many low- and middle-income countries (LMICs), where radiology infrastructure and human resources remain critically limited. In Tanzania, for example, the number of practicing interventional radiologists was recently reported as zero, underscoring the depth of the workforce gap. By contrast, in high-income nations, radiologist-to-population ratios can exceed 100 per million people.² This disparity illustrates the scale of the global radiology divide and the urgent need for sustainable strategies to expand access.

Compounding these shortages are barriers such as inadequate infrastructure, limited imaging equipment, and insufficient training.³ These gaps can delay critical diagnoses, exacerbate preventable illnesses, and contribute to avoidable deaths.

Similar challenges face radiation oncology. Cancer remains the second leading cause of death worldwide.⁴ By 2030, most cancer deaths are expected to occur in LMICs,⁵ where access to radiation therapy remains severely limited. Indeed, more than 90% of low-income country populations lack basic radiation therapy services.⁶

Addressing these inequities requires a global commitment and coordinated strategies across multiple organizations and disciplines. They include governments, intergovernmental organizations such as the World Health Organization and the International Atomic Energy Agency, nongovernmental organizations (NGOs) like RAD-AID International, and medical societies such as the Radiological Society of North America (RSNA) and the

American Society for Radiation Oncology (ASTRO).

Five Core Strategies

Recognizing the urgency of this challenge, Dartmouth Health has established the Division of Global Radiation Oncology (DGRO). An initiative dedicated to the principle that all nations deserve high-quality radiological services, the DGRO leverages 5 core pillars: implementation science, clinical training, virtual education, community engagement, and analysis of determinants of global health (Figure 1).

Implementation Science

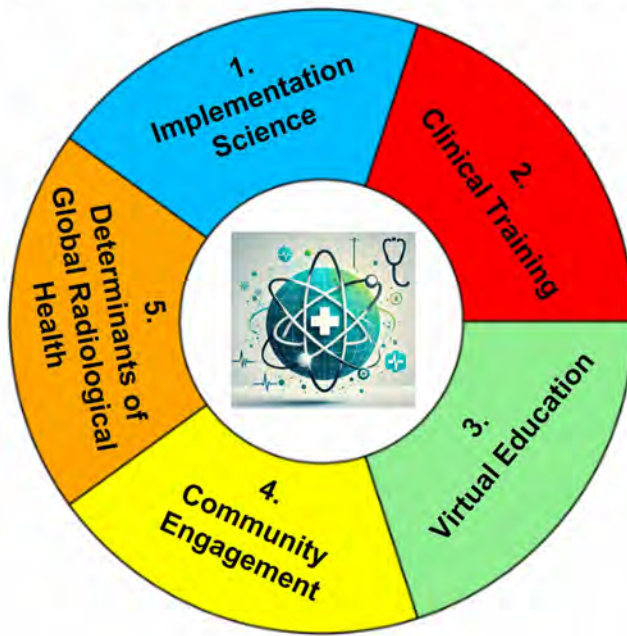
Leveraging evidence-based strategies to introduce and optimize advanced technologies and practices in resource-limited settings is foundational to the DGRO's efforts. As fundamentally technology-driven fields, Radiology and Radiation Oncology rely on sophisticated equipment and expertise to deliver effective care. The goal, however, is not merely

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Figure 1. Schematic drawing illustrating a 5-pronged framework for advancing global radiological services by leveraging 5 key pillars: implementation science, on-site clinical training outreach, virtual didactic education, community engagement, and the study of determinants shaping global health.

5 Core Principles of Advancing Global Radiological Health



to bring technology to LMICs but to develop sustainable systems that enhance care and empower local healthcare providers. This helps ensure that technologies are appropriately integrated to meet the unique needs of each setting.

Optimizing imaging protocols is one example of how implementation science can help achieve these goals in both specialties. Tailoring workflows to a given institution's needs can enhance image quality, mitigate geometric uncertainties, and ensure more accurate diagnoses and treatment planning. Another example is customizing hypofractionated radiation therapy protocols to reduce the number of treatment sessions, thereby improving patient throughput without compromising care quality.

Together, these efforts illustrate how implementation science can harmonize radiology and radiation oncology to deliver meaningful, worldwide reductions in radiological disparities.

Clinical Training

Improving clinical training is a second important strategy. Building radiological capacity in LMICs depends not just on the availability of technology but also on the expertise of the professionals using it. During our trips to underserved LMICs, we have witnessed how much sophisticated equipment goes unused or abandoned due to inadequate clinical training.

Training can take many forms. These include sending clinical teams to provide hands-on training with partner institutions in LMICs and, in our case, hosting

observerships at Dartmouth Health. By focusing on practical techniques and workflows, these initiatives foster skills development for radiologists, radiation oncologists, medical physicists, and other support personnel.

For example, technologists can be taught how to optimize protocols to improve diagnostic accuracy; medical physicists can be taught to refine their quality assurance practices to ensure safe equipment operation. These exchanges enhance individual expertise, strengthen institutional capacity, and help local teams sustain high-quality patient care.

We believe that clinical training outreach achieves its greatest impact when it goes beyond one-time, short-term engagements and focuses on building long-term relationships. Dartmouth Health, for example, collaborates with local institutions to hold regularly scheduled case discussions, conduct technical troubleshooting, exchange ideas, and even develop mentorship programs.

These measures offer local practitioners a trusted resource for guidance and support as they navigate complex cases or implement new practices. Equally valuable, ongoing relationships like this help cultivate a sense of community and alleviate the isolation that many clinicians in LMICs feel because of the reduced availability of peer networks in their regions.

Virtual Education

Offering virtual didactic education comprises the third of DRGO's strategies. LMICs face critical deficits in radiology and radiation oncology personnel. According to some estimates, the number of radiation oncologists must increase more than 20-fold to meet global radiation

therapy needs by 2030.⁷ Similarly, the demand for radiologists, medical physicists, and imaging technologists far exceeds the capacity of current training programs, leaving resource-limited regions struggling to sustain essential medical imaging services. As it allows for the delivery of high-quality training without requiring travel or costly infrastructure, virtual education offers a promising and accessible solution.

To this end, Dartmouth faculty are leading web-based initiatives tailored to the educational needs of radiology and radiation oncology professionals. These include a continuing lecture series on topics ranging from the principles of imaging modalities to advanced radiation therapy techniques.

