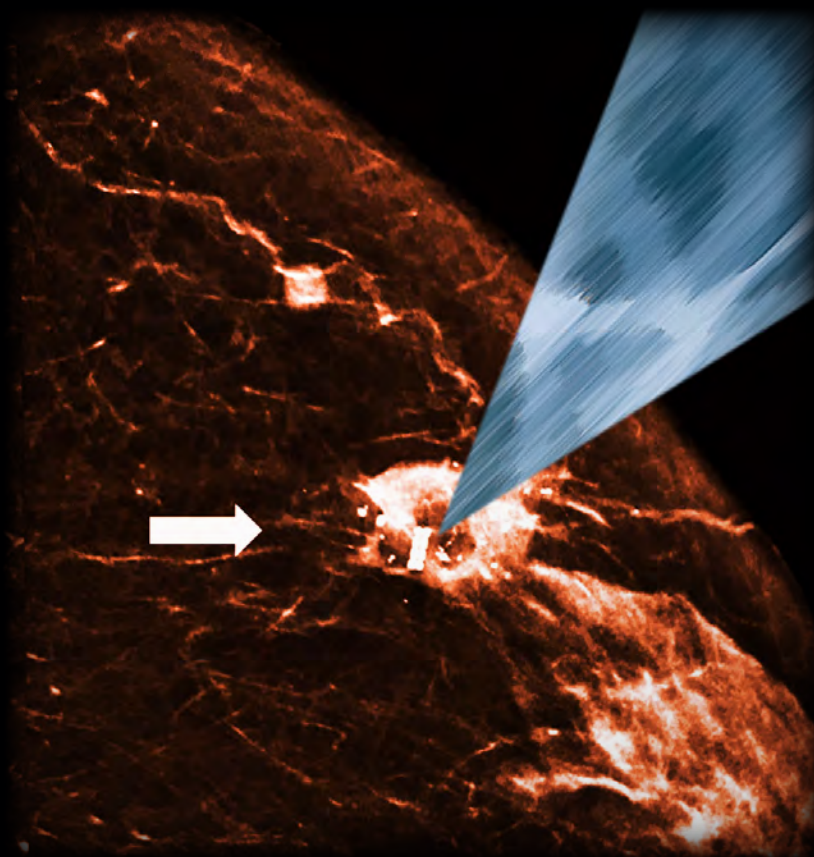


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# AppliedRadiology®

The Journal of Practical Medical Imaging and Management



Breast Cancer  
Cryoablation: Past,  
Present, and Future

Spectrum of Cystic  
Mediastinal Lesions:  
An Imaging Review

New Frontiers in  
Breast Imaging

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## Breast Cancer Cryoablation: Past, Present, and Future

Kenneth Tomkovich, MD, FACR, FSIR;  
Amy Deipolyi, MD, PhD, FSIR; Monica Huang, MD

Image-guided breast cancer cryoablation has evolved from an experimental technique to an emerging minimally invasive treatment option for selected patients with low-risk breast cancer. In this review, the authors summarize clinical evidence and procedural considerations, discuss its use in palliative care, and consider the immunologic effects of cryoablation and its potential combination with immunotherapy.

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## Spectrum of Cystic Mediastinal Lesions: An Imaging Review

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Cystic and cyst-like mediastinal lesions encompass a broad range of congenital and acquired abnormalities, as well as important mimics. This article highlights characteristic findings across radiography, CT, MRI, and PET/CT and presents a structured imaging approach to lesion characterization and management.

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## WET READ

### Please. Just Tell Me Something

C. Douglas Phillips, MD

**On the cover:** Image adapted from Figure 1 of 'Breast Cancer Cryoablation: Past, Present, and Future,' by Kenneth Tomkovich, MD, FACR, FSIR. Cover design by *Applied Radiology*.

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# New Frontiers in Breast Imaging

Nina S. Vincoff, MD

October is Breast Cancer Awareness Month, a time when many of us reflect on the extraordinary progress made in breast cancer detection, diagnosis, and treatment over the course of our careers. Few areas of radiology have evolved more dramatically than breast imaging.

When I began my training, the role of the breast imager was relatively well defined: detect abnormalities on screening mammography, characterize findings with diagnostic mammography and US, and perform image-guided biopsies and surgical localizations. Those responsibilities remain at the heart of our specialty.

Over time, however, the field has broadened considerably. Today, breast imagers routinely incorporate advanced modalities such as MRI and contrast-enhanced mammography into clinical practice. We have also assumed new responsibilities related to breast density notification, risk assessment, and personalized screening.

In this issue of *Applied Radiology*, we highlight additional ways that the scope of breast imaging is evolving. Our “Eye on AI” column, authored by Dr Alyssa T. Watanabe and colleagues, examines the growing role of artificial intelligence in the assessment of breast arterial calcifications (BACs) on screening mammography. BAC is increasingly recognized as a marker of cardiovascular risk, creating an opportunity for mammography to support not only breast cancer screening but also the identification of women who may benefit from cardiovascular risk assessment and preventive interventions.

In “Radiology Matters,” our interview with Drs Rajshri N. Shah and Julie A. Ritner explores the evolution of remote diagnostic mammography interpretation. Remote diagnostic imaging offers a means to expand access to subspecialty breast imaging expertise while helping address workforce shortages. Advances in communication technology are making it possible for radiologists, technologists, and patients to interact in ways that previously required everyone to be physically present in the same location. These innovations may help extend high-quality breast imaging services to underserved communities and create new models for delivering specialized care.

Finally, Dr Kenneth R. Tomkovich and colleagues review the emerging use of breast cancer cryoablation. Their article reminds us that radiologists are increasingly contributing not only to diagnosis but also to treatment. Advances in image-guided therapy have brought the possibility of treating selected breast cancers through minimally invasive procedures closer to reality, further extending our involvement across the continuum of care.

Taken together, these articles point toward a common theme. The future of our field will be defined not only by how effectively we detect cancer, but also by how broadly we serve our patients. From opportunistic assessment of cardiovascular risk, to improved access to specialized care, to image-guided treatment, breast imaging continues to evolve in ways that would have been difficult to imagine when many of us entered the field.

# Breast Cancer Cryoablation: Past, Present, and Future

Kenneth R. Tomkovich, MD, FACR, FSIR; Amy Deipolyi, MD, PhD, FSIR; Monica Huang, MD

## Abstract

The field of radiology is always changing, particularly with respect to image-guided breast cancer cryoablation. While this therapy has been studied for decades, the results of recent clinical trials have made the concept of treating breast cancer without surgery closer to reality. The technique closely resembles that of percutaneous image-guided breast biopsy, and the skill set to perform this procedure can be acquired by breast and interventional radiologists. Small, low-risk breast cancers can be treated with cryoablation, and there is an opportunity to use it for palliative care. Potential immune benefits of cryoablation add to the appeal and interest in this procedure.

**Keywords:** breast cancer, cryoablation, palliative care, immunologic effect, abscopal effect

## Introduction

Radiology continues to be a leader in advancing the field of medicine, challenging old thoughts, refining proven concepts, and utilizing new imaging and interventional technology. This is particularly true in the field of breast cancer. Radiology has championed the field of women's health by improving the quality of diagnostic imaging throughout years of research, while educating the medical and lay community on the appropriate use of such imaging advances. This has led to finding smaller, more treatable breast cancers, with an overall

reduction in morbidity and mortality. Today a new and exciting chapter is emerging: image-guided breast cryoablation for the non-surgical treatment of breast cancer.

## A Historical Perspective

Cryoablation devices were invented in 1961 when Irving Cooper, MD, PhD, and colleagues developed a device using liquid nitrogen circulating through an insulated probe.<sup>1</sup> In 1976, LePivert reported on "cryosurgery" for 7 cases of advanced breast cancer.<sup>2</sup> From 1982 to 1995, Suzuki

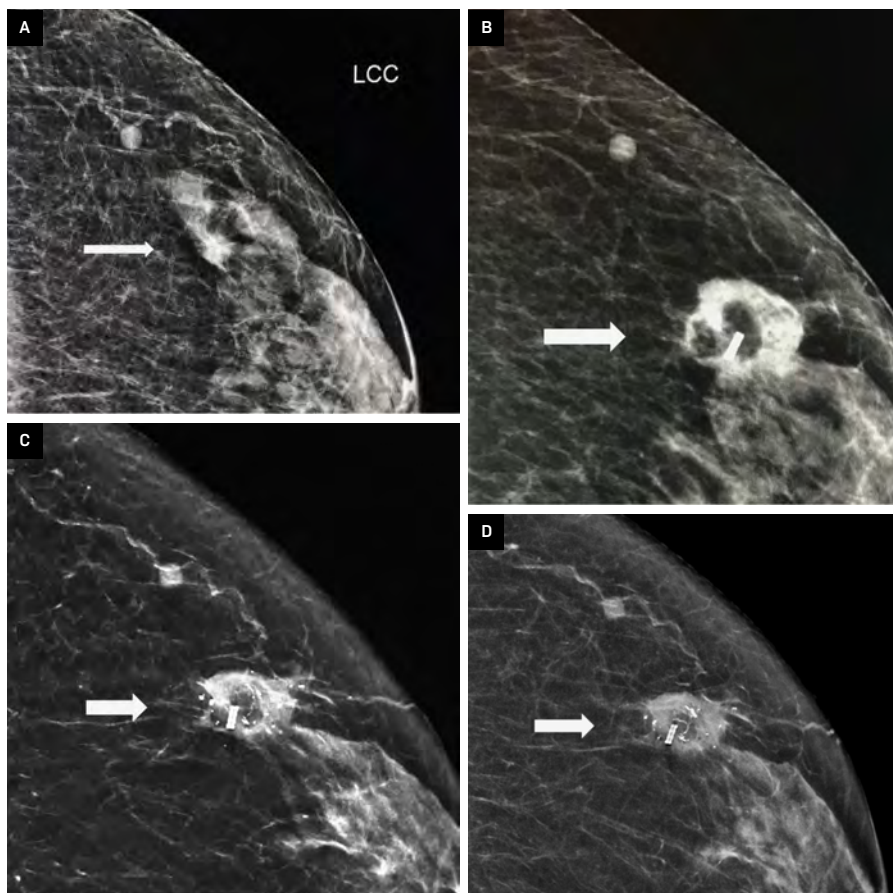
performed cryosurgery on patients with stage IV breast cancer, reporting rates of survival ranging from 6 months to 5 years.<sup>3</sup> In 2004, Roubidoux and Sable published their work on a feasibility study to treat breast cancers  $\leq 2$  cm with cryoablation followed by surgical excision, with 7 out of 9 patients having no residual cancer at surgery.<sup>4</sup> In 2009, Littrup and colleagues published one of the first trials using image-guided cryoablation on 22 cancers in 11 patients with no local recurrence at up to 18 months follow-up. This was a cohort of patients with all stages of breast cancer and with tumors treated up to 58 mm.<sup>5</sup> These early works led to ACOSOG Z1072, the first multicenter, large-scale trial testing the feasibility of using cryoablation as a primary treatment for unifocal predominantly invasive ductal carcinomas 2 cm or less. Nineteen centers contributed 99 patients; 87 cancers in 86 patients were treated with cryoablation followed by surgical excision. When multifocal disease outside of the ablation zone was excluded, 80 out of 87 (92%) of all

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**Declaration on the use of AI:** The authors of this manuscript declare that in the writing process of this work, no generative artificial intelligence (AI) or AI-assisted technologies were used to generate content, ideas, or theories. The authors utilized AI solely for the purpose of enhancing readability and refining language. This use was under strict human oversight and control. After the application of AI technologies, the authors carefully reviewed and edited the manuscript to ensure its accuracy and coherence.

**Figure 1.** (A) Imaging findings, left craniocaudal (LCC) view, of a patient from the ICE3 trial, showing a 6-mm invasive ductal carcinoma prior to cryoablation (arrow). (B) 12 months post ablation. Note the formation of a thickened rim of dense tissue around the ablation zone (arrow). (C) 36 months post ablation. The rim of dense tissue remains, and there has been interval development of dystrophic calcifications (arrow). (D) 60 months post ablation. The dystrophic calcifications persist and have increased over time. The rim of dense tissue has become less dense (arrow).



cancers and 100% of all cancers 1 cm or less were successfully ablated.<sup>6</sup>

### The ICE3 Trial

The ICE3 trial was the first multicenter trial to assess the safety and efficacy of image-guided cryoablation as a primary treatment for low-risk breast cancers without surgical excision. This prospective trial enrolled 194 women ages 60 and older across 19 centers with unifocal, US-visible breast cancers 1.5 cm or less. All patients were clinically lymph node-negative with biopsy-proven invasive ductal carcinomas that were hormonal receptor (HR)-positive and HER2-negative. All patients with lobular carcinoma and extensive ductal

carcinoma in situ were excluded due to the difficulty in assessing tumor borders with US imaging for those pathologies. A total of 162 patients completed the 5-year imaging follow-up (Figure 1). The 5-year follow-up data, published in 2024, demonstrated an overall ipsilateral tumor recurrence rate of 4.3%. Of the patients who also received endocrine therapy only, the recurrence rate was 3.7%,<sup>7</sup> which was comparable to the current standard of care with surgical excision.<sup>8</sup>

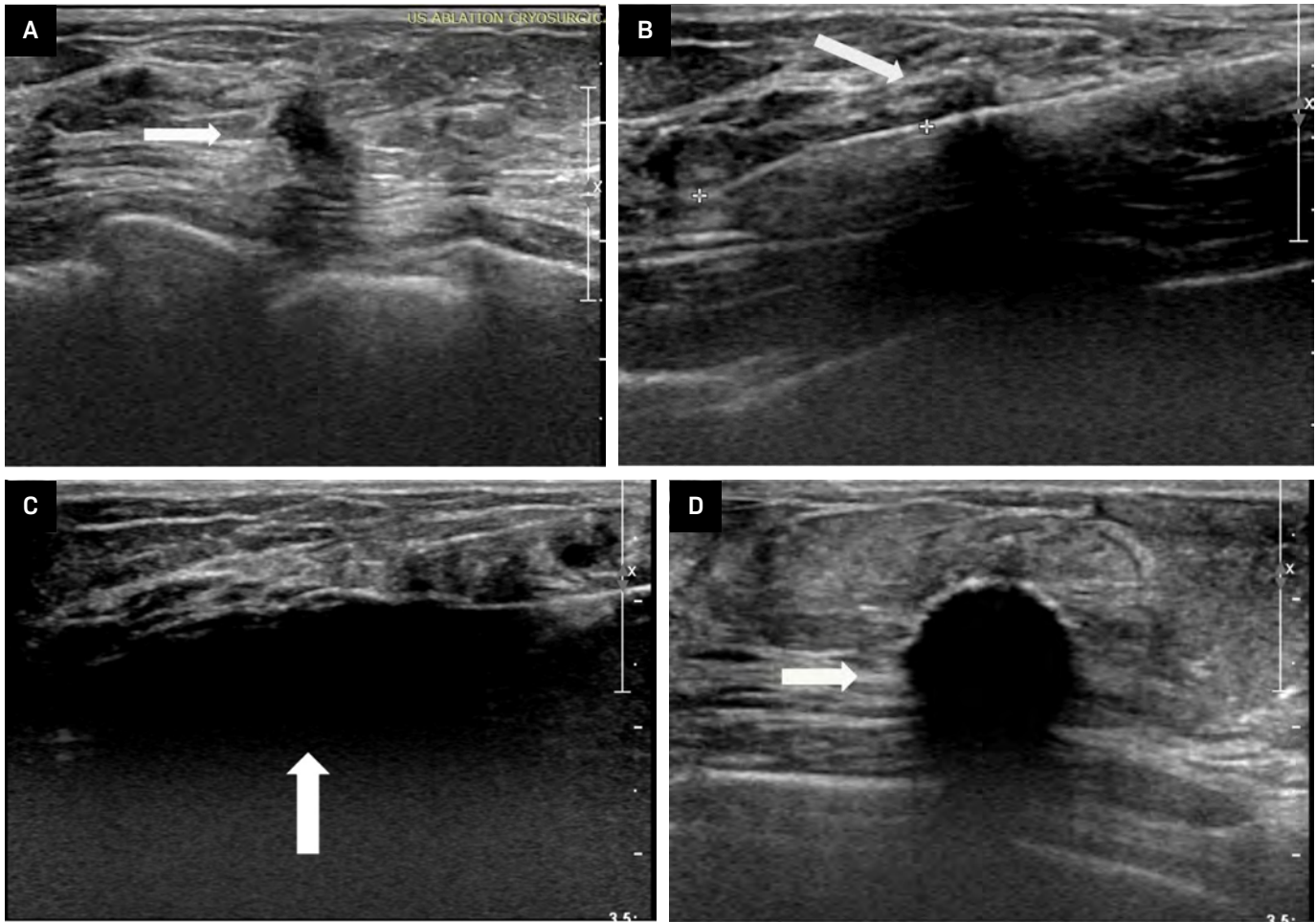
### Techniques and Clinical Considerations

The technique for performing image-guided breast cancer cryoablation

requires proficiency with image-guided breast biopsy procedures as well as the proper techniques and safety considerations for performing percutaneous image-guided cryoablation. While the procedure can be performed with multiple cryoprobes using US, CT, or MRI guidance for larger tumors, a single-probe US-guided procedure is preferable for small,  $\leq 1.5$  cm, unifocal low-risk breast cancers as defined in the ICE3 trial. Breast cancer cryoablation can be performed in an outpatient setting with patients awake and alert under local anesthesia. This allows the patients to return to normal activities almost immediately following the procedure and for treatment of patients who are poor surgical candidates.

