SA-CME CREDIT

Imaging brachial plexus pathology
JTP Hallinan, National University Health System and Yong Loo Lin School of Medicine, Singapore; MN Pathria and BK Huang, UC San Diego Health System, San Diego, CA

Update: Radiologic-pathologic correlation of hepatocellular adenoma
S Dhingra, Baylor College of Medicine, Houston, TX; C Thupili, S Chua, K Shirlakar, and V. Surabhi, University of Texas Health Sciences Center, Houston, TX; and SR Prasad, University of Texas MD Anderson Cancer Center, Houston, TX

Computed tomography of the acute abdomen
B Wildman-Tobriner, WL Ehieli, AX Dixon, and BC Allen, Duke University Medical Center, Durham, NC

Radiological Case
Diffuse alveolar hemorrhage
Why does Bayer invest in indications?

For the rigor and reassurance you and your patients deserve

At Bayer, we believe that confidence comes from evidence—so it is our responsibility to provide you with rigorous scientific data supporting our products.

That’s why we invest in FDA registration trials that build the knowledge base for specialty magnetic resonance (MR) procedures and patient populations. This commitment is why Gadavist has the most FDA-approved indications of any macrocyclic GBCA1,2.

Approved Gadavist Indications

See full Indications below.

<table>
<thead>
<tr>
<th>Year</th>
<th>CNS MR</th>
<th>FIRST AND ONLY</th>
<th>Breast MR</th>
<th>FIRST</th>
<th>CNS MR, patients aged less than 2 years</th>
<th>FIRST AND ONLY</th>
<th>Supra-aortic magnetic resonance angiography (MRA)</th>
<th>Renal artery MRA</th>
<th>FIRST AND ONLY</th>
<th>Cardiac MR in adults</th>
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Indications

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

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

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

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

Important Safety Information

**WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)**

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

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

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

Please see brief summary on adjacent pages.
For the rigor and reassurance you and your patients deserve in indications? Why does Bayer invest?

Gadavist® has the most FDA-approved indications of any macrocyclic GBCA. This commitment is why we invest in FDA registration trials that build the knowledge base for specialty magnetic resonance (MR) procedures and patient populations. That’s why we take utmost care to ensure the safety of our patients.

Important Safety Information

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

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

See full Indications below.

Approved Gadavist Indications

Please see brief summary on adjacent pages.

Please see brief summary on adjacent pages.

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

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

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

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

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

Please see brief summary on adjacent pages.


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Join the 3,000+ US institutions that use Gadavist³
GADAVIST (gadobutrol) injection, for intravenous use

Initial U.S. Approval: 2011

<table>
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<th>WARNING: NEPHROGENIC SYSTEMIC FIBROSIS (NSF)</th>
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</tr>
<tr>
<td>• For patients at highest risk for NSF, do not exceed the recommended Gadavist dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration [see Warnings and Precautions (5.1)].</td>
</tr>
</tbody>
</table>

1 INDICATIONS AND USAGE

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

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

1.2 MRI of the Breast

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

1.3 Magnetic Resonance Angiography (MRA)

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

1.4 Cardiac MRI

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

4 CONTRAINDICATIONS

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

5 WARNINGS AND PRECAUTIONS

5.1 Nephrogenic Systemic Fibrosis

Gadolinium-based contrast agents (GBCAs) increase the risk for nephrogenic systemic fibrosis (NSF) among patients with impaired elimination of the drugs. Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR < 30 mL/min/1.73m²) as well as patients with acute kidney injury. The risk appears lower for patients with chronic, moderate kidney disease (GFR 30 to 59 mL/min/1.73m²) and little, if any, for patients with chronic, mild kidney disease (GFR 60 to 89 mL/min/1.73m²). NSF may result in fatal or debilitating fibrosis affecting the skin, muscle and internal organs. Report any diagnosis of NSF following Gadavist administration to Bayer Healthcare (1-888-842-2937) or FDA (1-800-FDA-1088 or www.fda.gov/medwatch). Screen patients for acute kidney injury and other conditions that may reduce renal function. Features of acute kidney injury consist of rapid (over hours to days) and usually reversible decrease in kidney function, commonly in the setting of surgery, severe infection, injury or drug-induced kidney toxicity. Serum creatinine levels and estimated GFR may not reliably assess renal function in the setting of acute kidney injury. For patients at risk for chronically reduced renal function (for example, age > 60 years, diabetes mellitus or chronic hypertension), estimate the GFR through laboratory testing. Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA and degree of renal impairment at the time of exposure. Record the specific GBCA and the dose administered to a patient. For patients at highest risk for NSF, do not exceed the recommended Gadavist dose and allow a sufficient period of time for elimination of the drug prior to re-administration. For patients receiving hemodialysis, consider the prompt initiation of hemodialysis following the administration of a GBCA in order to enhance the contrast agent’s elimination [see Use in Specific Populations (8.6) and Clinical Pharmacology (12.3)]. The usefulness of hemodialysis in the prevention of NSF is unknown [see Clinical Pharmacology (12.3)].

5.2 Hypersensitivity Reactions

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

• Before Gadavist administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to Gadavist.

• Administer Gadavist only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.

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

5.3 Gadolinium Retention

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

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

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

Minimize repetitive GBCA imaging studies particularly closely spaced studies, when possible.

5.4 Acute Kidney Injury

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

5.5 Extravasation and Injection Site Reactions

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

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

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

5.7 Low Sensitivity for Significant Arterial Stenosis

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

6 ADVERSE REACTIONS

The following serious adverse reactions are discussed elsewhere in labeling:

• Nephrogenic Systemic Fibrosis (NSF) [see Boxed Warning and Warnings and Precautions (5.1)].

• Hypersensitivity reactions [see Contraindications (4) and Warnings and Precautions (5.2)].
6.1 Clinical Trials Experience

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

The adverse reactions described in this section reflect Gadavist exposure in 7,713 subjects (including 184 pediatric patients, ages 0 to 17 years) with the majority receiving the recommended dose. Approximately 52% of the subjects were male and the ethnic distribution was 62% Caucasian, 28% Asian, 5% Hispanic, 2.5% Black, and 2.5% patients of other ethnic groups. The average age was 56 years (range from 1 week to 93 years).

Overall, approximately 4% of subjects reported one or more adverse reactions during a follow-up period that ranged from 24 hours to 7 days after Gadavist administration. Adverse reactions associated with the use of Gadavist were usually mild to moderate in severity and transient in nature. Table 2 lists adverse reactions that occurred in ≥ 0.1% subjects who received Gadavist.

Table 2: Adverse Reactions

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

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

6.2 Postmarketing Experience

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

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

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

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

Data

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

Animal Data

Gadolinium Retention

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

Reproductive Toxicology

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

8.2 Lactation

Risk Summary

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

Data

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

8.4 Pediatric Use

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

NSF Risk
No case of NSF associated with Gadavist or any other GBCA has been identified in pediatric patients ages 6 years and younger. Pharmacokinetic studies suggest that clearance of Gadavist is similar in pediatric patients and adults, including pediatric patients age younger than 2 years. No increased risk factor for NSF has been identified in juvenile animal studies of gadobutrol. Normal estimated GFR (eGFR) is around 30 mL/min/1.73m² at birth and increases to mature levels around 1 year of age, reflecting growth in both glomerular function and relative body surface area. Clinical studies in pediatric patients younger than 1 year of age have been conducted in patients with the following estimated GFR (eGFR): 31 mL/min/1.73m² (age 2 to 7 days), 38 mL/min/1.73m² (age younger than 1 year), and 38 mL/min/1.73m² (age 8 to 28 days), 62 mL/min/1.73m² (age 1 to 6 months), and 83 mL/min/1.73m² (age 6 to 12 months).

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

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

10 OVERDOSAGE
The maximum dose of Gadavist tested in healthy volunteers, 1.5 mL/kg body weight (1.5 mmol/kg; 15 times the recommended dose), was tolerated in a manner similar to lower doses. Gadavist can be removed from the body by hemodialysis [see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)].

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No carcinogenicity studies of gadobutrol have been conducted.

Gadobutrol was not mutagenic in in vitro reverse mutation tests in bacteria, in the HGPRT (hypoxanthine-guanine phosphoribosyl transferase) test using cultured Chinese hamster V79 cells, or in chromosome aberration tests in human peripheral blood lymphocytes, and was negative in an in vivo micronucleus test in mice after intravenous injection of 0.5 mmol/kg. Gadobutrol had no effect on fertility and general reproductive performance of male and female rats when given in doses 12.2 times the human equivalent dose (based on body surface area).

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

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

Nephrogenic Systemic Fibrosis
Instruct patients to inform their physician if they:
• Have a history of kidney disease and/or liver disease, or
• Have recently received a GBCA

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

Common Adverse Reactions
Inform patients that they may experience:
• Reactions along the venous injection site, such as mild and transient burning or pain or feeling of warmth or coldness at the injection site
• Side effects of headache, nausea, abnormal taste and feeling hot

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

Instruct patients receiving Gadavist to inform their physician if they:
• Are pregnant or breastfeeding
• Have a history of allergic reaction to contrast media, bronchial asthma or allergic respiratory disorder

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Manufactured for:

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

6905905BS1
Imaging brachial plexus pathology
MRI remains the best modality for assessing the brachial plexus, due to its superior soft-tissue contrast compared to CT or ultrasound. This review article will provide an overview of anatomy and practical, up-to-date BP imaging techniques for general radiologists, followed by a step-wise discussion of common pathology.