Other online initiatives have included an MRI course for medical physicists in Turkey, a curriculum for radiation oncology residents in Kenya, and a lecture series for radiology residents in Guyana. Our faculty have also directed practical treatment planning workshops for physicists and dosimetrists and taught online courses on hypofractionated radiation therapy for specialists across sub-Saharan Africa.

Community Engagement

This fourth of the 5 core pillars emphasizes integrating radiology professionals into the broader healthcare community. Methods for achieving this goal include conference presentations, publishing research focused on global healthcare issues, and hosting forums for professionals to share their experiences at the international level.

The importance of global community engagement cannot be overstated. The wider healthcare

community has already developed innovative frameworks for building clinical capacity, expanding infrastructure, delivering education, and scaling care in resource-limited settings. For example, collaborations between governments and NGOs have supported the deployment of radiation therapy equipment, the establishment of national cancer treatment guidelines, and the training of technologists and clinicians to implement those services safely. These kinds of interventions can inform radiology's efforts² and help prevent duplication by offering tested models for equitable partnership, locally adapted solutions, and long-term sustainability.

Engaging with RSNA, ASTRO, and other professional groups is equally important. These groups provide platforms for advocacy, collaboration, and education to help integrate the priorities of the radiology and radiation oncology communities with those of global healthcare organizations.⁸ Non-governmental organizations such as RAD-AID International, Radiating Hope, and Rayos Contra Cancer can help translate these priorities into action through capacity-building programs and sustainable interventions in which technology or expertise is introduced into clinics in LMICs. Indeed, fostering community engagement underscores the importance of replacing professional and specialty silos with collaboration to ensure that improving the health of people around the world becomes an integral part of the mission of the radiology community.

Determinants of Global Health

The goal of examining the determinants of global health, our fifth core pillar, is to direct

more effective and sustainable outreach initiatives. Inequities in access to radiological services are shaped by a web of economic, geographic, historical, political, and cultural factors.⁹ Although they fall outside the scope of radiology professionals, these factors directly influence the success of healthcare efforts. Broadening their understanding of these determinants allows institutions to move beyond surface-level solutions to address the deeper causes of inequities.¹⁰

However, this requires a willingness to engage with specialists outside of radiology and radiation oncology, including experts in the social sciences, public policy, health diplomacy, and international development. By embracing this multidisciplinary approach, institutions can create more informed strategies to drive meaningful, lasting access to medical imaging and radiation oncology services.

Conclusion

Nearly 4 billion people currently lack access to basic imaging services.¹ The magnitude of this disparity represents an opportunity for the radiology community not just to greatly expand the reach of its services but also to help improve healthcare equity on a potentially unprecedented scale.

We believe the strategic framework outlined here, based on the principle that people of every nation deserve equal access to high-quality healthcare, can help achieve both of these goals.

Ultimately, this is not just about meeting a challenge. It is a moral imperative—one that demands vision, collaboration, and sustained action by the entire healthcare community. Through

commitment and innovation, the radiology community has the capacity to profoundly reshape global healthcare and create a future where equitable access to care is a reality for all.

REFERENCES

- 1) Ngoya PS, Muhogora WE, Pitcher RD. Defining the diagnostic divide: an analysis of registered radiological equipment resources in a low-income African Country. *Pan Afr Med J.* 2016;25:99. doi:10.11604/pamj.2016.25.99.9736
- 2) McKenney AS, Garg T, Kim E, Kesselman A. Addressing global radiology disparities: increasing access to interventional radiology education. *Radiographics.* 2021;41(5):E142-E144. doi:10.1148/rg.2021210176
- 3) Jalloul M, Miranda-Schaeubinger M, Noor AM, et al. MRI scarcity in low- and middle-income countries. *NMR Biomed.* 2023;36(12):e5022. doi:10.1002/nbm.5022
- 4) Wang H, Naghavi M, Allen C. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the global burden of disease study 2015. *Lancet.* 2016;388(10053):1459-1544. doi:10.1016/S0140-6736(16)31012-1
- 5) Bray F, Jemal A, Grey N, Ferlay J, Forman D. Global cancer transitions according to the human development index (2008-2030): a population-based study. *Lancet Oncol.* 2012;13(8):790-801. doi:10.1016/S1470-2045(12)70211-5
- 6) Zubizarreta EH, Fidarova E, Healy B, Rosenblatt E. Need for radiotherapy in low and middle income countries – the silent crisis continues. *Clin Oncol.* 2015;27(2):107-114. doi:10.1016/j.clon.2014.10.006
- 7) Elmore SNC, Prajogi GB, Rubio JAP, Zubizarreta E. The global radiation oncology workforce in 2030: estimating physician training needs and proposing solutions to scale up capacity in low- and middle-income countries. *ARO.* 2019;8:10-16. doi:10.37549/ARO1193
- 8) Lief E, Weygand J, Parker SA, et al. Global representatives' initiative of the American Association of Physicists in Medicine. *Med Phys Int.* 2023;11:16.
- 9) Parker SA, Weygand J, Bernat BG, et al. Assessing radiology and radiation therapy needs for cancer care in low-and-middle-income countries: insight from a global survey of departmental and institutional leaders. *Adv Radiat Oncol.* 2024;9(11):101615. doi:10.1016/j.adro.2024.101615
- 10) Acemoglu D, Johnson S, Robinson JA. The colonial origins of comparative development: an empirical investigation. *Am Econ Rev.* 2001;91(5):1369-1401. doi:10.1257/aer.91.5.1369

How AI Is Empowering Radiologists to Transform Cardiac Health Care

Orit Wimpfheimer, MD

People think of diagnostic radiology as a specialty where physicians provide insights about specific diseases or conditions from behind the walls of a darkroom. Often, they neglect to connect the impact of our field to improvements across the broader health care landscape.

For decades, radiology has been at the forefront of some of the most significant changes in medicine. In the acute care setting, for example, advances in imaging technologies such as CT, MRI, PET, and ultrasound have improved acute care by aiding the detection of conditions such as appendicitis, aortic dissection, and stroke, in addition to ‘what aches us,’ from broken bones to kidney stones.

Among the more notable contributions of our field are imaging-based screening programs. Early breast cancer detection, made possible through screening mammography, has reduced breast cancer mortality by 15–30% in women aged 40–74, depending on the frequency and starting age of screening.¹ Studies have shown that low-dose chest CT has reduced mortality from lung cancer significantly, with a 20% reduction

in the NLST and 24% in NELSON.^{2,3} Additionally, screening men aged <65 with ultrasound for abdominal aortic aneurysm has been shown to reduce rupture-related death by up to 50%.⁴

Chronic Conditions: A New Frontier for Radiology?