The US-guided technique follows that of a US-guided breast biopsy procedure with modifications. An US-visible well-defined tumor is localized. The approach is prepped and draped. Local anesthesia, typically 5 mL 1% lidocaine for the skin and 10 mL 1% lidocaine with epinephrine for the deeper tissues around the tumor, is delivered under US guidance. The cryoprobe is prepared and tested prior to insertion as per the manufacturer's guidelines. Sterile saline solution should be available for skin hydrodisplacement though a 20-gauge spinal needle if the ice ball approaches the skin surface to prevent thermal injury. A distance of  $\geq 5$  mm is preferred between the cryosphere and the skin during the procedure. Warming packs can also be placed on the skin surface. After a small skin incision, precise placement of the cryoprobe is the first key element to successful ablation. The probe should be placed under US guidance as close to the center of the tumor as possible, preferably along its long axis (Figure 2). Care should be taken to avoid crossing blood vessels between the skin and the target tumor during placement of the probe, if avoidable, as this can lead to ongoing bleeding and hematoma. The cryosphere grows from the probe outward from an isocenter as defined by the manufacturer's guidelines, and placement nearest the center of the tumor

**Figure 2.** (A) US image of the same patient as in Figure 1. Post biopsy, pre-ablation US demonstrates an irregular, poorly marginated hypoechoic mass (arrow). (B) US image with cryoprobe (echogenic line) through the center of the mass (arrow). Calipers present defining the ideal distance from the tip of the probe to the anterior border of the lesion for optimal cryosphere formation. (C) Early cryosphere formation in the longitudinal plane. (D) Early cryosphere formation in the transverse plane.



allows for the best possible outcomes for adequate freezing of the tumor and the optimal ablation zone. After placement, the probe is activated and the freeze cycle begins. This typically takes 8-10 minutes. The goal is to achieve a cryosphere that encompasses the breast cancer and the surrounding tissues so as to ideally provide a 10-mm margin of  $-40^{\circ}\text{C}$  to  $-20^{\circ}\text{C}$  lethal ice around the tumor. The cryosphere formed is highly visible anteriorly and laterally and nearly anechoic with an echogenic rim (Figure 3). The posterior margin is not visible by US but is deemed to be nearly the same depth as the anterior margin. Note is made that no protection is required for the chest wall during the procedure as there is no risk of significant thermal injury. However, patients may experience

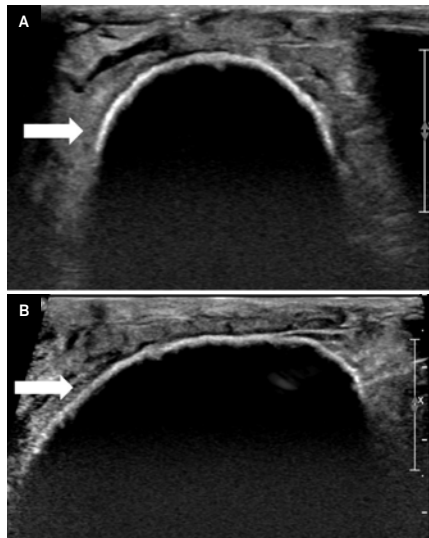
some chest discomfort if the ice ball grows posteriorly, near the chest wall, which can be treated by lifting the probe off the chest wall. The first freeze cycle is followed by a passive thaw of 8-10 minutes. This cycle is important as thawing causes osmotic gradients and fluid shifts into damaged cells, leading to swelling, bursting, and further cell death.<sup>9</sup> This is followed by a second freeze cycle of 8-10 minutes.

The second key element to successful ablation is remembering that the cryosphere can grow quickly in less than 8-10 minutes, but the internal temperatures of the kill zone may take significantly longer. Short freeze times can produce large ice balls in 3-5 minutes, but the  $0^{\circ}\text{C}$  isotherm, which defines the visible echogenic edge of the cryosphere,

is nonlethal. Cell death occurs at  $-40^{\circ}\text{C}$ , which is best achieved with longer freeze times.<sup>9</sup> The cryosphere, using a single probe technique, will not continue to grow significantly beyond a certain diameter, but the internal temperature will continue to drop. Adequate freeze time to achieve lethal ice, as well as a freeze, thaw, freeze cycle, are the keys to achieving cell death and tumor destruction in breast cancer cryoablation.

Following the second freeze cycle, a rapid thaw cycle is performed to facilitate probe removal. A dressing is applied, and after a brief observation period, the patient is discharged. The third key element to successful ablation is to manage patient expectations. Patients should be aware that as the ice ball melts, there can be

**Figure 3.** (A) Image of the same patient as in Figure 1. Highly visible, nearly anechoic cryosphere with echogenic border (arrow) in the transverse plane. (B) Highly visible nearly anechoic cryosphere with echogenic border (arrow) in the longitudinal plane.



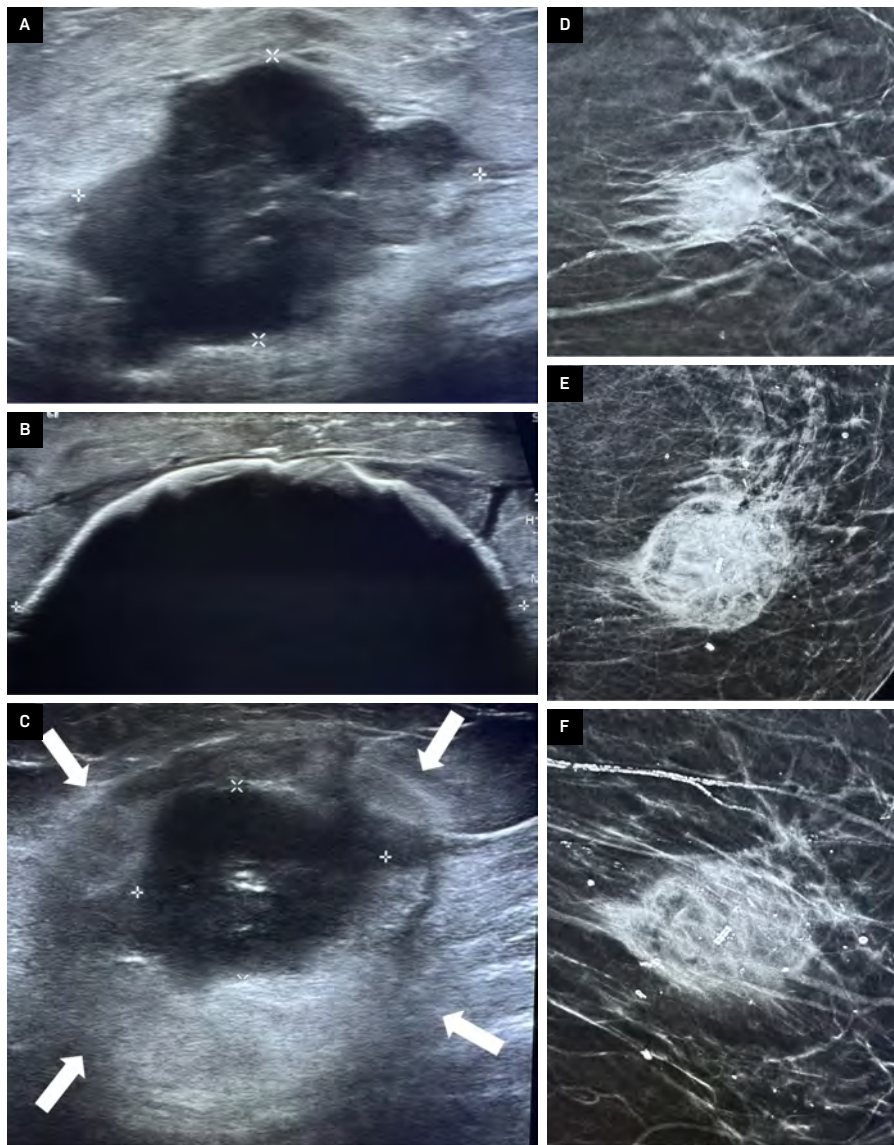
a leakage of fluid or bloody discharge from the entry site. Bruising and small hematomas are to be expected. There may be swelling and warmth at the site of the ablation due to a local inflammatory response. Most importantly, patients, who may have felt nothing in their breasts prior to ablation, will most certainly feel a lump in their breast for weeks to months after at the site of the ablation procedure. Communication of these common post-procedure occurrences will ensure that the patients are prepared for them should they happen.

### Breast Cryoablation with Palliative Intent

While the interim analysis results of the ICE3 trial published in 2021 by Fine et al<sup>7</sup> ignited renewed interest in breast cryoablation for the curative treatment of unifocal,  $\leq 1.5$  cm, low-risk breast cancer, breast cryoablation had been performed since the 1960s for the palliative treatment of advanced and recurrent breast cancer<sup>1,2</sup> (Figure 4).

From 1968 to 1994, breast and chest wall/mastectomy site cryoablation was

**Figure 4.** (A) Irregular poorly margined mass in a 90-year-old patient with multiple comorbidities measuring 3.4 cm  $\times$  2.4 cm. (B) Mass completely engulfed by 5.7 cm cryosphere post ablation using 3 freeze-thaw-freeze cycles and a single cryoprobe. (C) Hypoechoic mass “ghost” (centrally of treated tumor 3 months post ablation measuring 2.6 cm  $\times$  2.0 cm. Note the echogenic rim “cryohalo” defining the ablation zone margin (arrows). (D) Mammography of mass pre ablation. (E) Mammography of mass 3 months post ablation. Note the larger appearance due to inflammatory response in surrounding tissue following cryoablation. (F) Mammography of mass 18 months post ablation. Decreased density and size of mass with formation of some dystrophic calcifications.



performed in patients whose disease was resistant or unresponsive to standard of care surgical treatment, chemotherapy, and radiation therapy. These early studies, composed of small number ( $\leq 40$  patients) of case series with limited follow-up (6 months to 5 years), reported not only survival benefits,

resolution of pain, and local tumor size reduction but also regression of contralateral breast tumor and lymph node metastasis, noting the potential of systemic antitumor response.<sup>1,2</sup>

Additional retrospective small case studies from 2000 to 2024 continue to demonstrate that palliative breast

cryoablation treatments offer local tumor and pain control, with excellent patient tolerance and no significant complications. Pusceddu et al performed CT-guided breast cryoablation from 2010 to 2016 on 35 patients with metastatic breast cancer, including 17.1% with multicentric disease. This study demonstrated 100% tumor ablation (some requiring second cryoablation treatment), confirmed with 6-month follow-up MRI, although 20% experienced local recurrence and 20% died of tumor progression during follow-up (3-84 months, median 46 months).<sup>10</sup> In 2018, Beji et al reported their study of CT and US-guided breast cryoablation of 17 patients with metastatic breast cancer (following 1 or 2 cryoablation treatments), with resolution of breast mass pain in 5 patients and no residual, recurrent, or progression of primary breast tumor on MRI imaging follow-up (median 22 months, 15 patients with >12 month-follow-up) for 15 patients.<sup>11</sup> Huang et al reported in 2024 the results of their breast cryoablation treatment of 13 patients (18 lesions) with palliative intent (7 patients with nodal metastasis, 1 with scalp soft tissue metastasis, and 2 with multicentric disease). Treatment success was achieved in 100% of these patients during imaging follow-up (3-26 months, median 16 months; 14 treated tumors with >12 month follow-up), with one patient reporting resolution of nipple pain.<sup>12</sup> Despite these promising retrospective series, no prospective, large cohort, or long-term studies have been conducted on palliative breast cryoablation treatment.

### Immunologic Effects of Breast Cryoablation

Whereas surgical resection removes tumor tissue, cryoablation leaves the tumor in situ, inducing cell death while releasing intact tumor antigens that can stimulate local and systemic immune responses and potentially

generate abscopal effects. Freeze-thaw cycles preserve tumor antigens while releasing inflammatory mediators which activate immune pathways due to exposure of intact tumor-specific antigens to the immune system.<sup>13-16</sup> This process stimulates production of pro-inflammatory cytokines and nucleoproteins that activate innate immune cells such as natural killer cells and dendritic cells, while promoting adaptive immune responses, including cytotoxic T lymphocyte activation.<sup>13,17</sup> In preclinical triple-negative breast cancer models, compared with surgical resection, cryoablation results in increased populations of antitumor immune cells such as tumor-infiltrating lymphocytes, natural killer cells, and conventional type 1 dendritic cells.<sup>15,18</sup>

One ideal consequence of immune activation is the abscopal effect, in which treatment of a primary tumor generates systemic immune responses affecting distant tumors. In murine models, cryoablation of primary breast tumors resulted in reduced growth of distant tumors accompanied by increased natural killer cell activity and upregulation of leukocyte-mediated cytotoxicity.<sup>15</sup> Clinical studies similarly demonstrate increased tumor-infiltrating lymphocytes, CD8+ T cells, and granzyme B expression in distant tumors after cryoablation, suggesting enhanced cytotoxic immune activity.<sup>6</sup> These systemic immune responses may contribute to reduced recurrence and metastatic progression observed in some preclinical models compared with surgical resection alone.<sup>15,18</sup>

Despite these immunostimulatory effects, cryoablation alone may not fully overcome tumor immune escape mechanisms. Experimental studies show that cryoablation can also induce upregulation of PD-1/PD-L1 signaling pathways in the tumor microenvironment, limiting antitumor immune activity.<sup>19</sup> This observation provides a rationale for combining cryoablation with immune checkpoint inhibitors such as

anti-PD-1 or anti-CTLA-4 antibodies.<sup>13,20,21</sup> Preclinical studies demonstrate that PD-1 blockade enhances cryoablation-induced immune responses, producing synergistic antitumor effects.<sup>19</sup>

Early clinical studies support the feasibility of combining cryoablation with immunotherapy in breast cancer. One pilot trial demonstrated that preoperative cryoablation combined with single-dose ipilimumab was safe and well tolerated in patients with early-stage breast cancer and produced activation of systemic immune responses.<sup>22,23</sup> Building on these findings, an ongoing phase 2 study (NCT03546686) is evaluating perioperative checkpoint inhibition with ipilimumab and nivolumab combined with cryoablation in women with residual triple-negative breast cancer after neoadjuvant chemotherapy.<sup>24</sup> Patients undergo image-guided cryoablation shortly before surgery with perioperative checkpoint inhibitor therapy, followed by adjuvant systemic therapy. The study's primary endpoint is 3-year event-free survival.<sup>24</sup> Additional retrospective data evaluating thermal ablation combined with checkpoint inhibitors across multiple tumor types demonstrate acceptable safety profiles and suggest potential abscopal responses in a subset of patients.<sup>25</sup>

These findings suggest that cryoablation may function as an immune-modulating therapy capable of enhancing systemic antitumor immunity, particularly in combination with immunotherapy, in the hopes of improving outcomes in biologically aggressive breast cancer subtypes.<sup>20,26</sup> Cryoablation may provide a unique immunologic advantage over surgical resection by preserving tumor antigens and stimulating systemic antitumor immunity, supporting its investigation as both a local therapy and an immunologic adjunct in breast cancer management.