James Thomas Patrick Decourcy Hallinan, MBChB; Mini N. Pathria, MD; and Brady K. Huang, MD

Update: Radiologic-pathologic correlation of hepatocellular adenoma
Radiologists and pathologists have an equally important role to play in the diagnosis and morpho-molecular subtyping of Hepatocellular adenomas. This review focuses on the radiological and pathological features of HAs, its morphologic subtypes, and the differential diagnosis of HAs based on imaging characteristics.

Sadhna Dhingra MD, FCAP; Chakradhar Thupili, MD; Steven Chua, MD, PhD, Kaustubh Shirlakar MD; and Srinivasa R Prasad, MD, and Venkateswar R Surabhi, MD

Computed tomography of the acute abdomen
The causes of acute abdomen are numerous and span the medical and surgical spectrum, with many etiologies identifiable using medical imaging. This review will focus on common causes of the acute abdomen that are detected on imaging, particularly CT. Typical imaging findings as well as pitfalls and complications are discussed.

Benjamin Wildman-Tobriner, MD; Wendy L. Ehieli, MD; Austin X. Dixon, MD, MBA; and Brian C. Allen, MD
We all know that screening is the best way to detect breast cancer earlier and digital breast tomosynthesis (DBT) improves image quality for better detection. But now it’s time to get smarter about it.

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Times are changing

Erin Simon Schwartz, MD, FACR

As you read this we will be nearing the end of a decade. Hard to believe that the 20-teens are almost over; they have ushered in tremendous change—including here at Applied Radiology. Under the outstanding tenure of our former Editor-in-Chief, Applied Radiology grew into one of the most widely read radiology publications worldwide.

But we cannot rest on these laurels, and we must continue to change with the times.

To that end, in 2020 we will be introducing electronic, ahead-of-print publishing. This will dramatically decrease the time from manuscript acceptance to publication, as articles and cases will be assigned a digital object identifier (DOI) number once a portable document format (PDF) of their final, accepted publication can be created. For those not familiar with DOI numbers, they are used to permanently and uniquely identify each publication and its content.

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If you are lucky enough to be coming to the RSNA Annual Meeting this year, please stop by our booth in the Technical Exhibits Hall, South 1700. I look forward to meeting you.

I wish the best of health and happiness to you and yours in this holiday season and in the New Year (and decade) ahead.

Dr. Schwartz is the Editor-in-Chief of Applied Radiology. She is an Associate Professor of Radiology, Perelman School of Medicine, University of Pennsylvania, and a Pediatric Neuroradiologist at The Children’s Hospital of Philadelphia. She can be reached at erin@appliedradiology.com.
Imaging Brachial Plexus Pathology

Description
Brachial plexus disorders are a diagnostic challenge due to the complex anatomy and nonspecific symptomatology. MRI remains the best modality for assessing the brachial plexus (BP), due to its superior soft-tissue contrast compared to CT or ultrasound. Traumatic lesions are the most common cause of BP dysfunction, closely followed by neoplastic infiltration. Infection, inflammation and iatrogenic causes are less common.

This review article will provide an overview of anatomy and practical, up-to-date BP imaging techniques for general radiologists, followed by a step-wise discussion of common pathology. Clinically relevant advances such as dynamic thoracic outlet MRI will also be discussed.

Learning Objectives
After completing this activity, the participant will be able to:
• Explain the important role of MRI in the diagnosis of brachial plexus pathology,
• Identify the major pathologies of the brachial plexus including post-traumatic lesions, neoplastic infiltration and infection/inflammation, and,
• Use provocative MRI and ultrasound techniques in the evaluation of thoracic outlet syndrome.

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• Radiologists
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Brachial plexus disorders can be diagnostic challenges, owing to the region’s complex anatomy and nonspecific symptomatology. MRI remains the best modality for assessing the brachial plexus (BP), due to its superior soft-tissue contrast compared to CT or ultrasound. Trauma is the most common cause of BP dysfunction, closely followed by tumor infiltration. Infection, inflammation and iatrogenic causes are less common. This review article will provide an overview of anatomy and practical, up-to-date BP imaging techniques for general radiologists, followed by a step-wise discussion of common pathology. Clinically relevant advances such as dynamic thoracic outlet MRI will also be discussed.

Anatomy

The BP provides motor innervation to the ipsilateral chest, shoulder, and upper limb with the exception of the trapezius, which is supplied by the spinal accessory nerve. It is divided anatomically into roots, trunks, divisions, cords, terminal and collateral branches (Figure 1). These constituents may best be recalled using this mnemonic: Radiology (roots) Technicians (trunks) Drink (divisions) Cold (cords) Brew (terminal branches) Coffee (collateral branches)—a slight divergence from the usual alcohol-based memory tools.

The BP roots arise from the C5-T1 ventral rami of the spinal cord, with variable C4 and T1 contributions. As a result, the “roots” are actually the ventral rami of the spinal nerves formed from the dorsal and ventral rootlets arising from the spinal cord. Although “roots” is a misnomer, the term is well established in the literature and will be used throughout this article.

The roots exit through their respective neural foramina, and travel between the anterior and middle/posterior scalene muscles in the interscalene triangle,
or space (Figures 2, 3). Lateral to the middle scalene muscle the three trunks are formed: C5 and C6 combine into the upper trunk, C7 continues alone as the middle trunk, and C8 and T1 combine to form the lower trunk (Figures 2, 4). The trunks traverse posterosuperior to the subclavian artery behind the clavicle and each divides into anterior and posterior divisions within the costoclavicular space. The vessels lie inferiorly at the costoclavicular space with the subclavian vein anterior to the artery. This space, bounded by the clavicle superiorly, subclavian muscle anteriorly, and the first rib and middle scalene muscle posteriorly, is a common site of BP and subclavian vascular compression.

The conversion of the six divisions into three cords occurs at the lateral border of the first rib (Figure 5). The cords extend into the retropectoralis minor space and can be readily identified due to their relationship to the axillary artery;
The medial cord lies posteroinferiorly, lateral cord anterosuperiorly and posterior cord posterosuperiorly. The cords divide into five major terminal branches at the lateral border of the pectoralis minor: the median, ulnar, radial, musculocutaneous and axillary nerves. In addition there are numerous (~11) collateral branches that exit along the BP more proximally, eg, suprascapular nerve from the superior trunk. Table 1 shows the innervation of the cords and terminal branches.

### MR imaging protocol

Accurate visualization of the BP from the roots to terminal branches must take into consideration its oblique superomedial to inferolateral course. As such, oblique coronal and sagittal images are preferred, but not mandatory. Our protocol utilizes initial large field of view images for bilateral comparison of the brachial plexuses. These are typically performed with T1W fast spin echo images and three-dimensional T2W fat-suppressed sequences, which allows for multiplanar reconstructions. In a high-volume facility, isotropic imaging can shorten imaging time and decrease the need for custom-tailored exams.

Dedicated, multiplanar, small field of view images of the affected plexus are then performed. Coronal T2W fat-saturated sequences are useful for assessment of abnormal neural edema and enlargement; T1W sagittal images are especially useful for assessment of fat planes along with surrounding bony and muscular anomalies; eg, cervical ribs. High resolution, axial, pre-ganglionic, T2W images of the cervical region and nerve roots are also performed. These are useful for assessment of traumatic nerve root avulsions and pseudomeningoeles.

Both 1.5T and 3T platforms may be used, with a sample protocol shown in Table 2 (For 3T only). 3T is preferred due to better resolution and signal-to-noise profile over 1.5T, with 1.5T reserved for patients with hardware or contraindications to 3T. Neurovascular surface coils or a wrap-around body coil can be utilized.

Intravenous gadolinium-based contrast is not routinely required for BP imaging as most nerve pathology is well assessed on the high-resolution, fat-suppressed T2W images. Contrast administration is typically required in cases of suspected infection or tumor infiltration. Contrast allows for more accurate assessment of disease extent, identification of drainable collections and characterization of focal masses, such as neurogenic tumors.

Another common indication for imaging is thoracic outlet syndrome (TOS). The aim is to assess for the site of vascular and/or neural compression, which is typically at the costoclavicular space and may involve anomalous ribs
or musculature, or fibrous bands.  

Pro-vocative maneuvers, such as arm raising and head turning, can unmask the extent and location of the compression. Bilateral coronal T1W sequences and post-contrast MR angiography are commonly performed in each position (Table 2).

Diffusion tensor imaging (DTI) with fiber tractography has the potential to detect microstructural abnormalities beyond the resolution of conventional, anatomic MRI sequences. It is still an experimental tool, but has been shown to detect tract disruption, infiltration and internal disorganization, which could allow for earlier diagnosis of neoplastic or inflammatory neuropathies.  

CT of the brachial plexus

CT also plays a role in the diagnosis of BP pathology. Extension of neoplastic disease into the plexus (eg, Pancoast tumor), rib and clavicle anomalies, and adjacent fractures and hematomas can be visualized. CT angiography also provides a high-resolution and rapid assessment of arterial and venous patency in trauma and TOS.