While imaging has enabled the early and accurate diagnosis of numerous conditions for more than a century, with an immeasurable impact on global health, the field has yet to make inroads as significantly in the early detection of major chronic health conditions. According to the CDC, an estimated 129 million people in the United States have at least 1 major chronic disease (eg, heart disease, cancer, diabetes, obesity, and hypertension). Five of the 10 leading causes of death in the US are, or are strongly associated with, preventable and treatable chronic diseases.⁵ The prevalence of these conditions has increased steadily over the past two decades, and the trend is expected to continue.⁵

More than 944,800 Americans die of heart disease or stroke every year—that is more than 1 in 3 deaths. In addition to the toll that it takes on personal health, chronic disease costs the United States healthcare system \$254 billion per year and results in an estimated

\$168 billion in lost wages. Costs related to cardiovascular diseases are projected to hit roughly \$2 trillion annually by 2050.⁶

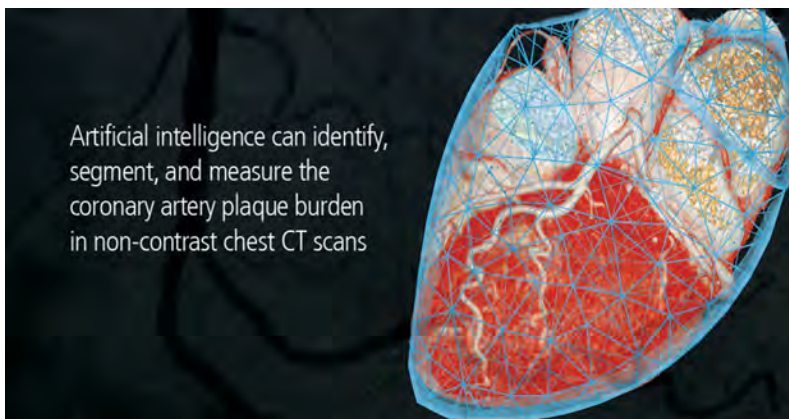
An Opportunity to Impact Cardiovascular Disease

Radiology, as a specialty, is in a prime position to reduce deaths resulting from the most prevalent chronic health condition: cardiovascular disease. It is well known in the cardiology literature that coronary artery calcium burden is the leading predictor of a cardiovascular event.^{7,8}

Calcium can be seen on non-contrast chest CT scans, including the lower-dose scans performed for lung cancer screening. While some radiologists will note the presence of coronary artery calcium in their evaluations, few will quantify the amount.⁹ The practice of “eyeballing” the degree of calcified plaque is subjective and not standardized, often rendering the radiology report less effective than it could be for making the diagnosis of cardiovascular disease and determining the extent. Therefore, the referring physician may not appreciate the actionable insights from the report. This is an unfortunate, missed opportunity.

Artificial intelligence can identify, segment, and measure the coronary

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artery calcium burden in non-contrast chest CTs, enabling radiologists to quantitatively diagnose and assess cardiovascular disease burden based on coronary artery calcium scoring and Agatston category. Several FDA-approved algorithms are commercially available in the United States and European Union. Recent findings have shown that 49% of individuals undergoing chest CT have moderate (100–399) or high (>400) Agatston units of coronary artery calcium,¹⁰ and 64% of those with detected plaque had no prior diagnosis of cardiovascular disease.¹¹

Consider the potential impact of identifying coronary artery calcium burden in the chest CTs of patients seen for other indications. Radiologists could trigger a preventive health pathway for these patients that includes lifestyle changes, such as diet and exercise, and a potential prescription for statins, which decrease the rate of a cardiovascular event by 25%.¹²

With the seamless integration of advanced AI systems into the radiology workspace, radiologists can significantly contribute to identifying patients at high risk

of cardiovascular events with minimal disruption to the radiology workflow. There will, however, be newly added patient information directed to primary care and related subspecialties, which could result in more work, but that should translate into improved patient care and, potentially, to improved long-term outcomes. As these technologies become more widely available, radiologists will increasingly play a pivotal role in preventive health care, shaping better health outcomes worldwide.

REFERENCES

- 1) US Preventative Services Task Force. Final Recommendation Statement, Breast Cancer: Screening. 2025. Accessed April 24, 2025. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening>
- 2) The national lung screening trial research team: reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med*. 2011;365:395-409. doi:10.1056/NEJMoa1102873
- 3) de Koning HJ, van der Aalst CM, de Jong PA, et al. Reduced lung-cancer mortality with volume CT screening in a randomized trial. *N Engl J Med*. 2020;382(6):503-513. doi:10.1056/NEJMoa1911793
- 4) Ashton HA, Buxton MJ, Day NE, et al. The Multicentre Aneurysm Screening Study (MASS) into the effect of abdominal aortic aneurysm screening on mortality in men: a randomised controlled trial. *Lancet*. 2002;360(9345):1531-1539. doi:10.1016/S0140-6736(02)11522-4
- 5) Benavidez GA, Zahnd WE, Hung P, Eberth JM. Chronic disease prevalence in the US: sociodemographic and geographic variations by zip code tabulation area. *Prev Chronic Dis*. 2024;21:E14. doi:10.5888/pcd21.230267
- 6) Centers for Disease Control. Fast Facts: Health and Economic Costs of Chronic Conditions. 2025. Accessed April 24, 2025. <https://www.cdc.gov/chronic-disease/data-research/facts-stats/index.html>
- 7) Detrano R, Guerci AD, Carr JJ, et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med*. 2008;358(13):1336-1345. doi:10.1056/NEJMoa072100
- 8) Pletcher MJ, Tice JA, Pignone M, Browner WS. Using the coronary artery calcium score to predict coronary heart disease events: a systematic review and meta-analysis. *Arch Intern Med*. 2004;164(12):1285-1292. doi:10.1001/archinte.164.12.1285
- 9) Osborne-Grinter M, Ali A, Williams MC. Prevalence and clinical implications of coronary artery calcium scoring on non-gated thoracic computed tomography: a systematic review and meta-analysis. *Eur Radiol*. 2024;34(7):4459-4474. doi:10.1007/s00330-023-10439-z
- 10) Kerndt CC, Chopra R, Weber P, et al. Using artificial intelligence to semi-quantitate coronary calcium as an “incidentaloma” on non-gated, non-contrast CT scans, A single-center descriptive study in west michigan. *Spartan Med Res J*. 2023;8(1):89132. doi:10.51894/001c.89132
- 11) Kimmel Y, Kurek A, Wimpfheimer O, Shalem O, Langholz D. Optimizing preventive cardiology: harnessing AI for early detection of coronary artery disease. *Journal of Cardiovascular Computed Tomography*. 2024;18(4):S13. doi:10.1016/j.jcct.2024.05.030
- 12) Blaha MJ, DeFilippis AP. Multi-ethnic study of atherosclerosis (mesa). *J Am Coll Cardiol*. 2021;77(25):3195-3216. doi:10.1016/j.jacc.2021.05.006