## Important Recent Developments

The US Food and Drug Administration (FDA) General and Plastic Surgery Devices Panel convened in Bethesda, Maryland, in November 2024 and voted “yes” to the proposal that the benefits of cryoablation for low-risk breast cancer outweigh the risks for the proposed indications for use, primarily based on the 20 of patients and results of the ICE3 trial. This led to the FDA granting Class II approval for the use of cryoablation as a primary treatment of biologically low-risk invasive ductal carcinoma 1.5 cm or less in patients 70 years old or older in combination with adjuvant endocrine therapy.<sup>27</sup> A post-market analysis trial was also requested by the FDA as part of the approval process and is currently recruiting sites. Following the FDA approval, the American Society of Breast Surgeons (ASBS) issued an updated resource guide in February 2026 on the use of percutaneous ablation for the treatment of benign and malignant tumors of the breast. In this document, the ASBS recommended consideration of image-guided cryoablation of the same specific cohort of patients approved by the FDA with additional clinical and technical considerations. It was also stressed that cryoablation must be considered in the context of a multidisciplinary team treatment plan, there is a significant learning curve for safe and effective breast cancer cryoablation, and that further evaluation of this procedure is ongoing.<sup>28</sup>

## Conclusion

Breast cancer cryoablation has been shown to be a safe and effective option for the curative treatment of small low-risk breast cancers as well as for palliation. The clinical skill set is already largely possessed by interventional and diagnostic radiologists with experience in breast biopsy noting

important technical considerations and a learning curve inherent to all new procedures. The potential for additional benefits of an immunological response adds to the appeal of this procedure and provides opportunities for future research. With the current guidelines and recommendations, as well as multiple ongoing studies throughout the world, the future of image-guided cryoablation as an alternative treatment for breast cancer is bright.

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# Spectrum of Cystic Mediastinal Lesions: An Imaging Review

Poonam Yadav, MD; Pooneh Jabbaripour Sarmadian, MD; Behrooz Masuodi, MD

## Abstract

Cystic and cyst-like lesions of the mediastinum encompass a broad spectrum of entities ranging from benign congenital abnormalities to inflammatory or malignant processes with cystic components. These lesions are frequently encountered with cross-sectional imaging and may present a diagnostic challenge due to overlapping imaging appearances. Accurate characterization is critical, as misclassification can lead to unnecessary surgical intervention or delayed diagnosis of clinically significant disease.

These lesions can be incidentally identified on routine chest radiographs as paramediastinal opacities. CT is typically the initial imaging modality for further evaluation of mediastinal lesions and provides essential information regarding lesion location, morphology, and relationship to adjacent structures. MRI offers superior soft-tissue characterization and plays a key role in problem-solving, particularly when CT findings are indeterminate.

The use of T1- and T2-weighted sequences, along with diffusion-weighted imaging, facilitates differentiation of simple cysts from lesions containing solid, proteinaceous, or malignant components. Awareness of characteristic imaging features of common congenital cysts, acquired cystic lesions, and important mimics further improves diagnostic confidence.

In conclusion, mediastinal cystic lesions require a structured imaging-based approach for accurate diagnosis. Integration of clinical context, anatomic location, and multimodality imaging findings, with particular emphasis on MRI, supports appropriate risk stratification and individualized patient management.

**Keywords:** mediastinal cysts, bronchogenic cyst, thymic cyst, pericardial cyst, esophageal duplication cyst, lymphangioma, mediastinal lesions

## Introduction

Cystic and cyst-like lesions of the mediastinum comprise a heterogeneous group of entities that frequently

pose diagnostic challenges, particularly when imaging findings are indeterminate.<sup>1-3</sup> These lesions span a broad spectrum, ranging from benign congenital lesions to malignant cystic neoplasms

or tumors undergoing cystic degeneration.<sup>1-3</sup> Accurate differentiation is essential, as misinterpretation may lead to unnecessary imaging follow-up, surgical intervention, or delayed treatment of clinically significant disease.<sup>1,4</sup>

Congenital mediastinal cysts include bronchogenic cysts, esophageal duplication cysts, thymic cysts, pericardial cysts, neuroenteric cysts, and lymphangiomas.<sup>2,3,5</sup> The classification, embryologic basis, and typical locations of mediastinal cystic lesions are summarized in Table 1. These lesions arise from distinct embryologic abnormalities such as aberrant foregut budding or

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**Table 1. Classification of Mediastinal Cystic Lesions**

| TYPE       | SUBTYPE                       | EMBRYOLOGIC/PATHOLOGIC BASIS                                      | TYPICAL LOCATION                  | REFERENCE |
|------------|-------------------------------|-------------------------------------------------------------------|-----------------------------------|-----------|
| Congenital | Bronchogenic cyst             | Abnormal budding of tracheobronchial tree                         | Visceral mediastinum, near carina | 5,6       |
|            | Esophageal duplication cyst   | Incomplete foregut recanalization, shares muscular wall           | Adjacent to esophagus             | 2,7       |
|            | Pericardial cyst              | Incomplete fusion of mesenchymal lacunae                          | Right cardiophrenic angle         | 8         |
|            | Thymic cyst                   | Persistent thymopharyngeal duct remnants                          | Prevascular mediastinum           | 9         |
| Acquired   | Lymphangioma                  | Sequestration of lymphatic tissue isolated from lymphatic system  | Prevascular mediastinum           |           |
|            | Cystic degeneration of tumors | Degeneration/necrosis in thymomas, germ cell tumors, and so forth | Variable                          | 1,2       |
|            | Non-neoplastic processes      | Infection, hemorrhage, abscess formation                          | Variable                          | 1,7       |

incomplete recanalization and typically demonstrate characteristic imaging features, including well-defined margins, thin walls, unilocular configuration, and homogeneous fluid attenuation on CT or fluid signal intensity on MRI.<sup>2,3</sup> Recognition of these features is highly important for confident diagnosis and appropriate clinical management.

In contrast, acquired cyst-like mediastinal lesions may result from cystic degeneration or necrosis within malignant tumors such as thymomas, germ cell tumors, lymphomas, or metastatic disease, or from non-neoplastic processes including infection, hemorrhage, or abscess formation.<sup>1-3,8</sup> Although these lesions may mimic benign cysts, the presence of thickened or irregular walls, enhancing or nodular internal septations, solid enhancing components, or restricted diffusion on MRI should raise concern for malignancy.<sup>1,3,9</sup> We will provide a practical, imaging-based approach to cystic and cyst-like mediastinal lesions, with emphasis on classification, embryologic origin, characteristic imaging features, important

mimics, and implications for diagnosis and management.

### Imaging Modalities and Technical Considerations

Larger mediastinal cysts can be identified as circumscribed opacities silhouetting the cardio-mediastinal border on routine chest radiograph. CT is typically the first-line imaging modality for evaluation of mediastinal lesions and allows accurate assessment of lesion location, attenuation, wall characteristics, calcification, and relationships to adjacent mediastinal structures.<sup>1,3,10</sup> CT plays a central role in initial lesion detection and anatomical localization; however, attenuation overlaps between proteinaceous fluid, hemorrhage, and necrotic tumors may limit diagnostic confidence in certain cases.<sup>1,3</sup> Additionally, beam-hardening and streak artifacts may falsely elevate the measured attenuation of simple cysts.

MRI provides superior soft-tissue characterization and is particularly valuable when CT findings are

equivocal.<sup>3,6,11</sup> T1- and T2-weighted sequences facilitate differentiation of simple fluid from hemorrhagic or protein-rich content, while contrast-enhanced imaging assists in identifying solid enhancing components suggestive of malignancy.<sup>3,11</sup> Diffusion-weighted imaging further improves lesion characterization by assessing diffusion properties and helps distinguish non-neoplastic cysts from solid or malignant lesions, demonstrating restricted diffusion.<sup>6,9</sup>

PET combined with CT may be useful in selected cases when malignancy is suspected. Increased fluorodeoxyglucose uptake suggests metabolically active components and supports the diagnosis of malignant or infectious processes rather than simple cysts.<sup>1,7</sup> Key imaging characteristics of mediastinal cystic lesions across different imaging modalities are summarized in Table 2.

### Pathology-Based Review of Mediastinal Cystic Lesions

#### Bronchogenic Cyst

Bronchogenic cysts arise from abnormal budding of the tracheobronchial tree during embryogenesis and represent one of the most common congenital cystic lesions of the mediastinum.<sup>12,13</sup> They are typically located in the visceral mediastinum near the carina or mainstem bronchi, although ectopic locations have also been described.<sup>2,3,12</sup> Most lesions are asymptomatic and incidentally detected, while larger cysts may produce cough, chest pain, or compressive symptoms due to mass effect.<sup>12</sup> Approximately 20% of these cysts are intraparenchymal and can cause recurrent infection and, rarely, pneumothorax.<sup>14</sup>

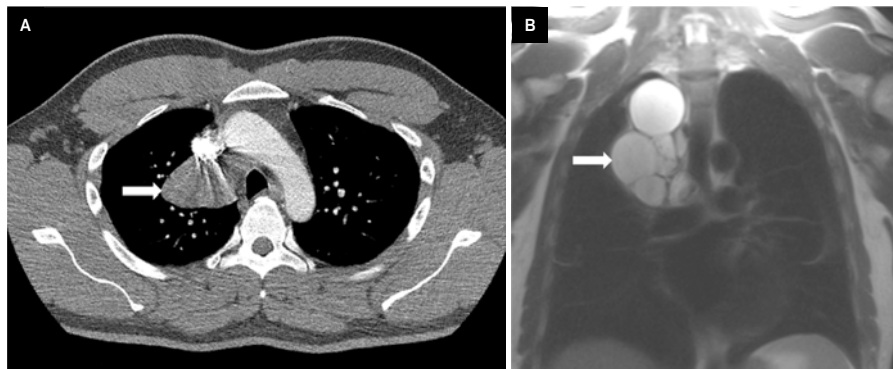
On imaging, bronchogenic cysts appear as well-defined, thin-walled cysts with simple fluid (water) attenuation or higher density fluid due to proteinaceous material on CT. These can be occasionally multilocular with thin internal septations. Air or hemorrhage is less common but

**Table 2. Imaging Features of Mediastinal Cystic Lesions**

| MODALITY | KEY DIAGNOSTIC FEATURES                                                                           | REFERENCE |
|----------|---------------------------------------------------------------------------------------------------|-----------|
| CT       | Defines attenuation, wall calcification, relation to adjacent structures                          | 1,12      |
| MRI      | Superior soft-tissue contrast; high T2 signal; absence of enhancement consistent with simple cyst | 3,13      |
| DWI      | Differentiates cystic lesions from solid tumors; useful for indeterminate CT findings             | 3,14      |
| PET/CT   | Identifies metabolic activity in malignant or solid components                                    | 4         |

*DWI, diffusion weighted imaging.*

**Figure 1.** Bronchogenic cyst. (A) Axial contrast-enhanced CT image demonstrates a well-defined, thin-walled, low-attenuation cystic lesion in the visceral mediastinum superior to the right main stem bronchus. (B) Coronal T2 MRI sequence shows a multilobulated hyperintense lesion superior to the right main stem bronchus with tissue characteristics of a simple bronchogenic cyst.



**Figure 2.** Esophageal duplication cyst. Axial contrast-enhanced CT image demonstrates a well-defined, unilocular, thin-walled cystic lesion in the posterior mediastinum in relation to the right lateral esophageal wall, consistent with an esophageal duplication cyst.



can be seen within these cysts. On MRI, these lesions are characterized by high T2 signal intensity with variable T1 signal based on proteinaceous content, without enhancement or diffusion restriction (Figure 1).<sup>1,3,14</sup> While most asymptomatic cases may be managed conservatively, symptomatic lesions or when diagnostic

uncertainty exists, surgical resection is recommended. Malignant transformation is rare but has been reported.<sup>4,12,14,15</sup>

### Esophageal Duplication Cyst

Esophageal duplication cysts result from incomplete recanalization of the foregut and are most commonly located adjacent to the esophagus in the visceral mediastinum.<sup>2,3</sup> These lesions are frequently asymptomatic but may present with dysphagia or chest discomfort depending on size and location.<sup>2,5</sup> Hemorrhage is a common complication of these cysts that can cause rapid enlargement of the cyst and chest pain.<sup>16</sup> Malignant transformation is exceedingly rare.<sup>2</sup>

Imaging typically demonstrates a unilocular cyst closely associated with the esophageal wall, with homogeneous fluid characteristics on both CT and MRI

(Figure 2).<sup>2,3</sup> Surgical excision is generally recommended in symptomatic patients or when the diagnosis is uncertain.<sup>4</sup>

### Pericardial Cysts

Pericardial cysts arise from incomplete fusion of mesenchymal lacunae during pericardial development and are most commonly located at the right cardiophrenic angle.<sup>13,17</sup> These lesions are usually asymptomatic and incidentally detected, although symptoms may occur due to compression of adjacent structures.<sup>17</sup>

On imaging, pericardial cysts appear as well-circumscribed, thin-walled lesions with homogeneous fluid attenuation on CT and high T2 signal intensity on MRI, without enhancement (Figure 3).<sup>3,17</sup> Larger pericardial cysts are detectable on frontal chest radiograph as well-defined basilar opacities silhouetting cardiac borders. The wall of the cyst can sometimes become calcified. There is no established malignant potential, and asymptomatic lesions may be managed conservatively, with intervention reserved for symptomatic or enlarging cysts.<sup>13</sup>