Ultrasound of the brachial plexus

Ultrasound of the BP is technically feasible, but challenging due to the complex anatomy and bony relations. In skilled hands, it is a useful bedside tool for assessing traumatic BP injury and is routinely used by anesthesiologists to perform nerve blocks. It is also commonly used for dynamic vascular assessment in suspected TOS. Lapeque et al (2014) provide a practical review on BP ultrasound. However, for the majority of BP injuries, MRI remains the standard examination, with ultrasound as a useful adjunct.

Brachial plexus lesions

BP lesions can be classified broadly into two categories: traumatic and non-traumatic lesions. Traumatic lesions form the majority of BP injuries, and are the major indication for imaging. Non-traumatic lesions are a heterogeneous group encompassing neoplastic processes, infection/inflammation and functional neurovascular compression or TOS.

Trauma

Motor vehicle accidents are responsible for the majority of traumatic BP injuries. Traumatic traction on the BP can lead to proximal spinal nerve root avulsion (pre-ganglionic) or more distal rupture (post-ganglionic). Clinical examination of the neurological injury should be documented promptly to determine the site and clinical course of lesions (recovery or stable deficit) and whether surgery is indicated. Upper limb paralysis is complete in approximately 75% of patients, with a supraclavicular site of injury seen in 72% of cases. Delineation of the site of injury is important for prognosis and management. Pre-ganglionic injuries may require early (<3 months) reconstruction using nerve transfers, whereas postganglionic injuries may be repaired after a longer period of observation.

Identification of pre-ganglionic lesions requires high-resolution 3D T2W images, which are typically viewed in the axial plane (Figure 6). Intradural nerve rootlets should be assessed for integrity from the root entry zone to the dorsal root ganglion within the neural foramen. These injuries are associated with traumatic pseudomeningoceles in 80% of cases. Other common associated findings in pre-ganglionic avulsion include contralateral cord displacement, syrinx, epidural hematoma and spinal cord edema. The posterior paraspinal musculature should also be assessed for denervation edema, which can occur due to a nerve root avulsion.
at or before the dorsal root ganglion. Stretching or incomplete avulsion of the pre-ganglionic rootlets is more challenging to diagnose, and may be suggested when there is differential enhancement of the rootlets.\textsuperscript{1,5}

Post-ganglionic avulsions distal to the neural foramina typically occur proximally at the scalene triangle, but may variably involve the trunks to distal branches. These can also be partial or complete; complete ruptures are usually associated with distal nerve retraction (Figure 7). Another finding is nodular thickening and mild enhancement due to a post-traumatic neuroma in continuity.

Indirect findings include formation of hematomas at the site of avulsion and denervation edema and enhancement at the shoulder girdle musculature.\textsuperscript{1,5,20} MRI is the mainstay for diagnosis, although ultrasound can provide an accessible bedside examination in critically injured patients.\textsuperscript{11} Ultrasound can be

\textbf{FIGURE 7.} Brachial plexus traumatic postganglionic avulsions in a 39-year-old man following a motorcycle accident. Coronal T2W, fat-saturated MRI (A) of the right brachial plexus shows apparent discontinuity of the postganglionic C5 and C6 nerve roots (between the arrowheads). There is extensive downstream edema within the upper trunk of the right brachial plexus (solid arrow). On sagittal T2W, fat-saturated MRI sequences (B-medial and C-lateral at the shoulder girdle) there is an absence of the C5 nerve root at the expected position compatible with complete avulsion (solid arrow in B), with diffuse enlargement of the C6 nerve root, likely due to severe stretching (dashed arrow in B). Associated denervation edema and atrophy of the right shoulder girdle musculature, including the rotator cuff muscles (arrowheads in C) and deltoid muscle (dashed arrows in C), are seen.

\textbf{FIGURE 8.} Nodal metastases with extracapsular extension at the brachial plexuses in a 67-year-old man with known thyroid carcinoma. Coronal, contrast-enhanced, T1W, fat-saturated MRI sequence shows numerous, enhancing, bilateral nodal metastases (arrowheads) with extensive involvement of the brachial plexuses and axillary regions (best seen on the left). There are additional pleural metastases at the left lung apex (solid arrow) with mediastinal lymphadenopathy (open arrow).

\textbf{FIGURE 9.} Pancoast (superior sulcus) tumor with invasion of the brachial plexus in a 43-year-old man. Coronal T2W, fat-saturated MRI shows a Pancoast tumor at the left lung apex (solid arrow) with extension into the lower neck and involvement of the mid to lower roots (mainly C6-T1) and trunks of the brachial plexus (dashed arrows). There was additional encasement of the left subclavian artery and vein (not shown), which along with the extensive neural involvement, precludes surgical resection.
FIGURE 10. Metastatic versus radiation plexopathy in a 67-year-old woman with metastatic breast carcinoma (known pulmonary metastases). Coronal, contrast-enhanced, T1W, fat-saturated MRI sequence (A). Additional coronal reconstruction from a subsequent FDG-PET/CT (B). There is extensive contrast-enhancement of the right brachial plexus, extending from the trunks to the axillary region (solid arrow). Prior scans had shown less marked aggregation and enhancement, likely in favor of post-radiotherapy plexopathy (images not shown). Due to the interval progression, metastatic disease was a key consideration and an FDG-PET/CT confirmed the presence of avid FDG uptake along the brachial plexus (solid arrow). This was highly suspicious for metastatic disease and a biopsy was confirmatory. In equivocal cases, FDG-PET/CT is a useful tool to distinguish radiation versus metastatic plexopathy.

FIGURE 11. Post-radiation brachial plexopathy in a 53-year-old with metastatic hypopharyngeal squamous cell carcinoma. Coronal, T2W, fat-saturated MRI sequence (A) and a coronal reconstruction from a subsequent FDG-PET/CT (B). There is extensive T2W hyperintense aggregation and thickening of the left brachial plexus (solid arrow in A), involving the roots through to the cords with overlying soft tissue and muscular thickening and edema. There is nodular soft tissue at the left lung apex (dashed arrow) with altered signal at the left first and second ribs (arrowheads in A). Compared to the pre-radiation studies (not shown) the edema and neural thickening showed interval increase in extent with no new focal mass. Along with the paucity of FDG avidity at the left brachial plexus (solid arrow in B) and thoracic inlet on the PET/CT, these findings were compatible with post-radiation plexopathy, left apical fibrosis and post-radiation osteonecrosis of the ribs. Continued surveillance was recommended as this patient remained at high risk of recurrence.

used to assess for post-ganglionic injuries at the interscalene triangle or distal to the costoclavicular space. Thickening or discontinuity of the trunks or cords can be assessed using the contralateral side as a readily accessible control.\textsuperscript{10,11,12} CT myelography also remains an accurate technique for assessing pre-ganglionic avulsions with clear depiction of the intradural rootlets.\textsuperscript{17,21}

Plexus traction injuries in neonates are well-recognized, although they are uncommonly imaged. Traction on the superior plexus at C5-7 (Erb-Duchenne palsy) is more common than the inferior plexus at C8 and T1 (Klumpke palsy). These injuries are usually managed conservatively, with surgery reserved
for those with poor functional recovery and suspected pre-ganglionic injury on imaging. 1,22

**Malignant neoplasms**

Malignant involvement of the BP is more common than primary benign lesions, and occurs in an older age group. The BP can be infiltrated by primary malignant tumors, local secondary malignancy or metastatic disease (Figure 8). Lesions arising directly from the plexus include malignant peripheral nerve sheath tumors and a plethora of uncommon sarcomatous lesions (eg, fibrosarcoma or radiation induced tumors). Local malignant extension commonly occurs secondary to a Pancoast tumor at the lung apex or due to a head and neck carcinoma (Figure 9). 1,3,15

These lesions can involve multiple structures including the vertebral bodies, ribs and clavicle with compression and direct invasion of the neural and vascular structures. Clinically, there is usually pain followed by paraesthesia and weakness at the upper limb, predominantly involving the inferior trunk and spinal nerves in a Pancoast tumor. In addition, adjacent infiltration of the sympathetic chain (stellate ganglion) may result in Horner’s syndrome. 6,23

Metastatic disease of the BP commonly arises in the adjacent regional lymph nodes. In particular, breast carcinoma can metastasize along the axillary and supraclavicular nodes resulting in focal masses or even diffuse plexus infiltration (Figure 10). Head and neck carcinomas and lymphoma are other common causes of metastatic infiltration. 16,17

MR imaging for suspected malignant involvement should include post-contrast sequences to assess for focal masses and any perineural or leptomeningeal enhancement extending to the spinal cord. The imaging report should also document potential involvement of the ipsilateral vertebral artery, which could be further evaluated using MR angiography. 1,5,6

**Radiation plexopathy**

Any discussion of malignant infiltration at the BP is incomplete without considering treatment complications. Radiotherapy is utilized for numerous malignancies and secondary nodal disease at the plexus, including breast, lung and head and neck carcinomas. Radiotherapy is a common cause of non-traumatic plexus injury with histology showing fibrous tissue sheathing the plexus and underlying neural degeneration. As in other forms of plexopathy, paraesthesias dominate the clinical picture, with motor loss less common. 1,13,17