Hemorrhagic Synovial Cyst

Patrick S. Chan, BS; John R. Bright, BS; Sangeeta Rao, MD; Katie C. Bailey, MD

Case Summary

An adult presented with a 10-day history of lower back pain following an episode of heavy lifting. Physical examination demonstrated pain radiating down the posterior left leg, accompanied by paresthesia in the medial thigh. This pain significantly affected the patient's mobility, but there was no bowel or bladder incontinence. Laboratory tests showed a supra-therapeutic international normalized ratio (INR) value of 4.03 due to coumadin treatment for a mechanical heart valve.

Imaging Findings

Lumbar spine MRI identified a 2.8 cm cyst with a hemorrhagic component at L4-L5, causing severe lumbar stenosis. Sagittal T1 (Figure 1) demonstrated hyperintense T1 signal, suggesting hemorrhagic or proteinaceous components. Sagittal T2 MRI revealed hypointense T2 signal. Axial imaging confirmed the hyperintense T1 signal and showed the lesion projecting medially from the left L4-L5 facet joint into the left dorsolateral epidural space.

Diagnosis

Hemorrhagic synovial cyst

Discussion

Synovial cysts are fluid-filled sacs that arise from a joint or tendon, often resulting from degenerative changes. When these cysts occur in the spine, they are typically associated with the facet joints. According to one retrospective cohort study, synovial facet cysts are found in approximately 6.5% of patients undergoing lumbar MRI.¹ Hemorrhagic synovial cysts are less common, reflecting only 10% of all synovial cysts.² Hemorrhagic cysts may be more clinically challenging owing to their often more acute symptomatology and association with more chronic degenerative spinal conditions.³

Spinal synovial cysts are encountered primarily in older individuals or in those with underlying spinal conditions such as spondylosis and spinal instability, which can result from degenerative changes or trauma. Clinically, patients typically present with lower back pain and lower extremity radiculopathy, which can be bilateral. This may sometimes lead to severe episodes resembling cauda equina syndrome.³ High-impact activities and certain sports such as tennis are linked to higher occurrence rates in younger populations, suggesting repetitive stress as a risk factor.⁴ Additionally, hemorrhagic

synovial cysts can arise secondary to anticoagulation therapy, underscoring an iatrogenic risk factor that is relevant to this case, in which the patient had a supra-therapeutic INR.⁵

A retrospective study of 303 lumbar MRI scans of patients referred for back pain and radiculopathy found posterior synovial cysts to be more common than anterior cysts, with a prevalence of 7.3% and 2.3%, respectively.⁶ Both types are associated with facet joint osteoarthritis and may be linked to degenerative spondylolisthesis, although no direct relationship with disc disease has been found. Anterior cysts can contribute to spinal stenosis and present with symptoms such as neurogenic claudication, whereas posterior cysts, located outside the canal, may be associated with back pain and radiculopathy but are less likely to cause claudication.⁷

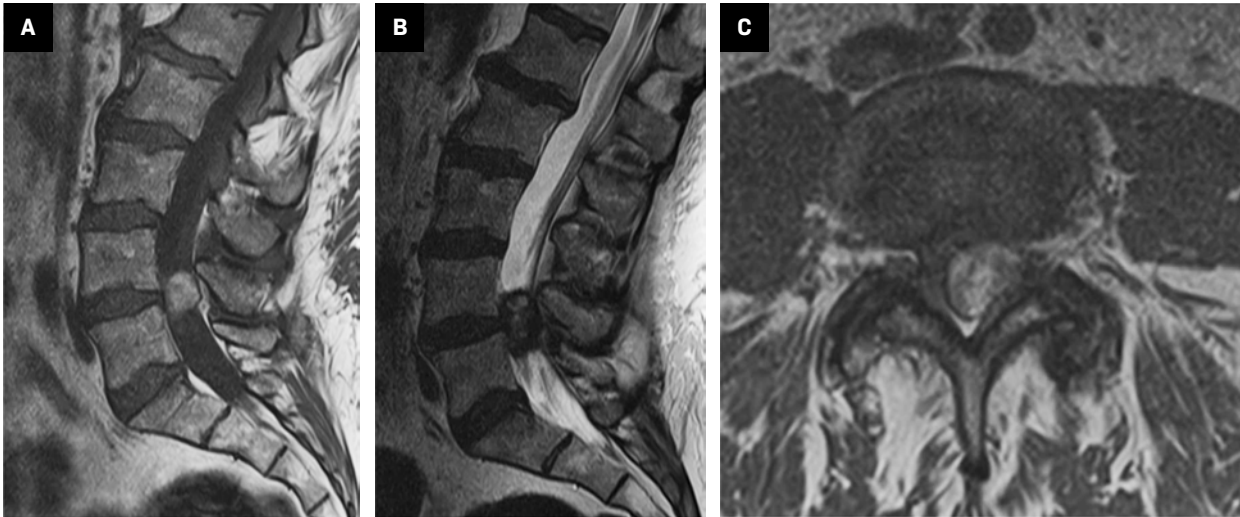
As seen in this case, synovial cysts manifest predominantly at the L4-L5 level, corresponding to this level's biomechanical stresses and load-bearing function.² MRI is the diagnostic modality of choice. Nonhemorrhagic cysts are typically T1 hypointense and T2 hyperintense. Hemorrhagic cysts are usually T1 hyperintense while T2 images may show varying intensities depending on protein content and age of hemorrhage within the cyst.^{2,3}

Treatment generally consists of surgical removal, particularly when conservative treatments fail or when cysts cause significant neurological

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Figure 1. MRI of lumbar spine without contrast. (A) Sagittal T1 image demonstrates the hyperintense T1 signal epidural mass at L4-L5. (B) Sagittal T2 image demonstrates the hypointense T2 signal epidural mass at L4-L5. (C) Axial T1 image demonstrates the hyperintense T1 signal mass projecting medially from the left facet joint in the left dorsolateral epidural space.



signs or symptoms. Specifically, cyst resection via laminectomy is a safe and effective management strategy for symptomatic relief. A retrospective analysis of 194 cases showed that fusion was rarely needed post-cyst resection. The postsurgical prognosis was very good, with 91% of patients reporting good pain relief and 82% showing improvement in motor deficits.⁸ A recent study discussed the efficacy of facet synovial cyst rupture under CT guidance, with the best success rates involving indirect percutaneous cyst rupture (IPCR) combined with direct fenestration in cases of IPCR failure.⁹

Conclusion

Presenting most commonly at the L4-L5 level, hemorrhagic synovial cysts of the lumbar spine pose a distinct clinical challenge.