### Thymic Cyst

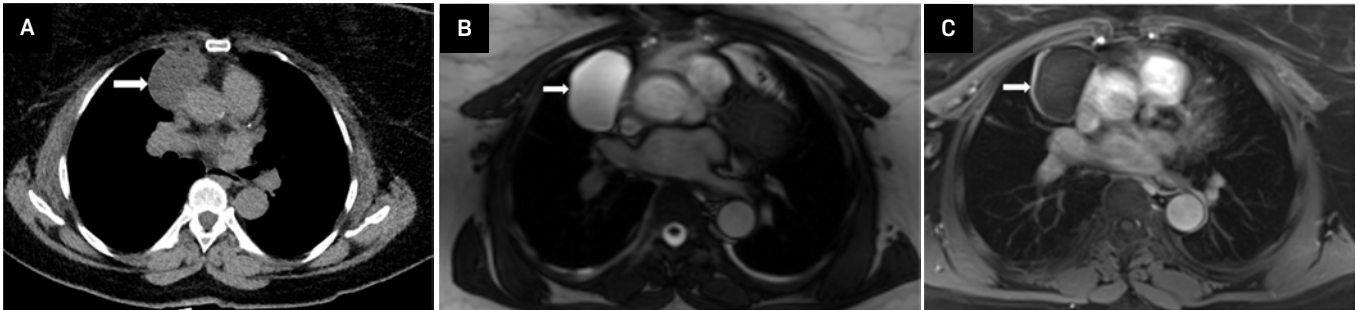
Thymic cysts arise from persistent thymopharyngeal duct remnants and are typically located in the prevascular anterior mediastinum.<sup>10,18</sup> Most lesions are asymptomatic and incidentally detected. While generally benign, multilocular thymic cysts may be associated with underlying thymic neoplasms.<sup>10,18</sup>

On imaging, thymic cysts appear as well-defined unilocular or multilocular cystic lesions with homogeneous fluid attenuation on CT and high T2 signal intensity on MRI (Figures 4, 5). MRI is particularly helpful in excluding internal solid or enhancing components that may raise concern for malignancy.<sup>3,10</sup> Surgical resection is considered when imaging findings are atypical or malignancy cannot be confidently excluded.<sup>4,18</sup>

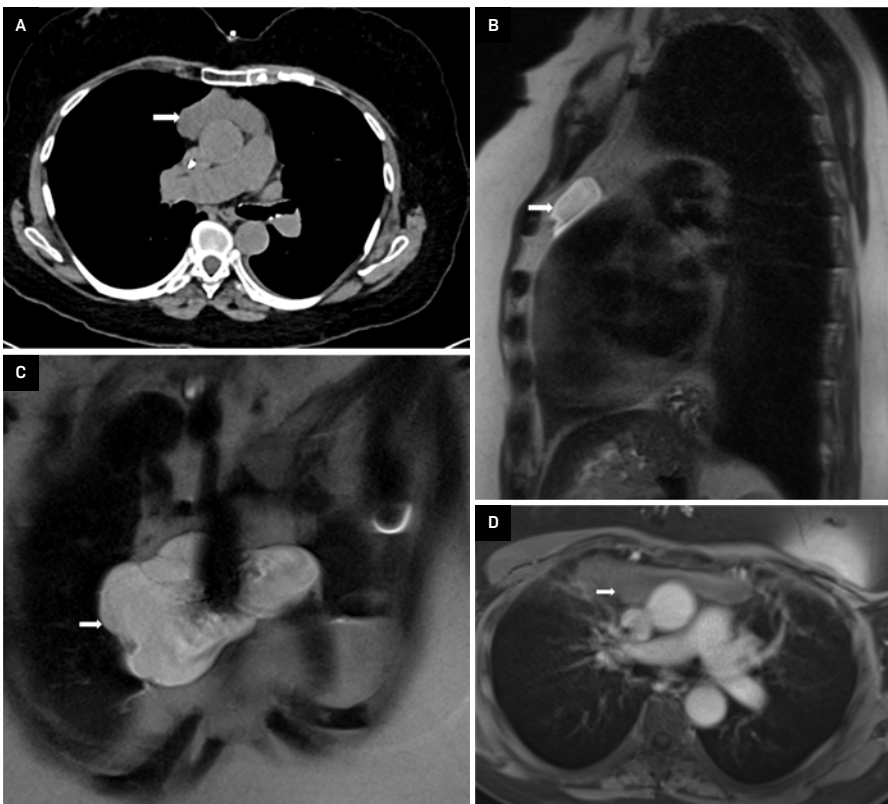
### Lymphangioma

Mediastinal lymphangiomas are uncommon benign cystic structures that

**Figure 3.** Pericardial cyst. (A) Axial noncontrast CT image demonstrates a well-circumscribed, unilocular, cystic mediastinal lesion abutting the ascending thoracic aorta with thin, imperceptible walls. (B) Axial T2-weighted MRI demonstrates homogeneous hyperintense signal of the cyst contents, consistent with simple serous fluid. (C) Axial T1-weighted fat-suppressed post-contrast MRI image confirms peripheral enhancement of the lesion with absence of solid components within the lesion, consistent with a simple pericardial cyst.



**Figure 4.** Thymic cyst. (A) Axial noncontrast CT chest image shows a low-attenuation lesion in the prevascular space. (B, C) Sagittal and coronal T2-weighted MRI images demonstrate the craniocaudal extent of the multilocular lesion with heterogeneous T2 signal, reflecting variable fluid composition across the cystic locules with internal septations consistent with a thymic cyst. (D) Axial post-contrast T1-weighted MRI image shows no enhancement of the lesion in the prevascular mediastinum.



arise from focal proliferation of lymphatic vessels and are most commonly found in the superior aspect of prevascular mediastinum.<sup>19</sup> They are usually asymptomatic and become apparent when there is mass effect on adjacent structures.<sup>20</sup> Complications associated with lymphangiomas include infection,

cystic hemorrhage, chylothorax, and chylopericardium. Standard treatment includes surgical excision if symptomatic. Recurrence is highly unlikely after excision. On CT, lymphangiomas appear as low-attenuation cysts with smooth contours and attenuation could be of simple to complex fluid and fat. On

MR, they are isointense to muscle on T1-weighted images and hyperintense on T2; however, signal could vary based on cystic and proteinaceous content (Figure 6).

Differentials include necrotic tumors, teratomas, thymic cysts, pericardial or bronchogenic cysts, hematomas, goiters, and infectious fluid collections.<sup>21</sup>

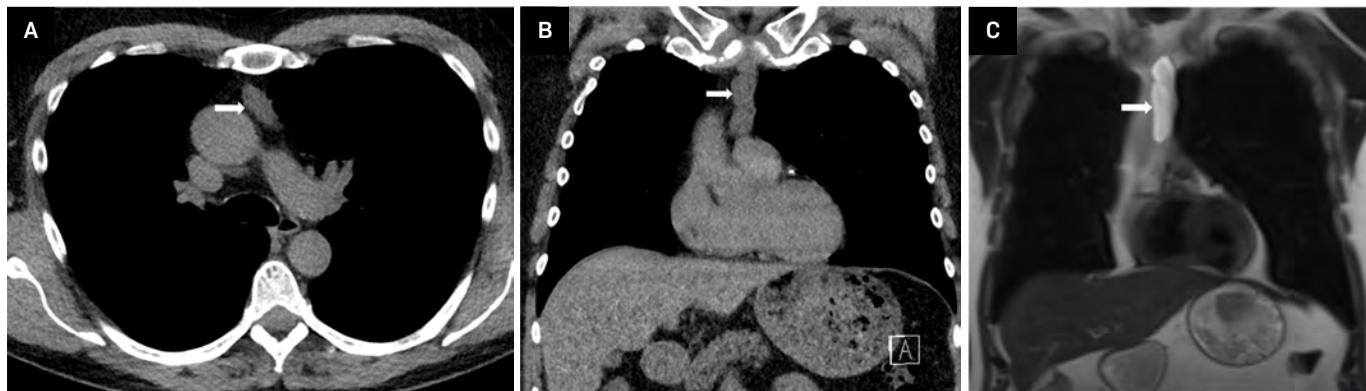
### Cystic Degeneration of Malignant Tumors

Cystic degeneration may occur within malignant mediastinal tumors such as thymomas, germ cell tumors, lymphomas, or metastatic disease.<sup>2,3,8</sup> These lesions may present incidentally or with systemic or compressive symptoms depending on tumor burden.<sup>8</sup> Imaging features suggestive of malignancy include irregular or thickened walls, internal septations, heterogeneous or nodular enhancement, and restricted diffusion on MRI.<sup>1,3,9</sup> Management requires tissue diagnosis and appropriate oncologic treatment.<sup>4,22</sup>

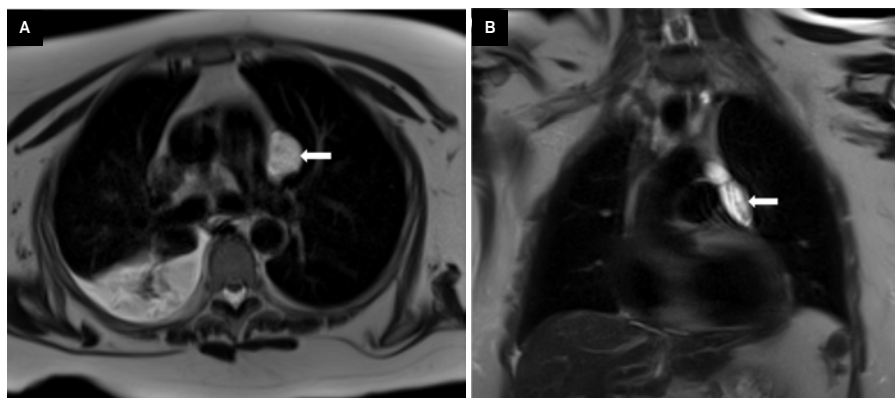
### Infectious and Inflammatory Cyst-Like Lesions

Cyst-like lesions may develop secondary to infection, hemorrhage, or abscess formation.<sup>1,8</sup> Pseudocysts resulting from pancreatitis can also extend into the visceral mediastinum.<sup>23</sup> Patients may present with fever, chest pain, or systemic signs of infection.<sup>1,3</sup> Imaging typically demonstrates complex cystic lesions with surrounding inflammatory changes and possible enhancement.<sup>3</sup> Management includes antibiotic therapy and drainage,

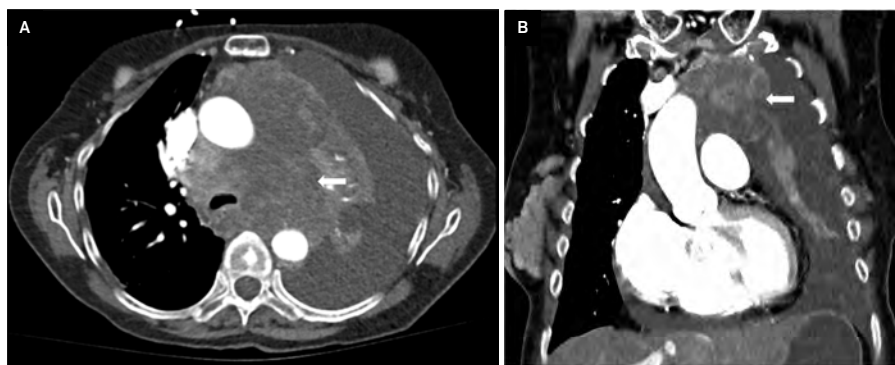
**Figure 5.** Thymic cyst. (A, B) Axial and coronal noncontrast CT images demonstrate a well-defined, low-attenuation cystic lesion in the prevascular anterior mediastinum. (C) Similar lesion on coronal T2-weighted MRI sequence shows hyperintense lesion consistent with thymic cyst.



**Figure 6.** Lymphangioma. (A, B) Axial and coronal T2-weighted MRI sequences showing a T2 hyperintense visceral mediastinal lesion abutting the pulmonary artery, which represents lymphangioma.



**Figure 7.** Necrotic mediastinal lymph nodes. (A, B) Axial and coronal contrast CT images show conglomerated enlarged mediastinal lymph nodes in the prevascular and visceral mediastinum. Extensive necrosis of lymph nodes is seen, mimicking complex cystic mediastinal lesions.



with surgical intervention reserved for complicated cases.<sup>4,22</sup>

### Important Mimics of Mediastinal Cystic Lesions

Several noncystic entities may closely mimic mediastinal cystic lesions on

imaging and should be carefully considered in the differential diagnosis.<sup>1-3</sup> Pericardial recesses represent normal anatomic variants that may appear as well-defined fluid collections along the pericardium, particularly adjacent to the great vessels.<sup>1,2</sup> Recognition of their

characteristic locations, continuity with the pericardial space, and lack of mass effect is essential to avoid misdiagnosis.<sup>3</sup>

Necrotic or cystic lymph nodes may also simulate mediastinal cysts, particularly in the setting of malignancy, infection, or inflammatory disease.<sup>1,2,22</sup> Unlike simple cysts, necrotic lymph nodes often demonstrate irregular or thickened walls, peripheral or nodular enhancement, and restricted diffusion on MRI, which can aid in differentiation (Figure 7).<sup>9,22</sup>

Other important mimics include cystic teratomas and chronic infectious or granulomatous processes.<sup>2,8,10</sup> These entities may demonstrate heterogeneous internal components, fat, calcifications, or variable enhancement patterns, features that are atypical for simple cysts.<sup>2,10</sup> Careful assessment of imaging findings in conjunction with clinical context and multimodality imaging is the key for distinguishing these conditions from true mediastinal cysts.<sup>1,5,22</sup>

### Treatment of Cystic and Cyst-Like Mediastinal Lesions

Management is individualized based on symptoms, lesion growth, imaging characteristics, and diagnostic certainty.<sup>4,12,22,24</sup> Surgical resection is recommended for symptomatic lesions, enlarging cysts, or lesions with suspicious imaging features, whereas conservative surveillance may be appropriate for asymptomatic congenital cysts with classic imaging appearances in patients with reliable follow-up.<sup>4,22</sup>

## Conclusion

Cystic mediastinal lesions and their mimics have overlapping imaging features. It is very important to adopt an organized approach, including lesion localization, imaging features, and clinical information, which helps to narrow down the differentials. Even though CT is the first-line imaging technique, MRI plays a critical role in differentiating simple and benign lesions from complex and malignant lesions. Together, these complementary modalities enable confident diagnosis and guide appropriate treatment.

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# Breast Arterial Calcifications on Mammography: AI Assessment and Cardiovascular Risk

Alyssa T. Watanabe, MD; Christopher Liu; Emma Yuguchi; Jared Patterson

Cardiovascular disease (CVD), not breast cancer, is the leading cause of death in women, who are more likely than men to be diagnosed at later stages of CVD and to experience poorer outcomes following myocardial infarction. Because mammography is performed worldwide for breast cancer screening, it also provides an opportunity to identify breast arterial calcification (BAC), a known cardiovascular risk marker, thereby serving the dual purpose of screening for breast cancer while providing potentially important information about cardiovascular risk. Despite this opportunity, radiologists infrequently report BAC when it is detected.

In 2023, the Canadian Society of Breast Imaging issued a position statement recommending BAC reporting, along with severity grading.<sup>1</sup> The recently released *BI-RADS v2025 Manual* (previously referred to as BI-RADS 6th Edition) now explicitly acknowledges the association between BAC and CVD, although BAC reporting remains optional.<sup>2</sup> On April 11, 2026, Maryland House Bill 1364 was unanimously passed, mandating that the presence of BAC on all screening mammograms be reported to patients

in lay-language result letters, effective October 1, 2026.<sup>3</sup> Other states may follow.

Artificial intelligence (AI) can assist with quantification of BAC severity and age-based percentile scoring on mammography, allowing for further stratification of cardiovascular risk.<sup>4</sup> A large-scale University of California San Diego study<sup>5</sup> of more than 18,000 women using an experimental AI model demonstrated that each 10-point increase in BAC score was associated with a higher risk of mortality (HR 1.08; 95% CI 1.06-1.11) and the composite of mortality and major adverse cardiovascular events (MACE) (HR 1.08; 95% CI 1.06-1.10) (Figure 1).