On imaging, it is challenging to differentiate radiation plexopathy from recurrent/residual tumor. MRI of radiation plexopathy in the acute phase (<6months) appears as a non-specific plexopathy with diffuse neural thickening, T2W hyperintensity and mild enhancement (Figure 11). In the more chronic fibrotic phase MRI can demonstrate T2W and T1W hypointense thickening without a focal mass. Enhancement is variable in the fibrotic phase, again making differentiation from tumor challenging. 24 Clinical history is crucial to assess for this entity, with information such as radiation dose (less likely if less than 50Gy) and time course (peak presentation is several years after therapy) especially useful. When doubt remains, early follow-up MRI or additional FDG PET-CT, which can assess for recurrent hypermetabolic tumor, can be utilized. 3,25

**FIGURE 12.** Brachial plexus neurogenic tumors in a 47-year-old woman with chronic neck pain and right arm numbness following a motor vehicle accident 2 years ago. Coronal T2W, fat-saturated MRI sequences of the right brachial plexus show two round, T2W hyperintense masses at the right brachial plexus. The dominant mass (solid arrow) involves the cords and branches of the right brachial plexus at the costoclavicular space, with the smaller lesion (dashed arrow) in the retropectoral space in close relation to the proximal branches. Both lesions demonstrate a target sign (better seen at the dominant lesion), with relative central T2W hypointensity. These findings are most compatible with schwannomas or neurofibromas. No surgical intervention is planned at the current time with continued imaging follow-up advised.
Benign neoplasms

Numerous benign lesions can arise directly from or in the vicinity of the BP. Peripheral nerve sheath tumors (PNST) such as schwannomas and neurofibromas are the most common primary benign lesion of the BP. The majority of PNST are not associated with underlying neurofibromatosis. Patients usually report a painless supraclavicular mass without parasthesia or weakness. A positive Tinel sign may be present. On imaging the lesions are usually well-circumscribed, ovoid (parallel to the course of the BP), with T2W hyperintensity and avid enhancement. A target sign may also be demonstrated (more commonly in neurofibromas) consisting of central low signal and surrounding peripheral T2W hyperintensity (Figure 12). Schwannomas also demonstrate the salt and pepper fascicular sign, and can undergo degenerative cystic changes (ancient schwannoma).

Other compressive benign lesions arising in the vicinity of the BP include lipomas, fibroproliferative conditions, and vascular lesions (e.g., hemangioma, arteriovenous malformations or pseudoneurysms).

Lipomatous lesions are well characterized on both ultrasound and MRI. On T1W and T2W images the lesions are hyperintense with loss of signal on fat suppression. Differentiating lipomas from low-grade liposarcomas remains difficult, although imaging features such as numerous thick septations, extensive non-fatty components and a large size (>10cm) suggest a more malignant potential.

Fibroproliferative conditions can present as large masses and include fibromatosis (locally aggressive extra-abdominal desmoid tumor) and nodular fasciitis. The former is typically painless with MRI demonstrating avid enhancement, heterogeneous T2W and hypointense T1W signal and infiltrative margins. In contrast, nodular fasciitis usually presents as a markedly tender mass with similar MR signal characteristics but less marked enhancement. Surgical resection is typically curative in nodular fasciitis, whereas fibromatosis is prone to recurrence following resection and is therefore difficult to treat. For this reason, close MRI follow-up is common in fibromatosis, and may coincide with additional radiation or chemotherapy.

Brachial plexitis

Inflammation of the BP, termed brachial plexitis, typically presents with acute onset of severe shoulder pain, parasthesias and delayed weakness with muscular atrophy. On clinical follow-up the typical clinical course of pain improvement followed by muscle weakness can differentiate the condition from cervical spondyloarthropathy. The supraspinatus nerve is most commonly affected (~97%) and is involved solely in half of cases.

The cause of brachial plexitis remains uncertain with viral, post-vaccination or auto-immune mechanisms postulated. It is therefore usually termed acute sporadic brachial plexitis or Parsonage-Turner syndrome. A subset of brachial plexitis can occur due to autosomal dominant hereditary neuromuscular amyotrophy. Another condition
to be aware of is chronic inflammatory demyelinating polyneuropathy, which is rare but classically leads to marked, diffuse thickening of the cervical nerve roots and plexus. MRI is the preferred examination and in the acute phase may show denervation edema in the shoulder girdle musculature, which can progress to fatty atrophy with chronicity (Figure 13). Less commonly, MRI can show nerve root thickening and edema with increased T2W signal. Contrast administration is not strictly required, but can highlight neural enhancement, indicative of ongoing active inflammation. Practically, the major role of MRI is to exclude a compressive mass, which may require surgical intervention. Ultrasound does not have a major role in brachial plexitis, but may highlight fatty atrophy of the shoulder girdle musculature, and can also exclude compressive lesions; eg, a spinoglenoid notch cyst leading to suprascapular nerve compression.

Infection

Infection of the BP is uncommon and can occur secondary to penetrating trauma or adjacent soft tissue infection, vertebral osteomyelitis, septic arthritis of the glenohumeral joint or direct extension of infection from the lung apex. In patients with suspected infection, especially the immunocompromised, there should be a low threshold for contrast-enhanced MRI. This allows for assessment of infective extent, any adjacent primary source; eg, spinal infection, and for any fluid collections, which could then be targeted for aspiration or surgical debridement. Numerous pathogens are implicated with bacterial infections most common, especially staphylococcus aureus or tuberculosis.

Thoracic outlet syndrome

Compression of the subclavian vessels and BP as they traverse the thoracic outlet may produce symptoms such as paresthesia, pain, or swelling. Three potential sites of entrapment exist: interscalene triangle, costoclavicular space (most common site of arterial compression) and the retropectoralis minor space. The clinical evaluation of this syndrome is challenging, and provocative ultrasound and MRI can be used in tandem to aid diagnosis. Ultrasound can provide real-time evaluation of vessel stenosis or occlusion.

FIGURE 14. A 30-year-old man with mild neurogenic symptoms (numbness and tingling without weakness) during overhead activities. B-mode ultrasound was performed for suspected bilateral thoracic outlet syndrome with arms up and down as indicated. Dynamic imaging demonstrates narrowing of the subclavian veins upon arm raising at the costoclavicular spaces. These changes are more apparent on the left-side (solid white arrows highlight the caliber of the subclavian veins). This patient did not want to proceed with MRI, which would allow better evaluation of any neural compression or underlying compressive lesion.
A 19-year-old male with numbness in an ulnar distribution at both hands on arm raising, more marked on the left. Contrast-enhanced MR angiography was performed using Time Resolved Imaging of Contrast KineticS (TRICKS) for suspected thoracic outlet syndrome. Dynamic imaging with arms up and down demonstrates narrowing of the subclavian veins upon arm raising. These changes were more apparent on the left-side with >50% narrowing (solid white arrows). No evidence of neural edema or thickening was seen to suggest neural impingement (images not shown).

A 30-year-old woman with intermittent right arm swelling and pain. Contrast-enhanced MR angiography (A and B with arms raised) was performed using Time Resolved Imaging of Contrast KineticS (TRICKS) for suspected thoracic outlet syndrome. The arterial phase (A) shows narrowing of the right subclavian artery (solid arrow) at the costoclavicular space. Minimal narrowing of the contralateral left subclavian artery is also apparent. On the venous phase (B) there is narrowing of both subclavian veins, more marked on the right (dashed arrow) in the same region. Coronal T2W, fat-saturated MRI of the right brachial plexus (C) shows additional edema and enlargement of the trunks and proximal divisions of the brachial plexus (arrowhead), again at the costoclavicular space. No enlargement or edema of the nerves was noted on the left-side (images not shown). These findings were compatible with right-sided neurovascular thoracic outlet syndrome. There was an incomplete improvement with physical therapy, so the patient underwent external neurolysis of all the brachial plexus trunks, anterior and middle scalenectomy, and resection of the first rib. After 4 months follow-up there was >70% improvement and the patient resumed athletic activities.

 Provocative maneuvers typically involve arm hyperabduction, which accentuates any narrowing at the costoclavicular and retropectoralis minor spaces. The syndrome may result from a variety of causes including a cervical rib, anomalous muscle (eg, subclavius posterior muscle), clavicular fractures with callus formation, fibrous bands or neoplastic lesions. Diagnosis can be challenging as some degree of venous compression is apparent in most asymptomatic patients on arm abduction. In this regard, bilateral imaging may high-
light the region of abnormal narrowing on the symptomatic side (Figure 16).

### Cervical spondylosis

Due to the vague and non-specific symptoms of BP lesions, it is important to first exclude much more common cervical spondylotic changes. Disc bulges, osteophytes, uncovertebral and facet joint arthropathy can combine to cause cervical cord and/or nerve root compression. Although the cervical spine is covered to some degree on BP protocols, initial dedicated cervical spine MRI may identify the cause of the clinical complaint avoiding the need for the more time-intensive BP examination.

### Conclusion

The BP can be imaged in detail using dedicated MRI protocols, which allow for accurate interpretation by the radiologist. A dedicated BP protocol should include bilateral coronal and unilateral sagittal sections to identify normal anatomy and highlight pathology. A plethora of lesions occur at the BP, predominantly associated with trauma, but also including primary and secondary neoplasia, inflammation and less commonly infection. Practical reporting should include the site of the BP lesion (pre versus post-ganglionic), involved segment (eg, root, division, etc.), and any associated mass or compressive structure (eg, cervical rib). In the latter, a dedicated thoracic outlet MRI protocol in tandem with Doppler ultrasound can be used to assess dynamic changes in adjacent subclavian vascular caliber and flow.