Radiological imaging plays a pivotal role in diagnosis, and surgery remains the primary treatment strategy. Prognosis depends largely on individual patient characteristics and the presence of underlying spinal conditions.

References

- 1) Janssen SJ, Ogink PT, Schwab JH. The prevalence of incidental and symptomatic lumbar synovial facet cysts. *Clin Spine Surg.* 2018;31(5):E296-E301. doi:10.1097/BSD.0000000000000648
- 2) Lyons MK, Atkinson JL, Wharen RE, et al. Surgical evaluation and management of lumbar synovial cysts: the mayo clinic experience. *J Neurosurg.* 2000;93(1 suppl):53-57. doi:10.3171/spi.2000.93.1.0053
- 3) Cannarsa G, Clark SW, Chalouhi N, Zanaty M, Heller J. Hemorrhagic lumbar synovial cyst: case report and literature review. *Nagoya J Med Sci.* 2015;77(3):481-492.
- 4) Rajeswaran G, Turner M, Gissane C, Healy JC. MRI findings in the lumbar spines of asymptomatic elite junior tennis players. *Skeletal Radiol.* 2014;43(7):925-932. doi:10.1007/s00256-014-1862-1
- 5) Eck JC, Triantafyllou SJ. Hemorrhagic lumbar synovial facet cyst secondary to anticoagulation therapy. *Spine J.* 2005;5(4):451-453. doi:10.1016/j.spinee.2005.01.005
- 6) Doyle AJ, Merrilees M. Synovial cysts of the lumbar facet joints in a symptomatic population: prevalence on magnetic resonance imaging. *Spine.* 1976;29(8):874-878. doi:10.1097/00007632-200404150-00010
- 7) Khan AM, Girardi F. Spinal lumbar synovial cysts. diagnosis and management challenge. *Eur Spine J.* 2006;15(8):1176-1182. doi:10.1007/s00586-005-0009-4
- 8) Ramieri A, Domenicucci M, Seferi A, et al. Lumbar hemorrhagic synovial cysts: diagnosis, pathogenesis, and treatment: report of 3 cases. *Surg Neurol.* 2006;65(4):385-390. doi:10.1016/j.surneu.2005.07.073
- 9) Yang AY, Hutchins TA, Shah LM, et al. CT-guided indirect percutaneous facet synovial cyst rupture combined with direct fenestration: 10-year review at a single institution. *Interv Pain Med.* 2024;3(4):100447. doi:10.1016/j.inpm.2024.100447

Navajo Neurohepatopathy

Kathryn A. Szymanski, BS; Karis Houser; Michael S. Kuwabara, MD

Case Summary

A Native American infant initially presented with increased abdominal girth and a tense abdomen. Laboratory abnormalities included elevated bilirubin. An ultrasound and liver biopsy were performed. Pathology noted decreased mitochondrial quantity, large and numerous lysosomal granules, microvesicular steatosis, and bile canaliculi distention. The patient was referred for genetic testing.

In childhood, the patient represented with new-onset ascites. Electroencephalography (EEG) and brain MRI were performed due to agitation and a decline in mental status.

Imaging Findings

The patient underwent serial ultrasound examinations. The initial scans were normal, while the last demonstrated a cirrhotic liver with multiple nodules and ascites. A subsequent MRI examination of the abdomen with liver elastography

demonstrated numerous subcentimeter-sized hepatic nodules, most compatible with regenerative nodules, and increased mean liver stiffness (6.03 kPa), consistent with cirrhosis (in children aged 3–5 years, the mean is ~3.7, and the 75th percentile is ~3.9).¹

Altered mental status prompted an EEG and brain MRI. The EEG showed left hemispheric abnormalities, including continuous diffuse polymorphic delta slowing and continuous mild voltage attenuation. The MRI demonstrated bilateral white matter T2 hyperintensity, diffusion restriction, and bilateral multifocal periventricular heterotopic gray matter of unknown significance, although gray matter heterotopia is associated with a wide range of neurodevelopmental disorders (Figure 1). A follow-up brain MRI several months later demonstrated a worsening abnormal white matter signal throughout the supratentorial brain and cerebellum with associated diffuse restriction, as well as slight ventricular enlargement commensurate with the degree of parenchymal atrophy (Figure 2).

Diagnosis

Navajo neurohepatopathy.

Differential diagnoses that may be considered include idiopathic neonatal hepatitis, biliary atresia,

and metabolic liver diseases caused by enzyme defects, such as tyrosinemia, galactosemia, Wilson's disease, glycogen storage disorders, and lysosomal storage disorders, among others.

Discussion

Navajo neurohepatopathy (NNH) is a rare autosomal recessive mtDNA depletion syndrome (MDS) presenting in children of Navajo descent and primarily affecting the liver and nervous system.^{2,3} The estimated incidence of the disease in the western Navajo Reservation is 1 in 1,600 live births.⁴ The cause of NNH is an R50Q mutation of the nuclear *MPV17* gene that encodes an inner mitochondrial membrane protein thought to participate in mtDNA maintenance, which is necessary for normal cellular energy production.²

The average age at onset for NNH is 13 months; patients often do not survive past the first decade of life.⁵ Clinical features include liver disease, sensory and motor neuropathy, failure to thrive, corneal anesthesia and scarring, central nervous system demyelination, and recurrent metabolic acidosis, along with other concurrent illnesses.^{4,5} Based on the diagnostic criteria of Holve et al,⁴ NNH may be diagnosed with confidence if four of the criteria listed above are present or if three

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Figure 1. Brain MRI. Axial T2 (A) showing bilateral white matter T2 hyperintensities (orange arrowheads) and bilateral periventricular heterotopic gray matter foci (green arrowheads), and axial diffusion-weighted imaging (DWI) (B) showing foci of diffusion restriction (orange arrowheads).