BAC progression on serial mammography is also tied to a further elevation of cardiovascular risk. A study of over 10,000 women presented at the Radiological Society of North America in December 2025<sup>6</sup> showed that BAC can progress in as little as 1 year. The faster the progression, the greater the risk of cardiovascular events, especially for women under age 65. The risk of MACE and death in women who were BAC-negative and converted to BAC-positive was 41% higher, and 59% higher in those who transitioned from a lower to a higher

category of BAC. Those who started in the intermediate category and transitioned to the highest severity category had a 93% higher risk of MACE. Women in the highest BAC percentile category had up to twice the risk of MACE compared with women who did not have BAC.<sup>6</sup>

AI is widely used as an aid in mammography interpretation, with many products available to assist with breast cancer detection, density categorization, and risk scoring. Only 2 AI software vendors have commercially available products for binary reporting (presence/absence) of BAC: CureMetrix cmAngio version 1.0 (CureMetrix, San Diego, California) and DeepHealth BAC Assessment (Radnet, Cambridge, Massachusetts).

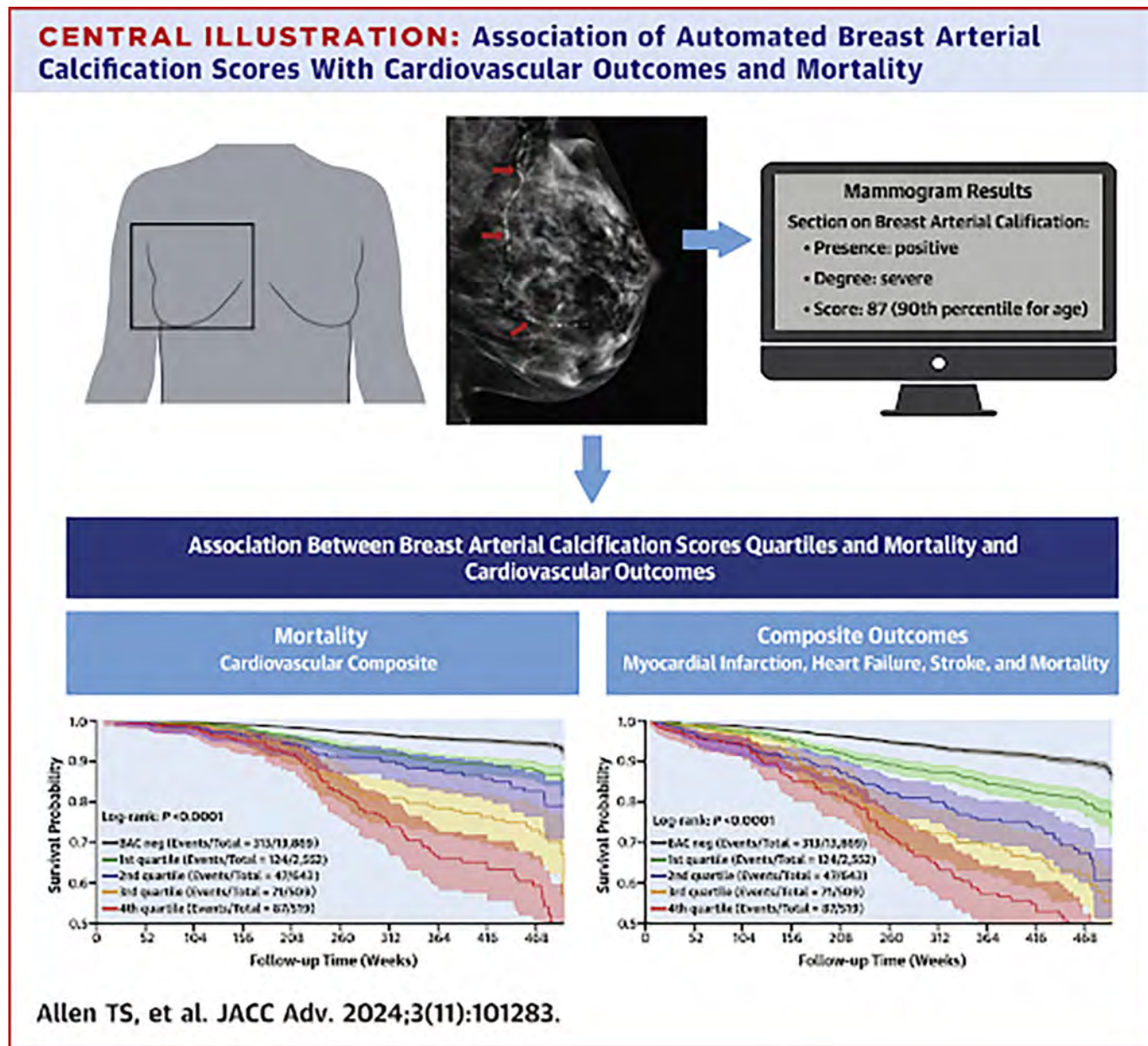
A newer version of CureMetrix's software (2.0), cleared in July 2026, also provides AI-based quantitative measurement of BAC based on BAC length and generates an age-based percentile score for comparison with reference data. The Deep Health and CureMetrix BAC detection products are cleared for both full-field digital mammography and digital breast tomosynthesis and show high performance across all tissue densities.<sup>7,8</sup>

Reimbursement remains a barrier to clinical implementation of AI-based BAC assessment. Coverage varies, and some facilities offer AI-assisted services on a self-pay basis. As of January 2025, BAC reporting is again included as a quality measure under Medicare's

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**Figure 1.** Association of breast arterial calcification with cardiovascular outcomes and mortality using artificial intelligence-based scoring. Reproduced with permission from Allen et al.



Merit-based Incentive Payment System (MIPS), designated QMM28.<sup>8</sup> Under the MIPS measure, the presence or absence of BAC must be reported for screening mammograms performed in women aged 40 years and older. When BAC is present, the report must include either a statement addressing its clinical relevance—for example, noting the association between BAC and CVD and/or coronary artery disease independent of other known

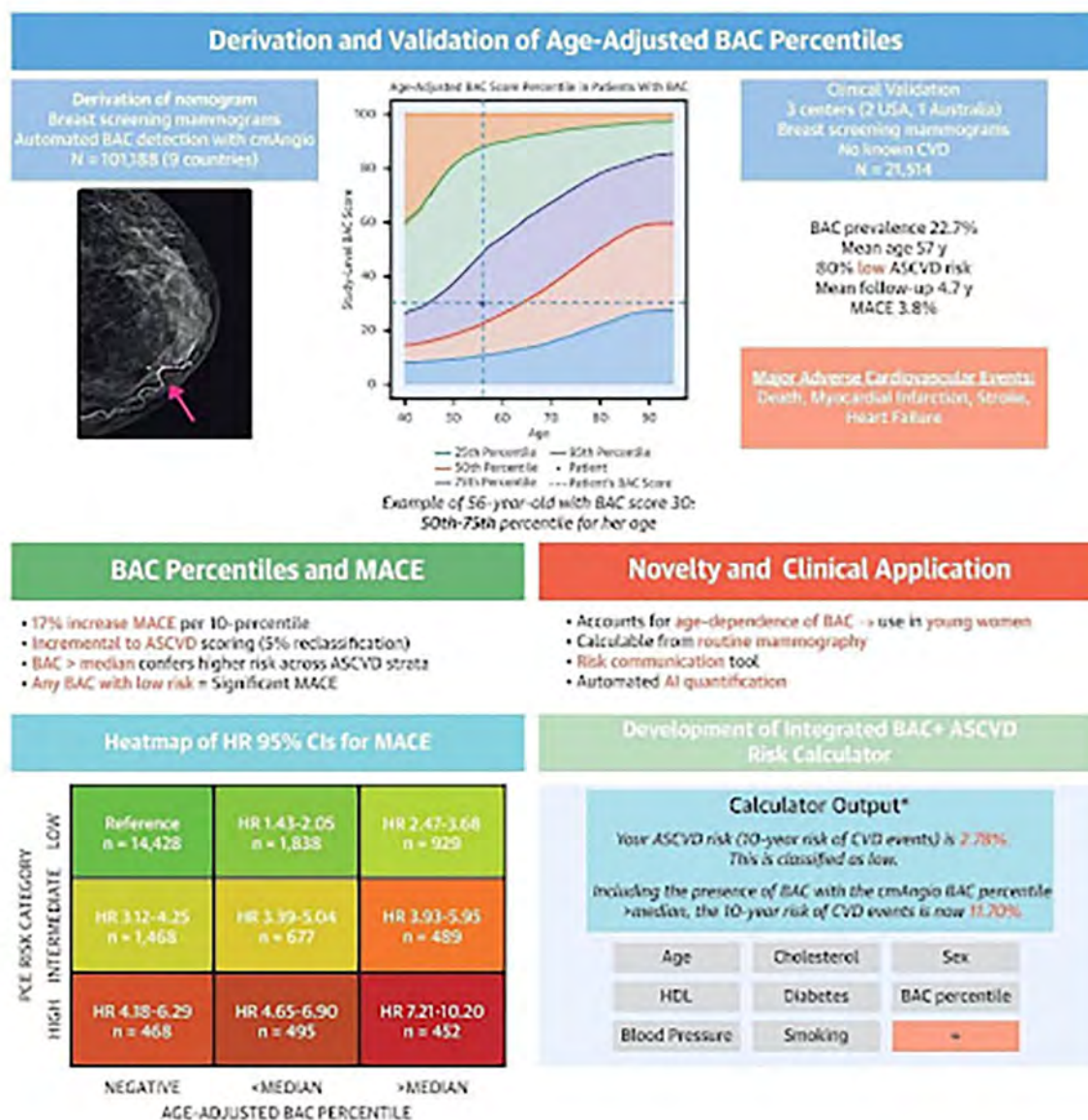
risk factors—or a recommendation for appropriate follow-up.

Current CVD risk assessment tools may underestimate risk in women. Mammography provides a simple, opportunistic means of identifying CVD risk without additional radiation exposure or a separate patient encounter. Unlike BAC assessment on an existing mammogram, coronary artery calcium scoring by CT requires

a separate examination and involves additional radiation exposure, procedural time, and potentially additional patient expense, depending on insurance coverage. A published survey found that most clinicians would prefer BAC to be reported, including the severity of calcification. Most physicians also indicated that the presence of BAC could prompt further evaluation for CVD and associated risk factors.<sup>9</sup>

**Figure 2.** Age-adjusted breast arterial calcification (BAC) percentile scores are tied to elevated risk of major adverse cardiovascular events (MACE). Reproduced with permission from Nerlekar et al.<sup>4</sup>

## CENTRAL ILLUSTRATION: Age-Adjusted BAC Percentiles Enhance ASCVD Risk Prediction in Women



Nerlekar N, et al. JACC Cardiovasc Imaging. 2026;19(6):735-748.

Reporting of BAC severity and progression on sequential mammograms may aid in identifying subgroups of women who are at the greatest cardiovascular risk. According to Matthew Nudy, MD, a cardiologist at Penn Health, “because BAC is already visible on

routine screening mammograms, I see it evolving into a standardized, artificial intelligence-enabled ‘cardiovascular risk enhancer’ that can be reported consistently and used to trigger a focused cardiovascular risk-factor assessment and subsequently used to intensify

guideline-based preventive therapies such as statins and intensive blood pressure control.”

AI-based severity scoring of BAC may help to further improve the ability to predict risk and prevent cardiovascular mortality in women (Figure 2). The next

step in building acceptance of this risk marker in clinical care is demonstrating that BAC-informed care can improve clinical outcomes, not just the prediction of risk.

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# Growth and Gains in Remote Diagnostic Mammography

Kerri Reeves, BA

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Remote interpretation is well established in screening mammography, helping health systems achieve timely reads and provide patient access to specialty expertise. As the radiologist shortage persists amid increasing breast imaging volumes, many systems now use a remote model for diagnostic reads, which presents new opportunities and challenges.

“Several factors are driving the growth of remote breast imaging, one of the biggest being the nationwide shortage of breast imaging radiologists,” says Rajshri N. Shah, MD, Medical Director of Breast Imaging, Radiology Care Division at Prisma Health, Greenville, South Carolina. “At the same time, demand for services continues to increase as screening programs expand, awareness improves, and more women undergo supplemental and high-risk screening.”

Diagnostic interpretations require more than quality image transmission; they demand continuity for timely clinical decision-making. As practices face the workflow, staffing, and technology complexities of maintaining this continuity, market forces continue to shift in support of this growing remote model.

“Remote diagnostic mammography is being driven by the convergence of several needs,” Dr Shah says, “addressing workforce shortages, improving access to specialized breast imaging expertise, supporting radiologist well-being, and ensuring that patients continue to receive timely, high-quality care.”

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### The Demand for Remote Reading

A shortage of breast radiologists is hindering timely access to diagnostic breast imaging

services—especially in rural and underserved areas—while radiologist burnout is adding to workforce challenges.<sup>1</sup> A recent study found that remote diagnostic breast imaging offers a practical, forward-looking solution for practices to expand service capacity, reach geographically distant populations, or mitigate burnout.<sup>1</sup>

Factors contributing to growth include expanded patient awareness of mammography, supplemental screening, and risk factors. As a health system grows its screening volumes, diagnostic reads also go up, increasing wait times, explains Julie A. Ritner, MD, staff radiologist at the Cleveland Clinic.

“We saw that if patients couldn’t get in here, they would go to a different hospital system to get in sooner,” which Dr Ritner says is “understandable.”

For hospitals, breast imaging is “a big pull to bring women in,” says Dr Shah, noting that “every hospital wants robust breast imaging—diagnostic mammography, interventional procedures, MRI—they want the full spectrum of breast imaging and intervention we can offer.”

This demand creates patient access challenges and delays that come at a cost. Remote diagnostic reading can help expand access to high-quality care, particularly in rural areas and satellite clinics, while freeing on-site breast imagers to focus on procedures including biopsies and pre-surgical localizations, Dr Shah adds.

From the physician perspective, flexibility has also become an important consideration. “Remote and hybrid work models can improve work-life balance and reduce burnout, which helps with retention of experienced breast imagers,” explains Dr Shah, particularly for highly specialized radiologists who may not live near the facilities they serve. “Given the workforce challenges facing

## Four Principles for Redesigning Radiologist Work

Remote diagnostic mammography interpretation is not just about redistributing reads across locations; it also provides an opportunity to reevaluate how tasks are organized.

According to Dr. Ritner, Cleveland Clinic developed an approach to managing growing case volumes by structuring the work of radiologists around four guiding principles:

- 1. Uniformity:** Group similar work functions within defined time blocks rather than repeatedly switching among different types of studies. For example, a radiologist might spend the morning interpreting remote diagnostic studies and the afternoon performing on-site procedures.
- 2. Predictability:** Establish a reasonable pace and defined workload for each time block. Assignments are standardized according to what the group can reasonably accomplish within the allotted time.
- 3. Flexibility:** Batch tasks that do not require an immediate response. Screening mammography, breast MRI, and automated breast ultrasound can be interpreted asynchronously, giving radiologists greater control over their workflow and more time for focused work.
- 4. Variability:** Vary the type of work from one time block to the next to improve engagement and reduce burnout. For example, moving from screening or MRI in the morning to diagnostic interpretation in the afternoon can provide a break from repetitive tasks and reduce monotony.

These principles support a workflow that is both structured and predictable without becoming rigid, Dr. Ritner says. For departments transitioning to remote diagnostic mammography interpretation, the model offers a way to improve efficiency and manage volume, while helping to address radiologist burnout.

our specialty, retaining skilled radiologists is just as important as recruiting new ones.”