### References

Hepatocellular adenoma (HA) is a relatively uncommon benign liver neoplasm that is typically seen in obese women of childbearing age who are on long-term oral contraceptives. It is also reported to occur in men secondary to androgen drug use and in patients with rare metabolic disorders such as glycogen storage disease, maturity onset diabetes of the young and metabolic syndrome. Accurate identification and characterization of HA is clinically relevant as there is an increased tendency of this distinctive tumor to rupture and cause hemorrhage, to increase in size during pregnancy as well as to undergo malignant transformation. Recent patho-genetic studies have revealed that HA is a heterogeneous entity that may be classified into specific subtypes based on unique molecular signatures, histological features and immunohistochemistry. Based on characteristic MRI characteristics, specific HA subtypes may be identified non-invasively. Radiologists and pathologists have an equally important role to play in the diagnosis and morpho-molecular subtyping of HAs. This review focuses on the radiological and pathological features of HAs and its morphologic subtypes, and in addition dwells on the differential diagnosis of HAs based on imaging characteristics.

Epidemiology and etiologic associations
Hepatocellular adenoma has an incidence of 1–1.3 million cases per year in North America and Europe. Several studies have consistently linked the occurrence of HAs to oral contraceptive pill (OCP) use. The risk of HA is associated with dose and duration of oral contraceptive use; HAs were particularly associated with use of older generation of OC pills with high-estrogen content. Regression of Hepatocellular adenoma has been reported to occur following cessation of OCPs. HAs have also been reported to occur in men secondary to anabolic steroid/an-drogen use. Other hormonal therapies and risk factors include: clomiphene, danazol, testosterone in patients with Fanconi anemia (FA) and without FA, Klinefelter’s syndrome, Glycogen storage disorders I, III and IV, alcohol, and metabolic syndrome. Hepatocellular adenomatosis, defined as development of >10 HAs in a patient, is usually related to germline mutations of HNF1-α gene and is also seen in patients with type 3 maturity onset diabetes of young (MODY 3).

Clinical presentation
The majority of HAs are clinically occult and are incidentally detected on imaging. The risk factors for hemorrhage are size >5 cm, a subcapsular location and longstanding OCP use. HCA associated with hemorrhage may present with acute abdominal pain, elevated liver enzymes, and hypovolemic shock. Inflammatory HCA has the highest risk of hemorrhage and may show elevated levels of acute-phase reactants. The β-catenin activated subtype has the highest predilection for malignant transformation of all HCAs and this may be seen as a rapid increase in the size of a previously known HCA.

Classification
Hepatocellular adenoma (HA) was considered a homogeneous entity until the early 2000s, when a French group of clinical researchers demonstrated somatic bi-allelic mutations of transcription factor 1 (TCF 1) gene encoding hepatocyte nuclear factor 1 (HNF 1) in a subset of HAs. Subsequently, they

Update: Radiologic-pathologic correlation of hepatocellular adenoma
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reported that telangiectatic focal nodular hyperplasias (T-FNHs) are monoclonal lesions and clinically behave similar to HAs without HNF-1-α mutation. These were later classified as inflammatory HAs. Ongoing genomic studies of HAs by the same French group led to the landmark paper in 2006 that introduced the genotype-phenotype taxonomy of HAs. According to this schemata, the HAs are classified into 4 subtypes, of which the first three have unique molecular signatures as well as histological, immunophenotypical and radiological features. These were: 1. HNF-1-α (HNF 1A) mutated HAs; 2. β-catenin mutated HAs; 3. Inflammatory-type HAs. The last group classified as “unclassified” refers to HAs that do not satisfy the diagnostic criterion described in the three other subtypes (Table 1). Using sequencing and gene expression

### Table 1. Clinical, Radiologic and Pathologic Features of Subtypes of HCA

<table>
<thead>
<tr>
<th>Subtype</th>
<th>Frequency</th>
<th>Clinical features and associations</th>
<th>Imaging features</th>
<th>Pathologic features</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory HCA (IL6ST mutations)</td>
<td>Most common: 40%–55%</td>
<td>• Obesity • Alcohol use • Hepatic steatosis • Metabolic syndrome</td>
<td>• Can mimic FNH • T2 moderate hyperintensity • Intracellular fat seen occasionally • Variable degree of uptake on hepatobiliary phase</td>
<td>• Pseudo-portal tracts with thick arteries, sinusoidal dilatation, and variable steatosis • Increased expression of inflammatory proteins CRP and SAA on immunostaining</td>
<td>• Bleeding is main complication • 10% also express β-catenin and hence may show malignant transformation</td>
</tr>
<tr>
<td>HCA with TCF1 gene mutation</td>
<td>30%–50%</td>
<td>• Hepatic adenomatosis • Maturity-onset diabetes of the young type 3</td>
<td>• Intracellular lipid</td>
<td>• Variable steatosis • Absence of expression of L-fatty acid binding protein on immunostaining</td>
<td>• No significant bleeding risk • No risk for malignant transformation</td>
</tr>
<tr>
<td>β-catenin–mutated HCA</td>
<td>10%–18%</td>
<td>• Glycogen storage disease • Male hormone administration</td>
<td>• Not usually steatotic • There can be washout during portal venous phase on non-hepatocellular gadolinium contrast agents</td>
<td>• May have cytologic and architectural atypia • Immunostain for β-catenin is positive in nuclei • Glutamine synthetase shows diffuse and strong cytoplasm expression</td>
<td>• Malignant transformation</td>
</tr>
<tr>
<td>Unclassified</td>
<td>10%</td>
<td>• No specific association</td>
<td>• No specific features</td>
<td>• No specific features</td>
<td>• Increased risk of bleeding in the subset with sonic hedgehog activation</td>
</tr>
</tbody>
</table>

CRP indicates C-reactive protein; FNH, focal nodular hyperplasia; HCA, hepatocellular adenoma; SAA, serum amyloid A.

**FIGURE 1.** HNF1A mutated hepatocellular adenoma. Immunostain for L-FABP showing loss of expression in tumor, versus retained expression in surrounding non-neoplastic liver.
profiling, this classification has further been refined recently to include 6 subgroups of HAs.\(^9,1,23\) The \(\beta\)-catenin mutated HAs (BHA and IHA with \(\beta\)-catenin mutations) are further split into: (a) BHA with exon 3 mutations; (b) BHA with exon 7/8 mutations. A subset of unclassified HA has been found to show constitutive activation of sonic hedgehog (shh) pathway due to overexpression of GLI family zinc finger 1 (GLI1). These HAs are associated with a higher risk of bleeding. They do not have specific morphological features or immunoprofile.

We will focus on four subtypes of HAs in this review, as radiologic features of the newer subtypes are not well defined. Clinical implementation of this classification in diagnostic medicine has brought about a paradigm shift in the management of HAs, as this helps determine the potential for complications including bleeding and malignant transformation, and thereby guide further management in terms of resection and/or surveillance.

**Pathology**

**Gross evaluation**

Hepatocellular adenomas are well-demarcated lesions that can occasionally be encapsulated and range in size from 1-30 cm.\(^3\) HA may present as a solitary mass or as multifocal, variably sized, soft tissue masses. They typically arise in non-fibrotic liver, however, they may

**FIGURE 2.** HNF1A mutated hepatocellular adenoma (Steatotic hepatocellular adenoma) in a 25-year-old woman. Arterial phase (A) shows a lesion in the right liver lobe with avid arterial enhancement. In-phase (B) and opposed-phase (C) shows uniform signal dropout of the lesion on the opposed phase suggestive of intracellular fat. Note that there is also signal drop out of background liver parenchyma indicative of underlying hepatic steatosis.

**FIGURE 3.** Inflammatory hepatocellular adenoma. Immunostain for L-fatty acid binding protein with retained cytoplasmic expression in tumor. X100.
occur in the background of cirrhosis. HAs reported in the setting of cirrhosis are usually of the inflammatory subtype. Rare cases of multiple HNF-1-α mutated HAs has been reported to occur in the background of congenital hepatocellular fibrosis. The cut surface of HA may be tan-yellow or red-brown depending upon the presence of steatosis or peliosis/hemorrhage/old hemorrhage, respectively. Inflammatory HA shows alternating pale red and dark-red surface.

**FIGURE 4.** Large inflammatory hepatocellular adenoma (IHA) in a 30-year-old woman along with associated focal nodular hyperplasia (FNH). (A) Moderately heterogeneous, mildly hyperintense lesion (IHA) is seen in the right lobe on a T2-weighted image (red arrow). Incidental iso-intense lesion (FNH) with a central scar (blue arrow). In-phase (B) and out-of-phase (C) images demonstrate no signal loss within the both lesions. Arterial (D) and portal venous phase (E) post gadoxetic acid images show marked heterogeneous hyperenhancement of the adenoma (IHA) (red arrow) and moderate enhancement of the FNH with a central scar (blue arrow). Hepatobiliary phase image (F) reveals the lateral lesion (IHA) with mild and heterogeneous retention of contrast (red arrow) and intense uptake within the medial lesion (FNH).
Microscopic evaluation

Hepatocellular adenoma is classically characterized by sheets of benign-appearing hepatocytes with interspersed thin-walled, unpaired arteries. The hepatocyte trabeculae are 1-3 cells thick and the reticulin framework is preserved. Portal tracts containing portal veins or bile ducts are absent. Few randomly distributed pseudo-portal tract areas with thick walled vessels and ductular reaction can be seen in some HAs. Other variable features include steatosis, inflammatory cell infiltrate, sinusoidal dilatation, myxoid changes and presence of pigments such as bile pigment, lipofuscin or Dubin Johnson-like pigment.