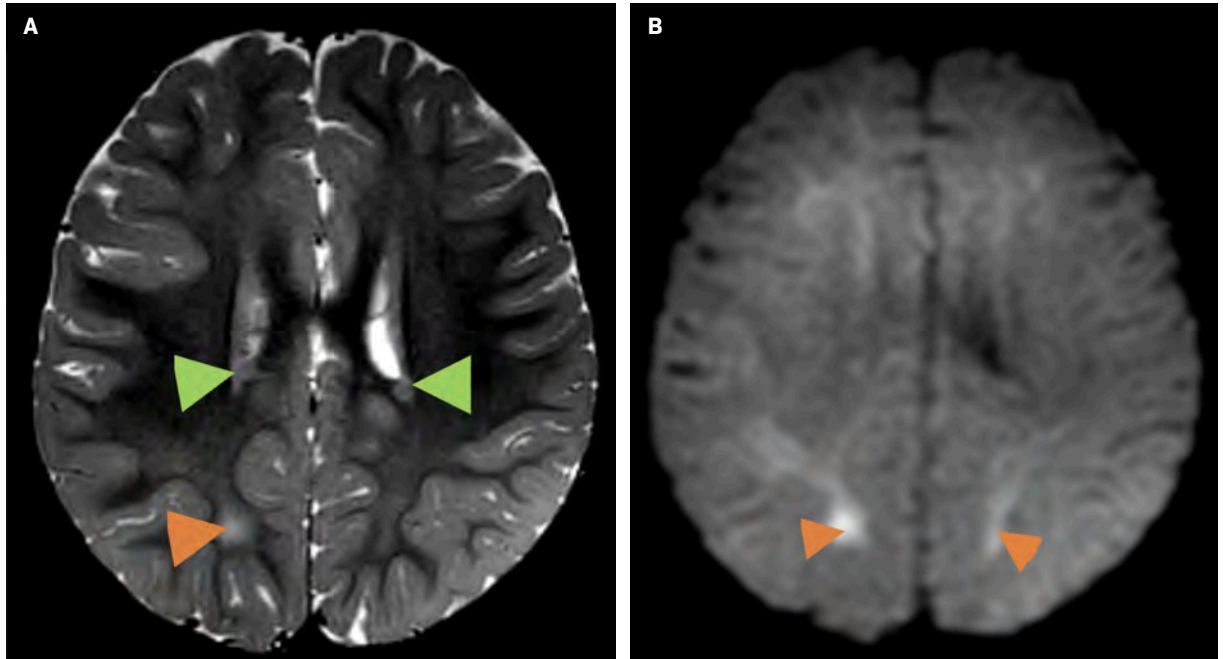
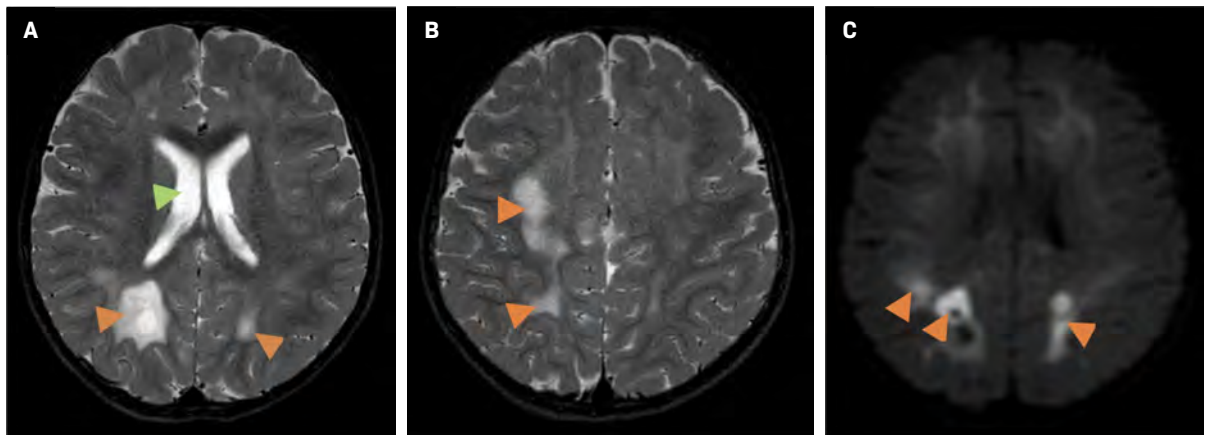


Figure 2. Brain MRI one year later. Axial T2 (A, B) demonstrates progressive abnormal white matter signal hyperintensity (orange arrowheads) and an interval ventricular enlargement (A, green arrow). Axial DWI (C) shows worsening restricted diffusion (orange arrowheads).



are present and the patient has an affected sibling.

As clinical diagnosis is difficult prior to disease progression, imaging studies are a key tool

in identification. Liver imaging and biopsy may offer a more timely diagnosis. However, the use of biopsy may be limited owing to uncommon knowledge of this rare disease among pathologists.

Therefore, genetic testing offers the most definitive and potentially earliest diagnosis.

Typical MRI brain imaging shows diffuse leukoencephalopathy,

manifesting as an abnormal, hyperintense T2 signal throughout the cerebral white matter, along with areas of restricted diffusion.^{2,4} This differs from other mitochondrial disorders that predominantly affect the cortex and deep gray nuclei. Currently, there is no curative treatment for NNH.^{6,7} The only treatment option for liver disease is transplantation;⁸ however, this is only palliative and does not alter long-term neurological decline.

This case demonstrates the difficulty of diagnosing NNH through imaging studies and liver biopsy alone. Suspicion of NNH should be high in pediatric patients of Navajo descent presenting with liver pathology and should prompt genetic testing for the disease as well as brain MRI.

Conclusion

Navajo neurohepatopathy is a rare and incurable mitochondrial disease affecting children of Navajo descent, causing liver disease and diffuse leukoencephalopathy. Health care professionals working near and serving Indigenous populations should be familiar with the signs and symptoms of NNH to enable prompt diagnosis and supportive treatment.