### Remote Setup Requirements

Remote breast imaging reads commonly occur at home workstations, while some practices leverage centralized remote reading hubs. While the pandemic normalized the practice, the technology has also become much more accessible, Dr Shah reports, noting that most radiology groups can easily implement remote reading with strong IT support. FDA-cleared high-resolution diagnostic monitors—typically two 5-megapixel monitors or one 10-12-megapixel monitor—which have dropped in price over the last several years, must be FDA-approved to achieve high brightness levels and calibrated to Digital Imaging and Communications in Medicine standards to ensure radiologists can distinguish subtle tissue density differences, Dr Shah explains. Secure virtual private network access, reliable high-speed internet, voice recognition software, and robust reporting and

picture archiving and communication systems are standard for remote mammography.

Quality assurance is typically performed annually by a trained physicist, or can be automated remotely to verify monitor performance and calibration. Remote diagnostic mammography requires compliance with the Mammography Quality Standards Act and applicable state licensure requirements, including quality-control and annual-survey requirements for remote review workstations, as well as facility accreditation.

Hardware aside, systems for real-time communication with technologists and patients are particularly critical, says Dr Shah.

“The [workstation] technology is increasingly accessible, but successful implementation depends just as much on communication, workflow integration, and collaboration.”

Diagnostic exams are dynamic in a way that screening isn't: radiologists may have to review images, direct technologists with additional instructions, integrate prior patient data, and communicate with clinical team members, all to determine next care steps for a patient who's at the imaging center.

“Communication is the most critical component. When the technology is in place and communication channels are strong, remote breast imaging can provide the same high-quality interpretation and patient-focused care as on-site reading,” Dr Shah asserts. “The goal is not simply to move the reading location; it’s to maintain the same level of expertise, collaboration, and responsiveness regardless of the radiologist’s location.”

Dr Shah messages with patients through Epic and uses videoconferencing tools or her iPhone to communicate with both the care team and patients. “Make sure that you make it very easy ... [for them] not to feel that lapse of face-to-face interaction,” Dr Shah advises radiologists. “Be open to the different types of workflows people feel comfortable with.”

Staffing highly trained mammography and US technologists is also critical, Drs Shah and Ritner agree, noting that strong relationships built on trust are paramount. Ongoing education, mentorship, and standardization of communication regarding exams facilitate quality diagnostic interpretation. Emerging real-time collaboration technologies are also making it possible for remote radiologists to view US exams and provide live direction to sonographers.

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### Efficient Workflow Considerations

At the Cleveland Clinic, where at one point wait times from an abnormal screening mammogram to a diagnostic appointment had exceeded 40 days, remote diagnostic mammography became a means to achieve smarter breast imaging coverage.

Increasing volumes and growing system inefficiencies meant that radiologists were being underutilized, Dr Ritner says, and experiencing “chaos and exhaustion.”

“There was a lot of [...] inefficiency for the radiologists traveling across our [12] sites.”

With the framing of breast care as a value stream and a plan to consolidate diagnostic cases in a central queue, Dr Ritner worked with Cleveland Clinic’s Continuous Improvement team on Lean principles to eliminate waste.

Dr Ritner explains that diagnostic imaging work is typically riddled with interruptive tasks, or “pushes” whenever a need arises. By transforming tasks into “pulls” that radiologists can perform during designated timeframes via a shared worklist, they are able to work with greater focus and efficiency. Using principles of uniformity, predictability, flexibility, and variability, the department determined a goal pace for remote diagnostic reads and batched them together, standardized processes, and dedicated other tasks to separate time blocks.

“The result was that you can see more patients, and that you can do more work.”

After optimizing diagnostic reads remotely, the clinic has consistently reduced the wait time to 10 days or less, with next-day availability at some sites.

“We always knew we had inefficiencies in our workdays, and our workflow restructuring has produced results that are even more dramatic than we ever expected,” Dr Ritner says of the improvements, noting the remote program has also become a tremendous recruitment advantage.

The department has hired 3 radiologists this year with more on the horizon, bringing their physician total to 25.

“Restructuring our work model has allowed us to offer more remote scheduling options, which has resulted in recruiting experienced remote radiologists while also providing local radiologists with greater flexibility in their schedules. This flexibility has allowed us to expand our capacity and improve access, enabling us to serve up to 14% more patients this year than in the past,” Dr Ritner concludes.

“This model allows you to provide the same level of expert care system wide. It’s really been transformative.”

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# Invasive Ductal Carcinoma in a Post-Transplant Male

Othria Ahmed, MD; Sarah Siddiqui, BS; Ekta Gupta, MD; Suzanne McElligott, MD

## ABSTRACT

Male breast cancer is rare, representing less than 1% of breast cancer cases, and is often diagnosed at a later stage due to a low index of clinical suspicion. This is the case of an invasive ductal carcinoma in a middle-aged man with a history of cardiac transplantation and long-term immunosuppressant use. The patient presented with a breast lump found on self-examination, which was then evaluated with diagnostic mammography and US. Imaging demonstrated a suspicious retroareolar mass with associated nipple retraction, and subsequent US-guided core biopsy confirmed moderately differentiated invasive ductal carcinoma (ER-positive, PR-positive, HER2-negative). This case highlights the importance of maintaining clinical suspicion for breast malignancy in male patients presenting with a new breast mass, even in the absence of traditional risk factors such as family history of breast cancer. Thorough clinical evaluation and appropriate diagnostic imaging can facilitate early detection and treatment of male breast cancer.

**Keywords:** male breast cancer, invasive ductal carcinoma, breast imaging, mammography, cardiac transplantation

## Case Summary

A middle-aged man presented to his cardiologist with a 1-month history of a newly noticed right breast lump. He had a history of nonischemic cardiomyopathy requiring a heart transplant and had been on immunosuppressants for the past 2 years. His family history was significant for colon cancer in his mother and prostate cancer in his father. He had no personal history of prior malignancy. Given the new palpable breast mass, the patient was referred for dedicated breast imaging for further evaluation.

## Imaging Findings

Diagnostic mammography of bilateral breasts was performed with a dermal marker placed over the patient's palpable lump. In the right retroareolar location, corresponding to the region of concern, a mass with irregular margins was identified with associated nipple retraction (Figure 1). US revealed a correlating 17-mm irregular hypoechoic mass at the right breast 10 o'clock retroareolar position (Figure 2). No abnormal axillary lymphadenopathy was identified on imaging.

Diagnostic imaging was reported as BI-RADS 4C "high suspicion for malignancy," with recommendation for US-guided core biopsy. Subsequent US-guided core biopsy demonstrated moderately differentiated invasive ductal carcinoma (IDC) (ER-positive, PR-positive, HER2-negative). Breast MRI demonstrated an 18-mm retroareolar enhancing mass with washout kinetics, associated skin thickening (Figure 3), and nipple retraction.

## Diagnosis

Ultrasound-guided core biopsy revealed moderately differentiated IDC (ER-positive, PR-positive, HER2-negative).

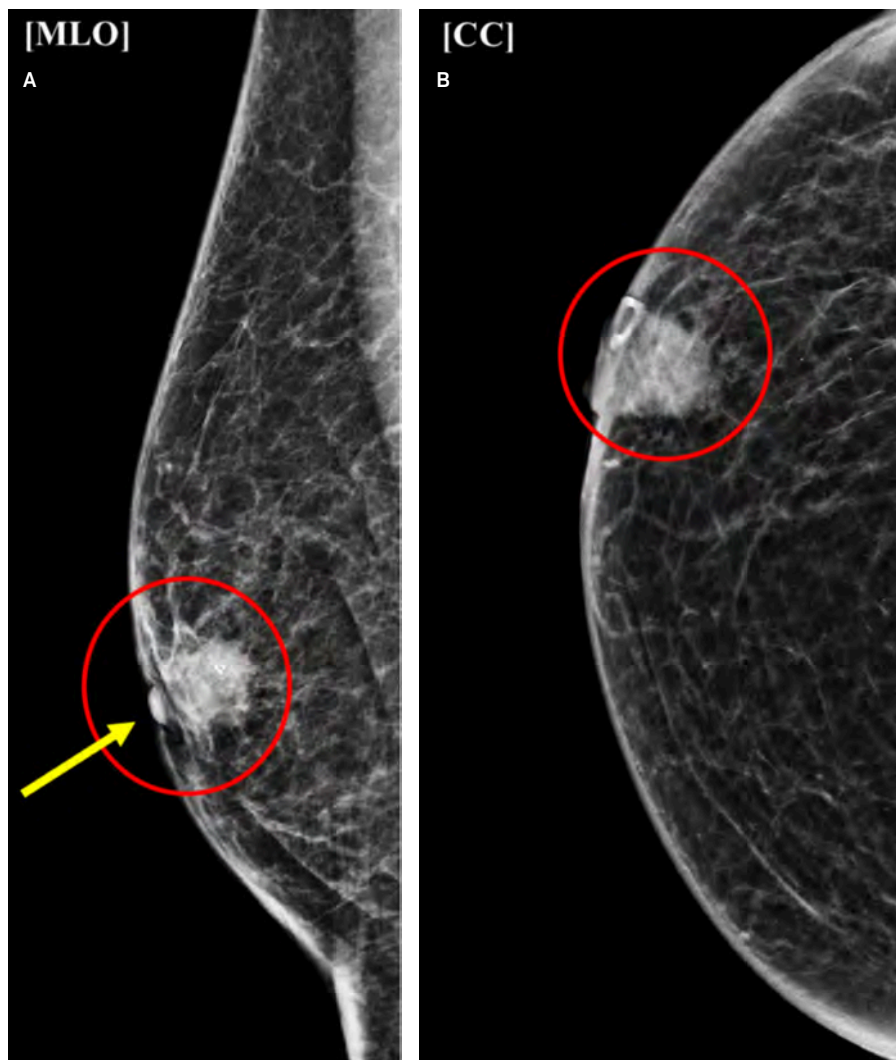
The differential diagnosis includes gynecomastia, intraductal papilloma, myofibroblastoma, and metastatic mass.

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**Figure 1.** Mediolateral oblique (MLO) (A) and craniocaudal (CC) (B) diagnostic mammogram views of the right breast. Palpable marker best seen on CC view (B) was placed over the lump as indicated by the patient. Within this region, there is a high-density irregular mass with indistinct margins (red circles). There is mild right nipple retraction (yellow arrow).



## Discussion

Breast cancer in males is rare, representing less than 1% of the cases of breast cancer. Although genetic factors are commonly discussed in relation to male breast cancer, the cause is largely multifactorial. Occupational exposure to ionizing radiation is associated with an increased lifetime risk of developing breast cancer. Additionally, underlying medical conditions that alter hormonal homeostasis, such as liver dysfunction and thyroid disease, may increase risk. Certain

medications can similarly contribute to altering the estrogen/testosterone balance in men, thereby increasing the risk of breast cancer.<sup>1</sup> There is no routine screening for male breast cancer, making assessment of risk factors key in detection. The most common presenting symptom in males is a painless, unilateral breast mass with possible secondary symptoms such as nipple retraction and discharge.<sup>1</sup>

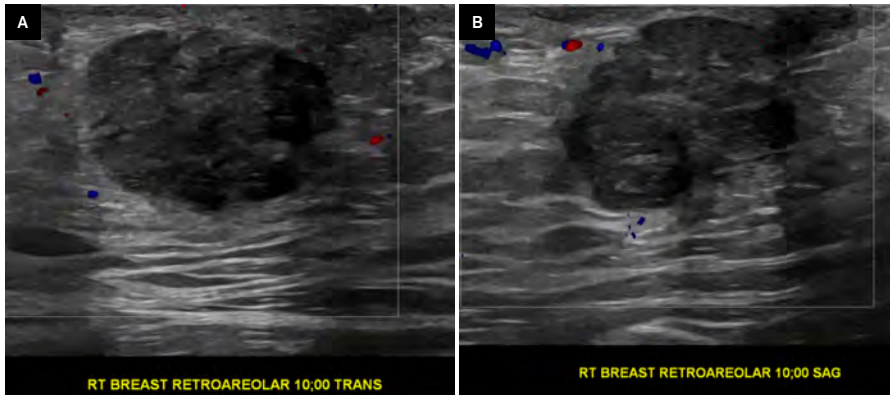
Invasive ductal carcinoma accounts for approximately 85% of male breast cancers. Due to lack of lobular development in males, the risk of developing tumors with

a lobular origin, including invasive lobular carcinoma, phyllodes tumors, fibroadenomas, and lobular carcinoma in situ, is less common than in women.<sup>2</sup> On imaging, male breast cancer typically presents as a round or irregular mass that is either subareolar or eccentric to the nipple and may demonstrate spiculated or circumscribed margins. Associated findings can include skin thickening and nipple retraction.<sup>3</sup> Calcifications may be present but are less common than in female breast cancer. On US, male breast cancers can show varying levels of posterior acoustic enhancement and shadowing as well as varying levels of internal vascularity.<sup>2,3</sup> Differentiation of atypical gynecomastia and other benign etiologies may not be possible with imaging alone. US can aid with further evaluation and planning for biopsy when needed.

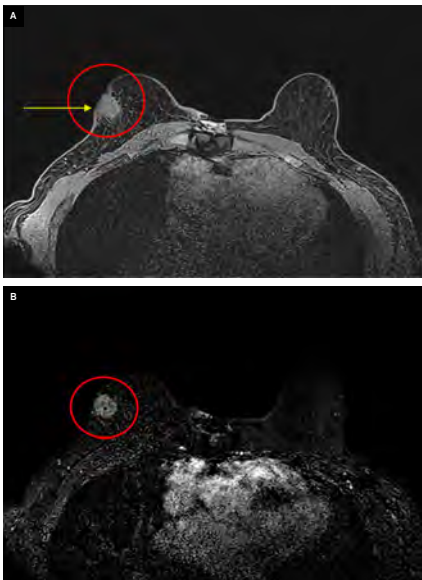
Despite representing less than 1% of cancer in men, male breast cancer carries a significantly lower 5-year survival rate compared with women.<sup>4,5</sup> Age of onset, stage at time of diagnosis, and low index of clinical suspicion are factors that contribute to the male breast cancer mortality rate. In this case, the patient had no history of cancer, negative family history for breast cancer, and unknown BRCA genetic testing, which would indicate a low suspicion for overall risk of breast cancer.<sup>3</sup> No formal lifetime-risk assessment is available for males currently as Tyrer-Cuzick and Gail risk assessments are optimized for women.

Additional risk factors include hormonal treatment and certain medications. Estrogen exposure has been linked to an increased incidence of breast cancer in males. In this case, the patient had been taking tacrolimus, an immunosuppressant, for more than 2 years. Chronic immunosuppression is routinely used following solid-organ transplantation and is associated with a higher risk of cancer, most notably nonmelanoma skin cancer.<sup>6</sup> Compounding the general risk of malignancy, studies have demonstrated the increased

**Figure 2.** Targeted US evaluation of the right retroareolar region of concern transverse (A) and sagittal (B) color flow images demonstrates an irregular hypoechoic mass with microlobulated margins. Internal vascular flow was not appreciated.



**Figure 3.** Contrast-enhanced breast MRI precontrast (A) and initial postcontrast subtraction (B) completed 1 month after initial diagnostic mammogram and US demonstrated an enhancing mass with overlying skin thickening (yellow arrow). No additional suspicious enhancing findings were identified.



risk of cancer in patients with overall cumulative tacrolimus exposure.<sup>7,8</sup> In the absence of traditional risk factors

like genetics, this history of organ transplant with chronic immunosuppression may have elevated the patient's overall risk for cancer. Although the evidence directly linking immunosuppressive therapy and male breast cancer is limited, this case highlights the need for further investigation into a potential relationship between immunosuppression, transplantation, and breast cancer in male transplant recipients.