Radiologic and pathologic features of subtypes of hepatocellular adenoma

Hepatocyte nuclear factor-1-α (HNF1A) mutated Hepatocellular adenoma

These comprise 35% to 40% of all HA. Their molecular signature is characterized by bi-allelic inactivating mutations of TCF-1, a tumor suppressor gene, located on long arm of chromosome 12, and encodes for transcription factor HNF-1A, which is involved in hepatocyte differentiation and expression of certain genes encoding for albumin, β-fibrinogen and α-1-antitrypsin.

The mutations are largely somatic, however, germline mutations of TCF1 (HNF1A) gene are associated with type 3 maturity onset diabetes of the young (MODY 3). This is an autosomal dominant disease, which presents in early adulthood and is associated with development of familial adenomatosias. HNF1A mutation down-regulates liver type-fatty acid binding protein (L-FABP) and causes lipogenesis by promoting fatty acid synthetase.

Gross examination of HNF1A mutated HA shows a well-demarcated solid tumor with a tan-yellow soft to firm cut surface. The phenotypic correlate of above-mentioned molecular alterations is presence of pigments such as bile pigment, lipofuscin or Dubin Johnson-like pigment.

Inflammatory hepatocellular adenoma (IHCA)

Historically, IHCAs were referred to as telangiectatic FNHs until 2004-2005, when studies showed these to be monoclonal neoplasms, which behave biologically similar to HAs. IHCA comprise about 30-35% of all HAs. This subtype of HA is characterized by activation of signal transducer and activation of transcription 3 (STAT 3) signaling pathway leading to induction of acute phase inflammatory response within the tumoral hepatocytes. About two-thirds of IHCA show mutations of interleukin 6-signal transducer gene (IL6ST gene), which encodes for glycoprotein 130 (gp130), a component of IL-6 receptor. Activation of IL-6 promotes the STAT3 signaling pathway. About one-third of the HAs do not show mutations of IL6ST gene, yet, show evidence of STAT 3 activation and gp130 protein expression through unknown mechanisms. About 10% of IHCA show concomitant β-catenin mutations.
Gross characteristics of IHCA include a well-demarcated tumor with red-brown variegated cut surface. Histologically, these are characterized by sinusoidal dilatation, peliosis, presence of pseudo-portal tracts like areas with dystrophic blood vessels, ductular reaction and varying degree of inflammatory infiltrates. Focal steatosis may be seen in some cases. Immunohistochemical staining with antibodies to acute phase inflammatory reactants, serum amyloid A (SAA) and C reactive protein (CRP), show diffuse cytoplasmic expression of both SAA and CRP. Immunostain for L-FABP shows retained cytoplasmic expression in tumoral hepatocytes (Figure 3). IHCA with β-catenin mutations show nuclear expression of β-catenin on immunohistochemical staining. Glutamine synthetase is a surrogate marker of β-catenin mutation.33

Some IHAs with β-catenin mutations maybe positive or negative for nuclear β-catenin expression on immunostaining, but will show strong diffuse/patchy cytoplasmic staining for glutamine synthetase.4 These β-catenin mutations may occur on exon 3 or exon 7/8.1,23

Inflammatory HAs show mild to moderate hyperintense signal on T2WI and are iso-intense or mildly hyperintense on T1WI with no significant signal drop-off with chemical shift imaging.32 After administration of extracellular gadolinium-based contrast material, IHAs usually show intense enhancement during the arterial phase, with persistent enhancement in the portal venous and delayed phases. IHAs may show uptake of hepatobiliary specific gadolinium agent and may show peripheral rim like uptake or heterogeneous internal retention of contrast on the hepatobiliary phase.32,35 Figure 4). Inflammatory HAs show the highest risk of bleeding due to the presence of sinusoidal dilatation, which can occur in about 30% of these tumors and particularly seen in tumors larger than 5 cm maximum dimension and subcapsular tumors (Figure 5). About 10% of inflammatory HAs show an increased risk of malignancy.10,18,19

**β-catenin–mutated hepatocellular adenoma (BHA)**

These adenomas comprise about 20% of all HAs,8 Wnt/β-catenin pathway is involved in hepatocellular development and zonation. In normal, non-neoplastic hepatocytes, activation of β-catenin protein is transient followed by degradation. Mutations of β-catenin gene (CTNNB1 gene) lead to production of mutant protein that has prolonged half-life and is resistant to degradation.36 In 10% of cases, there are deletions CTNNB1 exon 3 leading to decrease in β-catenin degradation.1,23 In other cases, there are point mutations targeting hotspots in exon 3 or those in exon 7/8.4,9

Gross characteristics of β-catenin–mutated HA are unremarkable. They may present as well-demarcated tumors with fleshy cut surface. Histologically, they lack a distinctive morphology. They are composed of sheets of hepatocytes with interspersed unpaired arteries. Some may show cytologic and architectural atypia characterized by pseudoacin formation. Steatosis is not a typical feature. Immunostain for beta-catenin will show nuclear beta-catenin staining, however, this can be very focal in distribution. Glutamine synthetase is a surrogate marker for β-catenin mutation. Immunostain for glutamine synthetase shows strong diffuse cytoplasmic staining, however, the staining can be heterogeneous and variable.23

No specific imaging findings have been reported to diagnose β-catenin–mutated hepatocellular adenomas on imaging. T1 and T2 signal of these tumors is variable depending on the presence of hemorrhage and/or necrosis.10,18,19

β-catenin–mutated HAs commonly demonstrate strong arterial enhancement with portal venous washout and no uptake on hepatobiliary phase (Figure 6). The risk of hepatocellular carcinoma is about 5%–10% in these HAs. β-catenin–
mutated HAs carry the highest risk of malignancy.\textsuperscript{10,18,19}

**Hepatocellular adenoma unclassified**

Unclassified HA constitutes 10% of all HAs and these tumors do not show any specific genetic abnormalities. No specific MR imaging findings are reported to identify unclassified HAs.\textsuperscript{10,18,19}

**Conclusion**

Hepatocellular adenomas are a diverse group of benign liver neoplasms with increased propensity to bleed and to undergo malignant transformation. Recent genetic studies have identified several subtypes with distinctive tumor genetics and pathways as well as specific risk factors and risks of complications. MRI plays a key role in the diagnosis and classification of HAs as well as in surveillance. Hepatocellular adenomas with \(\beta\)-catenin mutations frequently undergo malignant change, inflammatory HAs commonly bleed, and steatotic HAs typically portend a favorable prognosis. A knowledge of the clinical and imaging findings and associated complications of the subtypes of hepatocellular adenoma permit optimal patient management.

**REFERENCES**


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

• The risk for NSF appears highest among patients with:
  o Chronic, severe kidney disease (GFR < 30 mL/min/1.73m²), or
  o Acute kidney injury.

• Screen patients for acute kidney injury and other conditions that may reduce renal function. For patients at risk for chronically reduced renal function (e.g. age > 60 years, hypertension, diabetes), estimate the glomerular filtration rate (GFR) through laboratory testing.

• For patients at highest risk for NSF, do not exceed the recommended DOTAREM dose and allow a sufficient period of time for elimination of the drug from the body prior to any re-administration.

Indications and Usage
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Contraindications
History of clinically important hypersensitivity reactions to DOTAREM.

Warnings and Precautions
• Hypersensitivity Reactions: Anaphylactic and anaphylactoid reactions have been reported with DOTAREM, involving cardiovascular, respiratory, and/or cutaneous manifestations. Some patients experienced circulatory collapse and died. In most cases, initial symptoms occurred within minutes of DOTAREM administration and resolved with prompt emergency treatment.

• Before DOTAREM administration, assess all patients for any history of a reaction to contrast media, bronchial asthma and/or allergic disorders. These patients may have an increased risk for a hypersensitivity reaction to DOTAREM.

• Administer DOTAREM only in situations where trained personnel and therapies are promptly available for the treatment of hypersensitivity reactions, including personnel trained in resuscitation.

• Gadolinium Retention: Gadolinium is retained for months or years in several organs. The highest concentrations have been identified in the bone, followed by brain, skin, kidney, liver and spleen. The duration of retention also varies by tissue, and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs.

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• Acute Kidney Injury: In patients with chronically reduced renal function, acute kidney injury requiring dialysis has occurred with the use of GBCAs. The risk of acute kidney injury may increase with increasing dose of the contrast agent; administer the lowest dose necessary for adequate imaging.

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• The most common adverse reactions associated with DOTAREM in clinical trials were nausea, headache, injection site pain, injection site coldness and rash.

• Serious adverse reactions in the Postmarketing experience have been reported with DOTAREM. These serious adverse reactions include but are not limited to: arrhythmia, cardiac arrest, respiratory arrest, pharyngeal edema, laryngospasm, bronchospasm, coma and convulsion.

Use in Specific Populations
• Pregnancy: GBCAs cross the human placenta and result in fetal exposure and gadolinium retention. Use only if imaging is essential during pregnancy and cannot be delayed.