References

- 1) Mărginean CO, Meliț LE, Ghiga DV, Săsăran MO. Reference values of normal liver stiffness in healthy children by two methods: 2D shear wave and transient elastography. *Sci Rep*. 2020;10(1):7213. doi:10.1038/s41598-020-64320-w
- 2) Karadimas CL, Vu TH, Holve SA, et al. Navajo neurohepatopathy is caused by a mutation in the MPV17 gene. *Am J Hum Genet*. 2006;79(3):544-548. doi:10.1086/506913
- 3) Bitting CP, Hanson JA. Navajo neurohepatopathy: a case report and literature review emphasizing clinicopathologic diagnosis. *Acta Gastroenterol Belg*. 2016;79(4):463-469.
- 4) Holve S, Hu D, Shub M, Tyson RW, Sokol RJ. Liver disease in navajo neurohepatopathy. *J Pediatr*. 1999;135(4):482-493. doi:10.1016/s0022-3476(99)70172-1
- 5) Vu TH, Tanji K, Holve SA, et al. Navajo neurohepatopathy: a mitochondrial DNA depletion syndrome? *Hepatology*. 2001;34(1):116-120. doi:10.1053/jhep.2001.25921
- 6) El-Hattab AW, Scaglia F. Mitochondrial DNA depletion syndromes: review and updates of genetic basis, manifestations, and therapeutic options. *Neurotherapeutics*. 2013;10(2):186-198. doi:10.1007/s13311-013-0177-6
- 7) Aldossary AM, Tawfik EA, Alomary MN, et al. Recent advances in mitochondrial diseases: from molecular insights to therapeutic perspectives. *Saudi Pharm J*. 2022;30(8):1065-1078. doi:10.1016/j.jsps.2022.05.011
- 8) Holve S, Hu D. The long-term outcomes after liver transplantation in MPV-17 deficiency (navajo neurohepatopathy) are poor. *Pediatr Transplant*. 2023;27(3):e14437. doi:10.1111/petr.14437

Luc Abscess

Kathryn A. Szymanski, BS; Cerys Arnold, BS; Michael S. Kuwabara, MD

Case Summary

A previously healthy child presented to our institution after CT examination at another institution revealed mastoid air cell effusion and swelling of the left temporal soft tissues (Figure 1). Symptoms included headache, focal pain, and swelling over the left temporal region and decreased left auditory clarity. Physical examination demonstrated left tympanic membrane opacification, suggesting infection, and left temporal swelling anterior and superior to the left ear without edema or tenderness to palpation over the mastoid portion of the temporal bone.

Laboratory findings included elevated C-reactive protein (6.1 mg/dL), red blood cell sedimentation rate (77 mm/hour), and white blood cell count. Intravenous antibiotics were administered. Ultrasound of the left temporal soft tissues was performed, followed by MRI.

Imaging Findings

Ultrasound of the region of concern demonstrated asymmetric thickening

of the temporalis musculature measuring approximately 10.9 mm in thickness on the left versus 5.4 mm on the right. Loss of echotexture suggested edema. A small irregular hypoechoic area measuring approximately $9 \times 2 \times 11$ mm was visible.

MRI (Figure 2) demonstrated left temporal scalp diffusion-restricting collection with a thick enhancing peripheral rim and abnormal signal within the left squamous and temporal bones, expansion of the bone, irregularity of the cortex and intracranial extension, minimally involving the dura; left mastoid effusion; and edema and enhancement within the left medial pterygoid muscle, left masseter muscle, left mandibular condyle, and left temporomandibular joint place (not shown).

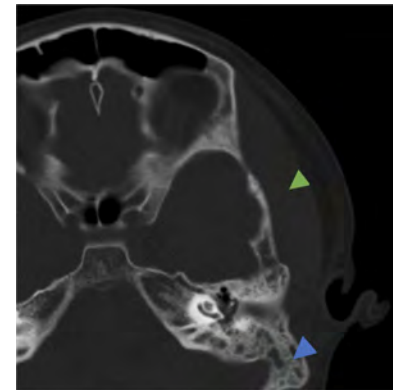
Diagnosis

Luc abscess

Discussion

Luc abscess is a rare but dangerous complication of acute otitis media, caused by the spread of infection from the middle ear and creating a subperiosteal suppurative collection beneath the temporal muscle.¹ The condition more frequently affects children (80.9%) as a complication of acute otitis media, but also in the setting of congenital

Figure 1. Temporal bone CT. Axial bone window demonstrating mastoid effusion (blue arrowhead) and abnormally thickened left temporal region soft tissues (green arrowhead).



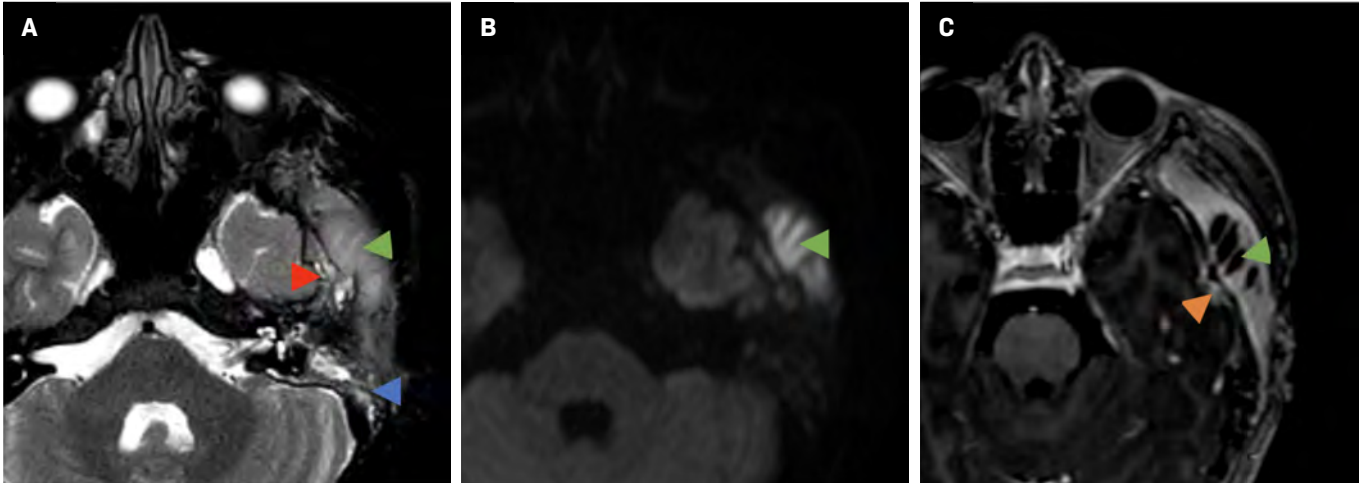
cholesteatoma.² The most common presenting signs and symptoms are preauricular and facial swelling with ipsilateral otalgia, tenderness on preauricular palpation, fever, malaise, trismus, and acute otitis media on otoscopy.³