## Conclusion

Male breast cancer is rare, with IDC representing the most common histological subtype. Mortality is generally higher in men than in women, largely due to delay in diagnosis. Mammography and US are valuable tools for detecting breast cancer, although they are not routinely performed in male patients. Despite the lower incidence of breast cancer in men compared with women, it is crucial to perform risk stratification. This includes assessing genetic predisposition, exploring comorbidities and medication history, and performing

thorough physical exams. In this case, the patient's self-examination led to swift dedicated imaging and multidisciplinary treatment evaluations. Although there is limited literature regarding the association between breast cancer and common immunosuppressant therapies such as tacrolimus, being aware of all these potential contributing factors is important and can reduce overall mortality in men through early detection and treatment.

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# Renal Arteriovenous Fistula

Luke Carson, BS; Martin Rindahl, MD

## Abstract

Arteriovenous (AV) fistulas are rare vascular anomalies that can cause high-output cardiac failure due to significant AV shunting. We report a case of a middle-aged patient presenting with progressive heart failure and abdominal pain. The patient was initially suspected of having hydronephrosis on grayscale US. However, color Doppler imaging subsequently revealed extensive vascular flow within the renal pelvis, excluding obstruction. CTA confirmed a large AV fistula between the right renal artery and right renal vein, with marked dilation of the renal vasculature and inferior vena cava. This case highlights the importance of Doppler imaging in avoiding misdiagnosis and demonstrates the role of CTA in characterizing renal vascular pathology. Early recognition of renal AV fistulas is critical given their potential for severe hemodynamic consequences.

**Keywords:** arteriovenous fistula, renal arteriovenous fistula, high-output heart failure

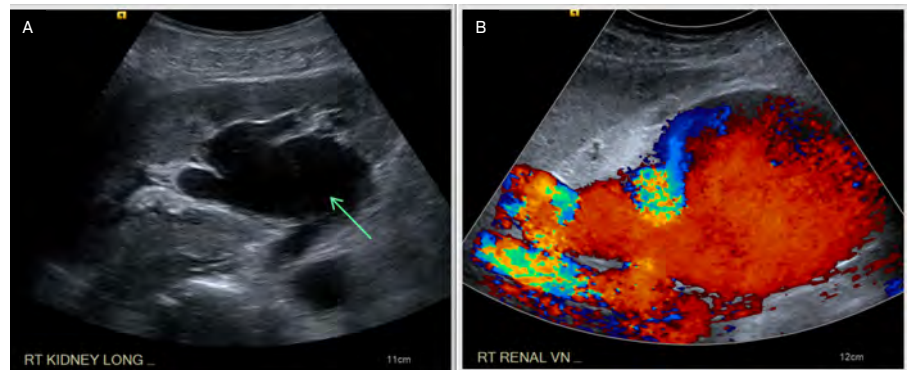
## Case Summary

An adult with a several-month history of progressive congestive heart failure presented to the emergency department with shortness of breath and generalized abdominal pain. Initial grayscale-only abdominal US demonstrated findings interpreted as severe right hydronephrosis. The patient was discharged but presented several weeks later to his primary care provider with continued shortness of breath, prompting concern for renal pathology based on the prior imaging findings.

## Imaging Findings

Grayscale sagittal US of the right kidney (Figure 1) demonstrated an anechoic region within the renal hilum concerning

**Figure 1.** (A) Sagittal grayscale US of the right kidney demonstrating an anechoic region within the renal hilum (arrow) concerning for collecting system dilatation. (B) Sagittal US with color Doppler showing marked color Doppler flow in the same region. Turbulent flow is noted in the dilated renal vein.



for renal collecting system dilatation. Color Doppler imaging, however, revealed extensive arterial and venous flow within the same region, excluding obstruction and raising concern for a high-flow

vascular abnormality. Marked turbulent flow was identified within a markedly dilated renal vein, suggesting the presence of an AV shunt.

Axial CTA (Figure 2) confirmed a large renal AV fistula with marked dilation of the right renal artery, right renal vein, and inferior vena cava. The right renal artery measured up to 1.6 cm in diameter, with direct communication to the right renal vein at the renal hilum. The right renal vein measured up to 9.8

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**Figure 2.** (A) Axial CTA image at the level of the mid right kidney demonstrating marked dilatation of the right renal artery (RRA), right renal vein (RRV), and inferior vena cava (IVC). Fistulous communication (F) is noted between the right renal artery and vein. (B) Coronal CTA image providing anatomic orientation with the aorta (Ao) and dilated RRA, RRV, and IVC. (C) Sagittal CTA image clearly depicting the fistula (F) between the RRA and RRV and the associated dilatation of these vessels.



cm in diameter centrally, tapering at its junction with the inferior vena cava. The inferior vena cava was enlarged, with reflux into the hepatic veins reflecting elevated right-sided pressures. Coronal and sagittal images (Figure 2) further delineated the fistulous tract and extent of venous dilation, with associated mass effect on adjacent structures.

## Diagnosis

Congenital right renal AV fistula resulting in high-output cardiac failure.

Differential diagnosis includes hydronephrosis, renal vein thrombosis, venous malformation, and arteriovenous malformation (AVM).

## Discussion

Renal AV fistulas are abnormal direct communications between the renal arterial and venous systems. Most of these entities are acquired, accounting for approximately 70% of cases, but about 20% are congenital.<sup>1</sup> Acquired fistulas most often result from iatrogenic injury following renal biopsy, surgery, or other percutaneous interventions.<sup>2</sup> Less commonly, they may arise from trauma, inflammation, renal malignancy,

or rupture of a renal artery aneurysm.<sup>2</sup> Their reported incidence ranges from 0.3% to 19% in native kidneys and 6% to 8% in renal allografts.<sup>1</sup> Renal AV fistulas significantly alter normal hemodynamics by allowing arterial blood to bypass the renal parenchyma and shunt directly into the venous system. This abnormal flow leads to progressive dilation of the renal vein and inferior vena cava and increases venous return to the heart. Over time, the chronic volume load may precipitate high-output cardiac failure, particularly in large, high-flow fistulas.<sup>3,4</sup>

Clinical manifestations include hematuria, flank pain, abdominal bruit, hypertension, and, in severe cases, high-output cardiac failure.<sup>2,5</sup>

Management depends on fistula size and symptomatology. Small, asymptomatic AV fistulas may resolve spontaneously, whereas large or symptomatic lesions generally require intervention. Endovascular embolization is the preferred treatment owing to its minimally invasive nature and high success rates.<sup>6</sup> Surgical options, including arterial ligation or nephrectomy, are typically reserved for cases where embolization is unsuccessful or not feasible.<sup>1</sup>

The differential diagnosis in this case also includes congenital renal AVM.

These lesions may present clinically in a similar fashion to renal AV fistulas and are treated using similar endovascular techniques. However, renal AVMs are characterized by abnormal communication between the renal arterial and venous systems through multiple tangled, dilated, and tortuous vessels forming a discrete vascular nidus. They may occur in isolation or in association with Osler-Weber-Rendu syndrome.<sup>7</sup>

In this case, there was no history of Osler-Weber-Rendu syndrome, no vascular nidus identified on CT angiography, and no history of hereditary hemorrhagic telangiectasia or prior renal intervention. Although an unrecognized remote traumatic etiology cannot be entirely excluded, the absence of identifiable acquired risk factors supports a presumptive congenital origin. This patient was successfully treated with endovascular embolization via arterial access.

## Conclusion

Renal AV fistulas are rare but potentially life-threatening vascular anomalies. This case demonstrates how grayscale US findings may mimic hydronephrosis and

emphasizes the essential role of color Doppler in detecting abnormal vascular flow. CTA allows definitive diagnosis and treatment planning. Early recognition is critical, as prompt intervention can prevent progressive cardiac decompensation and reduce morbidity.

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# Congenital Toxoplasmosis

Suchita Kumar, BS; Walter Dehority, MD, MSc; Asha Sarma, MD

## Abstract

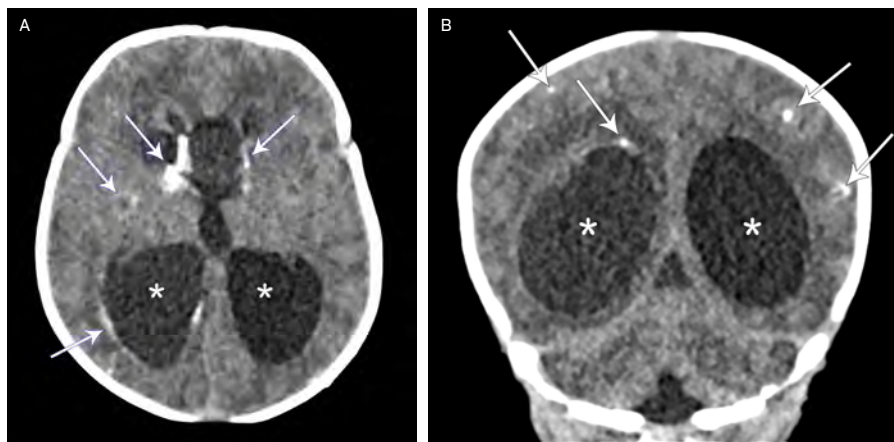
Congenital toxoplasmosis is a parasitic infection caused by vertical transmission of *Toxoplasma gondii*. Our case describes an early-term neonate presenting with poor feeding, abnormal movements, and hypothermia. Neuroimaging revealed hydrocephalus, randomly distributed intracranial calcifications, leptomeningeal and ependymal enhancement, and intraocular plaques. Diagnosis was confirmed by maternal and infant serologies. The patient was treated with pyrimethamine, sulfadiazine, and folinic acid, in addition to adjunctive neurosurgical and ophthalmologic interventions. Of note, there was no maternal exposure to cats or ingestion of undercooked meats, which are the typical risk factors associated with toxoplasmosis, but there was reported exposure to soil excavated in the yard during pregnancy. This case illustrates the variable presentation of congenital toxoplasmosis, which may be asymptomatic at birth and later present with the classic triad of hydrocephalus, chorioretinitis, and intracranial calcifications. Early recognition of imaging findings is critical for timely initiation of therapy, which improves neurodevelopmental and visual outcomes.

**Keywords:** congenital toxoplasmosis, TORCH infections, intracranial calcifications, pediatric neuroradiology

## Case Summary

A neonate born at early term presented to their pediatrician with decreased oral intake and a 3-day history of abnormal eye and neck movements. Pregnancy was uncomplicated, with unremarkable prenatal US, and the neonate had done well in the first 2 postnatal weeks. Owing to a core temperature of 93°F, the neonate was referred to the emergency department. Physical exam demonstrated dry mucous membranes, decreased interactivity, and 30-second episodes of rightward gaze deviation. Lumbar puncture was performed, followed by empiric treatment with ampicillin, gentamicin, and acyclovir. Analysis of cerebrospinal fluid demonstrated elevated protein, low glucose, and neutrophilic pleocytosis. The patient's

**Figure 1.** Axial (A) and coronal (B) head CT scans demonstrating hydrocephalus (\*) and extensive parenchymal calcifications (white arrows), including basal ganglia, subcortical, and periventricular calcifications.



complete blood count with differential and liver function panel were unremarkable.

Noncontrast CT of the head and contrast MRI of the brain were performed.

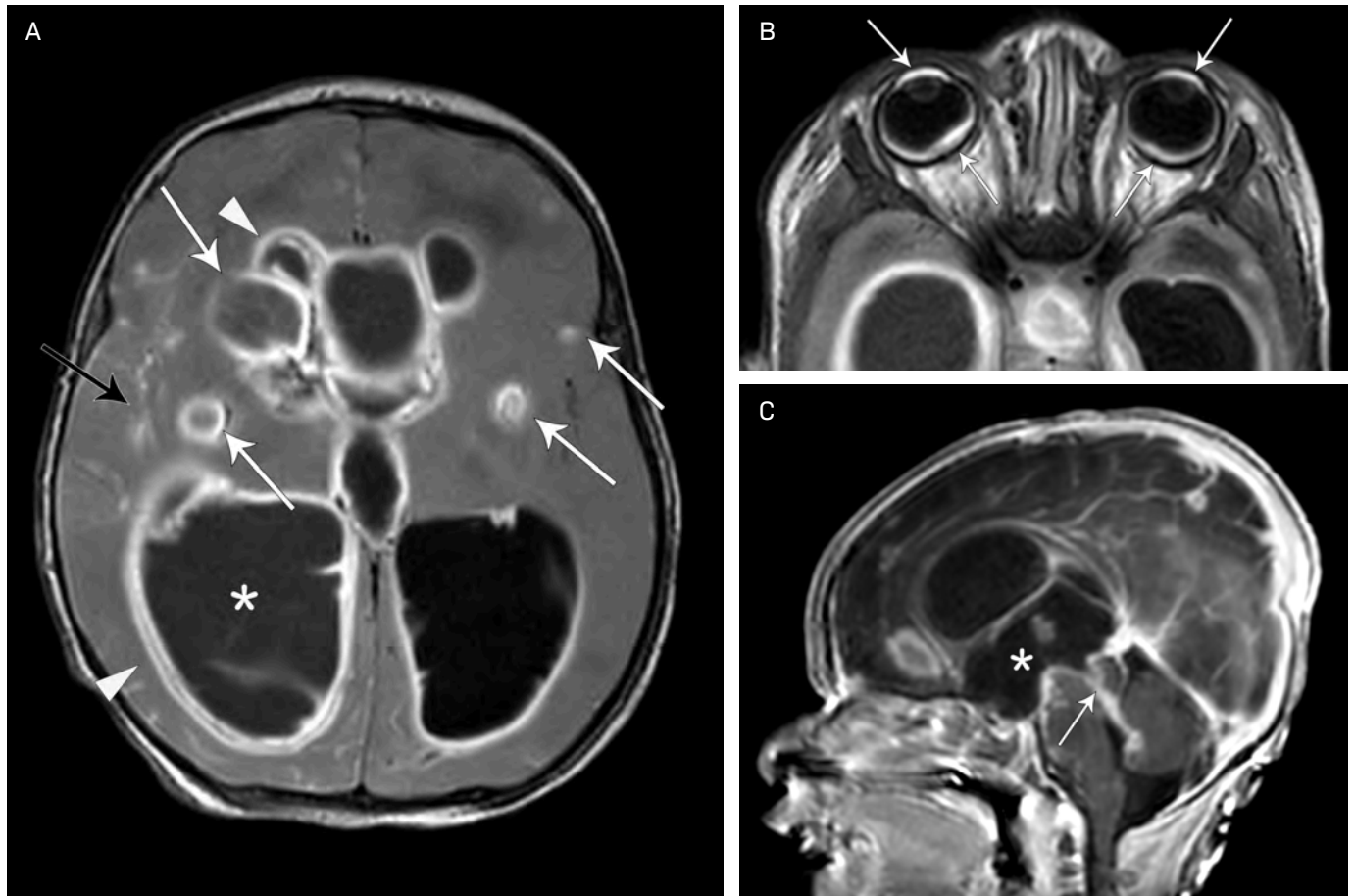
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## Imaging Findings

Noncontrast head CT (Figure 1) demonstrated marked enlargement of the lateral and 3rd ventricles and extensive parenchymal calcifications;

**Figure 2.** Axial post-gadolinium T2 FLAIR MRI of the brain (A) demonstrating hydrocephalus with incomplete suppression of signal in the intraventricular CSF (\*), multifocal enhancing parenchymal lesions in the basal ganglia and subcortical white matter (white arrows), leptomeningeal enhancement (black arrow), and thick ependymal enhancement (arrowheads). Axial image at a more inferior level from the same sequence (B) demonstrating enhancing, plaque-like, intraocular thickening in the anterior and posterior segments (arrows). Sagittal postcontrast T1 MRI (C) demonstrating dilatation of the third ventricle with dilated third ventricular recesses (\*) and aqueductal stenosis with thick ependymal enhancement (arrow).



these included basal ganglia, subcortical, and periventricular calcifications, raising concerns for a TORCH infection. The subsequent T2 FLAIR sequence on brain MRI (Figure 2) similarly demonstrated hydrocephalus and multifocal enhancing parenchymal lesions in the basal ganglia and subcortical white matter. This sequence further revealed leptomeningeal enhancement, ependymal enhancement, and enhancing plaque-like intraocular thickenings in the anterior and posterior segments. The T1 sequence demonstrated dilatation of the 3rd ventricle with dilated 3rd ventricular recesses and aqueductal stenosis with ependymal enhancement.