• Lactation: There are no data on the presence of gadoterate in human milk, the effects on the breastfed infant, or the effects on milk production. However, published lactation data on other GBCAs indicate that 0.01 to 0.04% of the maternal gadolinium dose is present in breast milk.

• Pediatric Use: The safety and efficacy of DOTAREM at a single dose of 0.1 mmol/kg has been established in pediatric patients from birth (term neonates ≥ 37 weeks gestational age) to 17 years of age based on clinical data. The safety of DOTAREM has not been established in preterm neonates. No cases of NSF associated with DOTAREM or any other GBCA have been identified in pediatric patients age 6 years and younger.

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*Dotarem was launched globally in 1989 and approved by the FDA for use in the US in 2013.

References:
A cute abdominal pain is a common symptom for seeking urgent medical evaluation. The term ‘acute abdomen’ has historically referred to patients needing immediate surgical intervention, but it has broadened to include any patient experiencing acute pain to a degree that requires medical evaluation. The causes of acute abdomen are numerous and span the medical and surgical spectrum, with many etiologies identifiable using medical imaging. Indeed, radiology in the emergency department and the acute setting plays an important role in the diagnosis and workup of these patients, with imaging adding value to patient care.1

This review will focus on common causes of the acute abdomen that are detected on imaging, particularly computed tomography (CT). Typical imaging findings as well as pitfalls and complications will be discussed.

CT Technique

While protocols will vary by institution, scanning is generally performed from the diaphragm through the pubic symphysis. Images are reconstructed as contiguous 2.5-5 mm axial images and reformatted as 2-3 mm coronal and sagittal images. Depending on the scanner, there are options for dose reduction with automated tube voltage and current modulation. Intravenous (IV) contrast material is essential, typically with a single acquisition in the portal venous phase that can be obtained using a fixed scan delay or bolus tracking with automated triggering.

At our institution, positive enteric contrast (iodinated water soluble contrast) is rarely utilized in the emergency department (ED). By not utilizing enteric contrast, studies have shown improved patient throughput while retaining high accuracy.2,3 Positive enteric contrast can be useful for select indications, including assessing for fistulae, enteric leak and mesenteric abscess; however, early intestinal ischemia and GI bleeding can be masked by enteric contrast. We find that with thin-image reconstruction and multi-planar reformatted imaging, the lack of enteric contrast does not affect our accuracy or confidence.

Dual energy CT (DECT), in which two different photon energies are used in a single acquisition, allows for the creation of a virtual non-contrast dataset. While there is potential for dual energy CT to allow characterization of incidental adrenal and renal lesions using a single post-contrast acquisition, small renal calculi can be missed on virtual noncontrast datasets, and in the setting of acute abdominal pain, the utility of DECT is unclear and research is ongoing.4-6

Differential diagnosis

The differential diagnosis for the acute abdomen is broad. For patients with right upper quadrant pain, cholecystitis should be considered. Appendicitis and gynecologic etiologies commonly present with right lower quadrant or pelvic pain. Diverticulitis most commonly affects the sigmoid colon and patients often present with left lower quadrant pain. Epigastric pain may suggest acute pancreatitis or peptic ulcer disease, while flank pain should suggest urinary tract pathology. Generalized abdominal pain should raise the suspicion for bowel obstruction and mesenteric ischemia. While a quadrant-based differential diagnosis may be useful, the specific abnormalities may present with nonspecific symptoms, and a careful search pattern on CT imaging is required.

Acute appendicitis

Acute appendicitis is a common acute surgical condition, with an incidence of 100 per 100,000 person-years in North America.7 Signs and symptoms can include right lower quadrant pain, nausea/vomiting, loss of appetite, fever, and leukocytosis. Imaging
findings include a dilated appendiceal lumen, wall thickening, mural hyperenhancement, and periappendiceal inflammatory changes (Figure 1). Mimics of appendicitis can include mucocele (dilated, fluid filled appendix without periappendiceal inflammatory change), inflammatory bowel disease, acute diverticulitis (ileal or colonic), carcinoma, epiploic appendagitis, and gynecologic abnormalities. Missed appendicitis may be caused by an unusual location of the appendix (right upper quadrant, left hemiabdomen), localized inflammation of the tip of the appendix (tip appendicitis), inflamed appendiceal stump following appendectomy, falsely reassuring presence of intraluminal gas, or a separate concurrent process causing the reader to overlook the appendix.

Complications of untreated appendicitis can include perforation, abscess formation, and septic seeding of the portomesenteric venous system. While antibiotic therapy alone is a validated option for the treatment of acute appendicitis, most providers and patients prefer definitive surgical management.

Acute cholecystitis

Acute cholecystitis is a common cause of the acute abdomen and patients most often present with right upper quadrant pain. The disease can be either calculous or acalculous, with the former representing the large majority of cases.

Acute cholecystitis is a clinical diagnosis that requires appropriate correlation between history and physical examination, laboratory studies, and radiologic examination. Cholecystitis can be demonstrated using ultrasound, CT, MRI, or nuclear scintigraphy, though the ACR appropriateness criteria lists ultrasound as the most appropriate initial imaging in a patient with suspected acute cholecystitis. CT findings of acute cholecystitis include wall thickening and luminal distention, though pericholecystic inflammatory change is often a central finding (Figure 2). CT also offers a complete picture of the surrounding tissues and allows for visualization of complications of acute cholecystitis such as perforation, emphysematous cholecystitis, hemorrhage, gallstone ileus, and postoperative complications. Gallstones can be seen on both CT and ultrasound, though ultrasound is more sensitive.

In addition to common findings, a number of CT signs have been described that suggest the diagnosis. The tensile gallbladder fundus sign, defined as the absence of gallbladder fundal flattening by the abdominal wall due to increased gallbladder pressures, has been shown to be useful, particularly early in the presentation. Similarly, the pope’s hat sign has been recently described as a thin crescent of low density between the gallbladder and liver and may also improve diagnostic performance in early acute cholecystitis.

Once the diagnosis is made, treatment options typically include cholecystectomy or percutaneous cholecystostomy tube placement. CT scans may be obtained post treatment to assess for postoperative complications or cholecystostomy tube position. Biliary scintigraphy is also used when bile leaks are suspected.

Acute diverticulitis

Approximately 10-20% of the millions of Americans with diverticulosis will develop acute diverticulitis, caused by impaction of a diverticulum and development of focal inflammation. The left colon is affected in 90% of cases and patients commonly present with left sided or left lower quadrant pain. Diverticula; however, can occur throughout the GI tract and cecal, ascending colonic, and small bowel diverticulitis are all possible.

CT is excellent at portraying findings of both uncomplicated and complicated diverticulitis. For the former, findings with a high sensitivity include colonic wall thickening and pericolonic inflammatory change (Figure 3).
confidence can be increased by finding a culprit diverticulum, i.e. a single out-pouching that appears acutely inflamed or at the epicenter of the surrounding stranding. Adjacent fascial thickening can also increase specificity. Complications of diverticulitis include perforation, intramural abscess, and pericolonic abscess. Perforation may result in localized foci of pneumoperitoneum, or may less commonly cause diffuse or large volume free air. If untreated or longstanding, chronic diverticulitis may lead to complications including colovesical and colocolonic fistulas, intramural tracts, and chronic fluid collections.

Various pitfalls and mimics exist when imaging acute diverticulitis. The most important mimic of diverticulitis is colon cancer, which can also cause wall thickening, fistulae, and surrounding inflammatory change. Cancers tend to be associated with pericolonic lymph nodes, intraluminal masses, asymmetric wall thickening, and shorter segments of involvement, though considerable overlap in findings exists. While some international guidelines recommend colonoscopy after every case of diverticulitis, a growing body of literature has suggested that colonoscopy is not routinely necessary following uncomplicated acute diverticulitis. Treatment of uncomplicated diverticulitis is often conservative and comprised of antibiotics and dietary change. Complicated cases may require percutaneous drainage of fluid collections or surgery for free intraperitoneal gas, and recurrent or chronic cases may eventually be referred for resection of the affected colon.

Acute pancreatitis

Acute pancreatitis is a common etiology of acute abdominal pain in patients presenting to the ED. The clinical diagnosis of acute pancreatitis requires two of three features: 1) epigastric pain 2) elevated serum lipase to three times normal and 3) characteristic findings on imaging. In the early phase of acute pancreatitis (first week), treatment is supportive and severity is determined by the presence or absence of organ failure caused by the systemic inflammatory response syndrome. Treatment during the late phase (beyond the first week) is determined by the presence of symptoms or complications of pancreatitis and is often based on imaging findings including pancreatic necrosis, fluid collections, and pseudoaneurysms. The Revised Atlanta Classification describes two morphologic appearances of acute pancreatitis: interstitial and necrotizing. Interstitial edematous pancreatitis (IEP) appears as focal or diffuse enlargement of the pancreas with homogeneous or slightly heterogeneous enhancement and peripancreatic soft tissue stranding and fluid. Necrotizing pancreatitis includes both pancreatic parenchymal and peripancreatic necrosis. Pancreatic parenchymal necrosis can be diagnosed when portions of the pancreas lack enhancement and should be described as <30%, 30-50%, or >50% of the gland. Peripancreatic necrosis can be distinguished by peripancreatic fluid that contains non-liquid/fat components (Figure 4).