Named for Henri Luc, the condition was first described in 1913 as Luc sought to identify the abscess as distinct from other subperiosteal abscesses related to acute otitis media and did not involve the mastoid bone. He argued that the infection spread via the notch of Rivinus as well as along branches of the deep auricular artery, which were the proposed pathways connecting the external ear canal to the subperiosteal area deep to the temporalis muscle.¹ In an era predating the widespread availability of antibiotics, Luc hoped to reduce unnecessary

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Figure 2. Brain MRI. Axial T2 (A) demonstrates mastoid effusion (blue arrowhead), hyperintense thickened left temporal region soft tissues (green arrowhead), and irregularity of the greater wing of the left sphenoid and squamous temporal bone (red arrowhead). (B) Diffusion-weighted imaging demonstrates left temporal scalp collection with increased signal (green arrowhead) and decreased ADC (apparent diffusion coefficient) (not shown) indicating restricted diffusion in the abscess. (C) Postcontrast T1 demonstrates left temporal scalp fluid collection consistent with abscess (green arrowhead) and a small focus of pachymeningeal enhancement along the temporal lobe surface (orange arrowhead).



mastoidectomies, especially in the absence of mastoiditis signs such as ongoing otorrhea and retroauricular swelling.⁴

Luc's theory has since been debated; as multiple cases have been reported of patients with subperiosteal abscesses below the temporal bone with concomitant mastoiditis, as seen in our case. In one study, 18 of 19 patients with a subperiosteal temporal abscess also had signs of acute mastoiditis on CT.³ This suggests the presence of an alternative pathway of direct extension from the mastoid air cells to the subperiosteal temporal space. Of note, tenderness of the mastoid and displacement of the pinna often develop days after the onset of preauricular swelling.³ Therefore, concurrent mastoiditis may develop secondary to the subperiosteal temporal abscess.

Contrast-enhanced CT is the preferred initial modality for assessment, including for additional complications such as adjacent venous sinus thrombosis, as well as to rule out other causes of facial edema such as orbital complications of sinusitis.^{4,5} MRI can assess for

sigmoid sinus thrombosis and other intracranial complications, though it may not be readily available in emergency settings and may require sedation in children.

The preferred treatment for Luc abscess includes incision and drainage with myringotomy and mastoidectomy. However, some believe conservative surgical management with incision and drainage of the subperiosteal temporal abscess is sufficient, even in patients with concurrent mastoiditis.³ Our case was successfully managed with incision and drainage of the abscess. However, mastoidectomy should be considered in patients with acute suppurative mastoiditis or those nonresponsive to antibiotics and drainage alone.

Conclusion

Luc abscess is a rare complication of acute otitis media, caused by the spread of infection from the middle ear to the subperiosteal area deep to the temporal muscle. Although the condition is uncommon with the widespread

use of antibiotics for acute otitis media, diagnosing and treating Luc abscess promptly is critical to prevent complications. Radiological studies can assess for the presence of concomitant mastoiditis or intracranial complications as these may alter the treatment plan.

References

- 1) Scrafton DK, Qureishi A, Nogueira C, Mortimore S. Luc's abscess as an unlucky complication of mastoiditis. *Ann R Coll Surg Engl.* 2014;96(5):e28-e30. doi:10.1308/003588414X13946184901281
- 2) Santhi K, Tang IP, Nordin A, Prepageran N. Congenital cholesteatoma presenting with luc's abscess. *J Surg Case Rep.* 2012;2012(12):rjs026. doi:10.1093/jscr/rjs026
- 3) Fernandez JJ, Crocetta FM, Pelligra I, Burgio L, Demattè M. Clinical features and management of luc's abscess: case report and systematic review of the literature. *Auris Nasus Larynx.* 2020;47(2):173-180. doi:10.1016/j.anl.2019.11.003
- 4) Mengi E, Tümkaya F, Sağtaş E, Ardiç FN. An unusual complication of otitis media: luc's abscess. *J Int Adv Otol.* 2018;14(3):497-500. doi:10.5152/iao.2018.4785
- 5) Chandran M, Saad MSM, Kailani A. Luc's abscess in a young adult – a unique presentation and approach. *Visual J Emerg Med.* 2023;31:101677. doi:10.1016/j.visj.2023.101677

"The life of the dead is placed in the memory of the living."
—Marcus Tullius Cicero

Losing a Colleague

C. Douglas Phillips, MD, FACR



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I had a particularly pithy and (hopefully) witty thing planned for this month, but as I've been told a few times, don't plan too far ahead. Maybe no further than that next step. I lost a good friend, colleague, and great man this week. That's actually being massively greedy, and I apologize. A *lot* of us lost a good friend, colleague, and great man this week.

Just a few observations about what we are all feeling.

Two competing lines of thought have been presented to me over the years about our value, not to our families and friends, but to our workplace. One of my prior chairs said repeatedly that "no one is irreplaceable." Okay.

Another one of my mentors said repeatedly that you instead *strive* to make yourself irreplaceable, and hopefully you get there. I choose to follow this thinking. Sure, you can hire someone to work a shift, make some widgets, fill a chair, or be around, but that is different than the feeling you get from a colleague who shares respect, life's moments, a drink or a meal, feelings, and dreams with you. That is entirely different and much more in line with reality, I think.

So, I have a heavy heart sitting here writing this all down. Mortality is a construct that becomes much more real to you as you get older (it really starts hitting when you receive that first mailing from AARP). Physicians are certainly not immune to the precarious nature of life. Maybe we are even more aware of it; I'm not sure.

I've been working long enough to say this with confidence: JT was one of the smartest folks I've had the pleasure of working with, an educator and a sharer of knowledge. He loved approaching an imaging study that others found confusing or inscrutable and often worked through the case, to a reasonable and (more often than not) correct answer, OUT LOUD, letting us all see how he was thinking. A superpower. Funny, and with a little edge that could be appreciated—never cutting, only insightful.

So, JT, we miss you already. You are, indeed, irreplaceable.

Work is going to be a little less happy for the next few months. I'm confident we will get someone to fill the chair, but we will never replace the man.

Keep doing that good work. Hug your kids, appreciate your colleagues. Mahalo.