### Diagnosis

Congenital toxoplasmosis.

The differential diagnosis included congenital toxoplasmosis, congenital cytomegalovirus (CMV), congenital lymphocytic choriomeningitis virus, *Escherichia coli* meningitis, and Aicardi-Goutières syndrome.

### Discussion

Congenital toxoplasmosis is a parasitic infection caused by the vertical transmission of *Toxoplasma gondii*

following acute maternal infection. In the United States, approximately 85% of women of childbearing age are susceptible to primary infection, with an incidence of 400-4000 cases annually.<sup>1</sup>

*T. gondii* is primarily transmitted through ingestion of raw or undercooked meat containing tissue cysts or inadvertent ingestion of oocysts found in cat feces, either from a litter box or soil.<sup>2</sup> In this case, there was no maternal exposure to cats or ingestion of undercooked meats, but maternal exposure to soil excavated from the patient's yard (presumably containing cat feces) throughout the pregnancy was reported.

Maternal infection with *T. gondii* is usually asymptomatic, but nonspecific symptoms such as cervical lymphadenopathy, fever, malaise, and myalgias may occur following an incubation period of 5-18 days. In immunocompetent adults, the clinical course is benign and self-limited. The overall risk of congenital infection from acute maternal infection during pregnancy is 20-50%. While this risk increases with more advanced gestational age, congenital toxoplasmosis is more severe when infection is acquired in the first trimester.<sup>3</sup> Since this patient had normal US and was asymptomatic at birth, transmission possibly occurred in the third trimester.

Congenital toxoplasmosis presents with a wide spectrum of outcomes ranging from a healthy neonate to significant neurological and ocular findings, including chorioretinitis, intracranial calcifications, hydrocephalus, seizures, hepatosplenomegaly, and jaundice.<sup>4</sup> Clinical findings may not be present at birth, as in the case of our patient. Typically, preterm infants with toxoplasmosis demonstrate neurological and ocular manifestations in the first 3 months of life, while term infants demonstrate milder disease with lymphadenopathy and hepatosplenomegaly within the first 2 months of life.<sup>4</sup>

Pre- or postnatal imaging may suggest a diagnosis of congenital toxoplasmosis. Prenatal US can reveal intracranial hyperechogenic nodular foci, ventriculomegaly, hepatosplenomegaly, and ascites.<sup>5</sup> Postnatally, bulging fontanelles or seizures can prompt head CT and MRI. While the findings can overlap with other congenital infections, several features help distinguish toxoplasmosis from CMV and Zika virus. Congenital toxoplasmosis typically demonstrates randomly distributed intracranial calcifications (often involving the cortex and basal ganglia), hydrocephalus (with various patterns such as aqueductal stenosis and ependymitis), chorioretinitis, and

normo- or macrocephaly. In contrast, congenital CMV presents with periventricular calcifications, ventriculomegaly, and migrational abnormalities such as polymicrogyria. Congenital Zika virus infection is characterized by striking microcephaly, periventricular and subcortical calcifications, and brain surface smoothness.<sup>6</sup> The clinical diagnosis is made with serological testing but, as in our case, empiric treatment was initiated based on imaging. The diagnosis was confirmed a few weeks later, with maternal *T. gondii* IgG values of 1:8000, and corresponding values of 1:2048 (normal  $\leq 1:16$ ) in the infant.

Treatment consists of pyrimethamine, sulfadiazine, and folinic acid for 12 months, along with steroids for severe chorioretinitis or CNS inflammation. Early initiation of therapy is recommended, as it is associated with a lower incidence of retinochoroidal lesions and improved neurodevelopmental outcomes.<sup>4</sup> Signs and symptoms of infection tend to resolve within the first month of treatment.<sup>7</sup> Management of hydrocephalus may require surgical CSF diversion.<sup>8</sup> In addition to antiparasitic therapy, our patient was treated with levetiracetam for seizure management, intravitreal clindamycin injections for chorioretinal scarring, and 2 ventriculoperitoneal shunts. The prognosis is generally favorable in children who receive early diagnosis and treatment, with most remaining asymptomatic or experiencing only mild sequelae, although a lifelong risk of ocular complications and neurological impairment remains, especially in cases of delayed diagnosis or inadequate therapy.<sup>7</sup>

## Conclusion

Congenital toxoplasmosis is a parasitic infection that can present in neonates with the classic triad of chorioretinitis, hydrocephalus, and diffuse intracranial calcifications. The condition may be

identified on prenatal US with intracranial echogenic nodular foci and ventriculomegaly. It can also be diagnosed postnatally with CT and MR images that demonstrate randomly distributed calcifications, hydrocephalus with aqueductal stenosis, ependymitis, and chorioretinitis, followed by confirmatory serological testing. Management involves antiparasitic therapy with pyrimethamine, sulfadiazine, and folinic acid and, depending on severity, steroids, intravitreal injections, and neurosurgical intervention.

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# Sphenoid Sinus Metastasis Secondary to Urothelial Carcinoma

Jessie Huang, MD; Devanshi Mistry, MD; Sarah Mohajeri Moghaddam, MD, MPH

## Abstract

Sphenoid sinus pathologies present with headache, cranial nerve dysfunction, and facial pain and require evaluation on CT and MRI. CT and MRI play a complementary role in assessing the extent of the lesion and involvement with neighboring critical structures, and the presence of destructive osseous changes. Imaging helps to narrow the differential diagnosis, which can include sinusitis, mucocoeles, bone cysts, primary malignancy, or metastases, in addition to aiding in preoperative planning. This case highlights the importance of considering rare metastatic sites on imaging in patients with a history of malignancy and suggestive symptoms.

**Keywords:** sphenoid sinus, metastasis, urothelial carcinoma, neuroradiology, CT sinus, MRI, FDG-PET

## Case Summary

A middle-aged patient presented with a history of left eye pain for 1 year and acute onset pressure behind the left eye with diplopia. The patient reported a prior history of FGFR-mutated urothelial carcinoma, which had been treated with radiation for metastases to the T9 vertebra and pelvic bone. The patient also reported a history of left cataract and left retinal repair surgeries, and had previously used eye drops for pain.

Physical exam revealed left abducens nerve palsy. An initial MRI brain scan demonstrated a cystic lesion in the left sphenoid sinus with a blood-fluid level. Follow-up CT sinus scans showed left sphenoid sinus opacification with osseous erosions and extension into the left cavernous sinus. The patient underwent septoplasty and left sphenoidotomy with

partial resection of the left sphenoid sinus mass. Pathology revealed HER+ metastatic urothelial carcinoma. The residual tissue exhibited continued growth prior to initiating trastuzumab deruxtecan and radiation therapy.

## Imaging Findings

The initial axial T2 postcontrast PROPELLER MRI demonstrated a well-circumscribed expansile mass in the left sphenoid sinus exhibiting T2 hyperintensity and an internal blood-fluid level (Figure 1, arrow). On axial postcontrast T1 CUBE MRI, there was smooth peripheral enhancement and thin linear enhancement along the superior aspect that could represent a vessel or a septation (Figure 2, arrow). No nodular enhancement corresponding to this mass

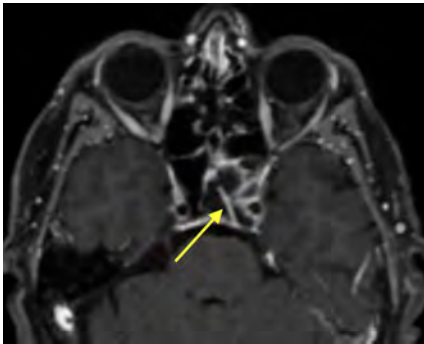
**Figure 1.** T2 FLAIR MRI demonstrating a well-circumscribed expansile mass in the left sphenoid sinus with a blood-fluid level (arrow) and T2 hyperintensity.



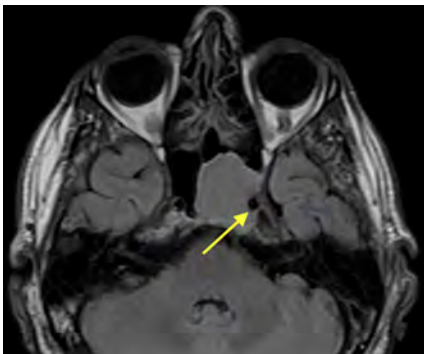
was noted. On axial T2 FLAIR MRI, the mass extended laterally to partially encase the left cavernous intracranial carotid artery (Figure 3, arrow). Additionally, there was thinning of the clivus dorsally without intracranial extension. Given the osseous thinning, CT sinus was recommended for further characterization. A subsequent CT sinus scan demonstrated osseous erosions of the clivus and lateral sphenoid sinus wall (Figure 4, arrow).

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**Figure 2.** Postcontrast T1WI demonstrating lateral extension of the mass to partially encompass the left cavernous intracranial carotid artery. There is also thinning of the clivus without intracranial extension dorsally.



**Figure 3.** Postcontrast T1 image demonstrating peripheral enhancement with thin linear enhancement along the superior aspect. No nodular enhancement is noted.



## Diagnosis

Sphenoid sinus metastasis secondary to urothelial carcinoma.

Differential diagnosis includes sphenoid sinus mucocoele, secondary aneurysmal bone cyst, and primary or secondary malignancy.

## Discussion

The sphenoid sinus, one of the 4 paranasal sinuses, is situated near the optic nerve, cavernous sinus, pituitary gland, cranial nerves, and internal carotid artery. Recognizing pathologies affecting the sphenoid sinus is critical, as they can lead to compression of these structures. Patients initially present with headache,

**Figure 4.** Sinus CT scan demonstrating osseous erosions of the clivus and lateral sphenoid sinus wall.



facial pain, visual changes, and cranial nerve dysfunction, most often abducens palsy.<sup>1</sup>

Common pathologies seen on MRI and CT include bacterial or fungal sinusitis and mucocoeles.<sup>1</sup> Although primary tumors in the sphenoid sinus are rare, they include squamous cell carcinoma, adenoid cystic carcinoma, and chondrosarcoma.<sup>2</sup> Metastasis to the sphenoid sinus, although also rare, is associated with poor prognosis. Sphenoid sinus metastasis most commonly arises from breast, prostate, lung, and colon primary cancers.<sup>3</sup> Metastasis from urothelial carcinoma, as seen in this patient, usually reaches the bones, lungs, and liver through lymphatic and hematogeneous routes. Urothelial carcinoma metastasis to the sphenoid sinus is exceedingly rare and, to our knowledge, has not been reported in the literature.<sup>4</sup>

CT and MRI are recommended for initial imaging of the paranasal sinuses. CT is better at evaluating bony changes like cortical erosion, destruction, and remodeling, while MRI is used to characterize soft-tissue components. Together, they help determine the size of the lesion, differentiate it from mucous and fluid, and assess for extension beyond the sinus walls.<sup>5</sup> Metastases in the sphenoid can present as a homogeneous soft-tissue masses; in some cases, they extend out of the sphenoid sinus or damage the sphenoid bone. Although 18F-fluorodeoxyglucose (FDG) PET/CT is used in

whole-body evaluation for metastases in patients with known malignancy,<sup>6</sup> biopsy is used to determine the diagnosis.

Mucocoele, a benign cystic lesion lined with respiratory epithelium and filled with mucoid secretions, was also considered based on this patient's MRI. A destructive mucocoele is a more aggressive form that erodes the bone and can spread to nearby structures.<sup>7</sup> On CT, mucocoeles appear as opacities with contents of varying density, as well as bowing and thinning of the osseous margins. On MRI, they can appear with high intensity on T2 imaging.<sup>8</sup> Mucocoeles and mucous retention cysts contain a mix of water, mucus, and protein, and rarely contain blood levels such as that seen on MRI in our case.<sup>7</sup> A third diagnosis considered was a secondary aneurysmal bone cyst, which are masses with blood fluid levels. These entities often demonstrate nodular enhancement on the periphery, which was not seen on this patient's MRI.<sup>9</sup>

Despite the well-circumscribed appearance of the mass in our patient, the presence of blood-fluid levels and osseous erosions at CT were highly suspicious for an aggressive process. Given the patient's history of urothelial carcinoma, metastasis was the leading differential and was eventually confirmed at histopathology. Metastasis to the sphenoid sinus can be treated with surgery, but total resection is difficult owing to the region's topography and nearby structures. In our patient, total resection was limited by the carotid artery, optic canal, and involvement of the cavernous sinus. Patients with inoperable tumors can receive radiation therapy, while recurrence can be treated with combined radiation and chemotherapy.<sup>2</sup> Repeat imaging is critical for timely identification of lesion growth.

## Conclusion

Sphenoid sinus pathologies typically present with headache, cranial nerve dysfunction, and facial pain and require CT and MRI evaluation. These modalities

play a complementary role in determining the extent of the lesion, involvement of nearby structures, and presence of destructive osseous changes. They also help to narrow the differential diagnosis, which can include sinusitis, mucocoeles, bone cysts, primary malignancy, and metastases, as well as aid in preoperative planning.

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*Sometimes what you don't say is more powerful than anything you could say.*

—A.D. Aliwat



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## Please. Just Tell Me Something

C. Douglas Phillips, MD, FACR

I remember reading (and also being told about this repeatedly in a million lectures on compliance and other unstated but critical physician tasks) that you need a reason for what you do. In imaging, that is often the clinical information provided in the request. Yes, a request. Someone is *requesting* that you perform the imaging study on their patient. Most of the time, it is a no-brainer: a simple match of the clinical question and of the study.

Stroke? Head MR. *Check. Match.* Pneumonia? Chest x-ray. *Check. Match.*

However, sometimes (as we all know), you may not have the best fit for the request.

Radiology is again under the microscope, and seems to be attracting a lot more interest than perhaps is warranted or deserved. AI is out there, lurking. It seems it is either going to replace us or generate the need for many more of us, depending on who you read.

There are several items that make me happy I am at the portion of the career arc I am now inhabiting—this is a big one.

I have thoughts, but I am not looking at another 30 years of doing this. Regardless of what side you may come down on in this debate, certain facts cannot be ignored. And, one of them, to me, is the clinical data generating the request.

Do you think AI machines will argue with one another about whether the study is indicated? This

AI looks through the data and says, *yes*; this AI looks through the data and says *no*.

Will they duke it out in the hallway? Try to pull each other's plugs? Figure out how to reboot each other? Resort to name-calling?

What made me think of this was a particular run of weird-odd-impossible-crazy-nonsensical items of clinical data to accompany exams today. A personal favorite was the provided clinical data for an IAC brain MR: "illness, unspecified." Another best-of-the-day close contender was this clinical data for spine MR: "long history of."

Yes.

I went to the EMR. You know how it is when not everyone the patient is seeing is on your own EMR? That big black hole of information that pertains to the current study? Yep. That happens much too often to be just chance.

I went to a patient data intake questionnaire for one of the studies. The patient circled the question when asked what they were being scanned for. Clearly, they were in on the "let's withhold data from the radiologist" game. Were the studies indicated? Well, as best as I can say, *yes*.

Just trying to keep moving forward.

Keep doing that good work. Mahalo.