Interstitial edematous and necrotizing pancreatitis can be complicated by both acute (< 4 weeks) and chronic (> 4 weeks) fluid collections that may be sterile or infected (Figure 4). Acute fluid collections in the setting of IEP rarely become infected and rarely require percutaneous or surgical intervention. Pseudocysts are chronic fluid collections in the setting of IEP which also rarely become infected but may require endoscopic or percutaneous drainage if symptomatic. Acute necrotic collections and walled off necrosis may require surgical, endoscopic or percutaneous drainage depending on a patient’s symptoms and do require therapy if infected.
Pseudoaneurysms or active hemorrhage can be diagnosed at CT imaging and are commonly treated with transarterial embolization. Venous thrombosis is common in the setting of severe acute pancreatitis, but treatment is largely supportive.

**Peptic ulcer disease**

Peptic ulcer disease (PUD) is most commonly caused by Helicobacter pylori bacteria and non-steroidal anti-inflammatory medication. Common complications of PUD include GI bleeding and perforation, with gastric outlet obstruction and fistulization occurring less frequently. There are direct signs (focal outpouching and mucosal enhancement defects) and indirect signs (edema, wall thickening, and adjacent soft tissue stranding) of ulcer disease (Figure 5).25 Inadequate luminal disten-
tion often limits evaluation of the stomach on CT and is a potential pitfall for identifying wall thickening accurately.\textsuperscript{26} While most ulcers are occult at CT, evaluation for direct and indirect signs and use of multiplanar reformatted imaging can improve sensitivity.\textsuperscript{27} Duodenal ulcers and marginal ulcers at a gastrojejunostomy are more difficult to identify and a high index of suspicion is required. Perforation related to PUD can be readily detected using CT; gastric ulcers will typically cause pneumoperitoneum, while duodenal ulcers may cause intraperitoneal or retroperitoneal air depending on the site of perforation.

**Small-bowel obstruction**

Patients with small-bowel obstruction (SBO) generally present with nausea and vomiting with a distended abdomen. Postoperative adhesions are the most common cause of bowel obstruction, followed by hernias and malignancy. Abdominal radiography is historically the first imaging test for patients with suspected SBO; however, CT imaging can add value for clinicians by revealing SBO etiology and severity.\textsuperscript{28} At CT, proximal loops of small bowel will be dilated (> 2.5 cm) and there will be a transition to normal caliber or decompressed loops of small bowel at the site of obstruction.\textsuperscript{29} In addition, bowel may contain gas-mottled material proximal to the site of obstruction, known as the “small bowel feces” sign. Patients with uncomplicated bowel obstruction are often treated conservatively with enteric tube decompression and bowel rest.

Complicated small-bowel obstructions include strangulation with ischemia, closed loop obstructions, and internal hernias. These entities often require urgent surgical evaluation, and CT can help with prompt diagnoses. Findings of early bowel ischemia include wall thickening, abnormal enhancement (hypo- or hyperenhancement), and mesenteric edema, with pneumatosis intestinalis, portal and mesenteric venous gas, and pneumoperitoneum seen in later stages.\textsuperscript{29}

Closed loop obstruction occurs when a segment of bowel is obstructed at two sites, isolating the obstructed segment and putting it at high risk of ischemia. A closed loop can be caused by a single adhesive band or a mesenteric twist/volvulus.\textsuperscript{30} The CT diagnosis of a closed loop obstruction is complex and the associated imaging findings of a C- or U-shaped obstructed segment, a “beak” sign, a mesenteric “swirl” sign, and interloop fluid/edema have variable sensitivity (Figure 6).\textsuperscript{31}

Internal hernias can be congenital or acquired but are increasingly seen in the setting of Roux-en-Y gastric bypass. Several signs have been described including swirled mesenteric vessels,
bowel wall thickening, and hypo- or ischemia, including dilatation (ileus), one should search for signs of bowel patency, and should be assessed for patency, and is seen in the setting of systemic hypotension and decreased mesenteric perfusion. At CT, the mesenteric vasculature can be difficult to identify, but clinical suspicion and the use of multiplanar reformatted images can help.

Vascular: Mesenteric ischemia/AAA

Most acute abdominal pain is not related to a vascular etiology, yet vascular causes of abdominal pain can be associated with high morbidity and mortality. The most common vascular causes of acute abdominal pain include mesenteric ischemia and abdominal aortic aneurysm (AAA).  

Mesenteric ischemia can be occlusive (70-80%) or non-occlusive (20-30%). In the former, there is occlusion of the superior mesenteric artery or vein (Figure 7) leading to bowel ischemia from either insufficient inflow or venous hypertension and congestion. Non-occlusive mesenteric ischemia is seen in the setting of systemic hypotension and decreased mesenteric perfusion. At CT, the mesenteric vasculature should be assessed for patency, and one should search for signs of bowel ischemia, including dilatation (ileus), bowel wall thickening, and hypo- or hyper-enhancement. Bowel wall thinning is occasionally seen and may indicate impending perforation. Pneumatosis and mesenteric/portal venous gas are generally late findings and indicate necrosis.

AAA is readily visualized on CT. The presence of high-density fluid in the retroperitoneum should raise concern for rupture (Figure 8). Findings suggesting impending rupture include increased aneurysm diameter (if prior imaging is available), acute intramural hematoma, perianeurysmal soft tissue stranding, and draping of the aorta over the spine. These findings warrant emergent surgical or endovascular intervention.

Non-ischemic bowel wall thickening

Small bowel and colonic wall thickening are nonspecific findings that may be the result of ischemic, infectious, or inflammatory etiologies. Normal wall thickness is less than 3 mm; however, thickness depends on distention. Non-distended small bowel will appear thicker and will enhance more than well-distended small bowel. In addition, the jejunum appears thicker and enhances more than the ileum due to increased mucosal surface area. With tube current modulation (80-100 kVp), the bowel wall can appear hyperemic following IV contrast, a result of obtaining images at a lower kVp (closer to the k-edge of iodine), an important pitfall to be aware of. Adjusting the window and level can negate this appearance.

Bacteria, viruses, and parasites are potential causes of infectious enteritis. Giardia and Strongyloides often affect the proximal small bowel, while Salmonella, Shigella and Yersinia preferentially affect the distal small bowel (Figure 9). The imaging appearance (bowel wall thickening with submucosal edema) is otherwise nonspecific, and stool cultures are often required. Infectious colitis often presents as a pancolitis with Clostridium difficile, Escherichia coli, and cytomegalovirus as common pathogens. Pseudomembranous colitis from C. difficile often results in marked wall thickening that may be low attenuation and edematous, creating the “accordion sign” (Figure 10).

Crohn’s disease is an idiopathic inflammatory disease that affects between 400,000-600,000 people in North America. The hallmark of Crohn’s disease is multifocal and asymmetric disease that affects the mesenteric border more than the antimesenteric border. Wall thickening and hyperemia are the most common imaging features associated with Crohn’s disease, and the terminal ileum is the most common site of disease. The presence of strictures, fistulae, and fibrofatty proliferation suggest Crohn’s disease.

Urinary tract

Urolithiasis is a common pathology affecting a wide variety of patients. Clinical presentation may include back or groin pain, nausea, and hematuria. Infection, including pyelonephritis, may also be associated with pain, but additional symptoms include fever and leukocytosis, typically in the setting of an abnormal urinalysis.

CT imaging of calculi is common, with the use of CT tripling between 1992 and 2009. Noncontrast CT is frequently performed, with stone detection sensitivity of 95%. Noncontrast imaging is preferred when suspicion is high,
so as to avoid potential contrast-related complications. Contrast enhanced CT may be performed when clinical presentation suggests a variety of other differential diagnoses, and presence of IV contrast does not significantly decrease the sensitivity of detection for urinary calculi.\(^4,1\) In addition, IV contrast highlights alternative diagnoses, increases sensitivity for identification of mild obstruction, and demonstrates heterogeneous renal enhancement seen with pyelonephritis.\(^4,2\)

Complications of renal calculi include obstruction with the potential for calyceal rupture. Another complication is infection, which may lead to abscess formation if left untreated. The combination of obstruction and infection can lead to urosepsis requiring temporary placement or percutaneous nephrostomy via retrograde ureteral stent lead to urosepsis requiring temporary nation of obstruction and infection can form if left untreated. The combined effects of obstruction with the potential for calyceal rupture. Another complication is infection, which may lead to abscess formation if left untreated. The combination of obstruction and infection can lead to urosepsis requiring temporary placement or percutaneous nephrostomy via retrograde ureteral stent lead to urosepsis requiring temporary nation of obstruction and infection can form if left untreated. The combined effects, while rarely encountered, may require surgical intervention or lithotripsy.\(^4,3\)

**Gynecologic etiologies**

While ultrasound is the initial modality of choice for acute gynecologic complaints, CT is frequently performed in the emergent setting given its wide availability and is often performed in patients with nonspecific pain.\(^4,4\)

Corpus luteal cysts and hemorrhagic cysts may be physiologic causes of acute pelvic pain; a rim-enhancing corpus luteal cyst may be seen on CT, or a high-attenuation adnexal cystic structure may suggest a hemorrhagic cyst. Endometriomas have a heterogeneous CT appearance and may demonstrate solid and cystic components with irregular margins and may be mistaken for malignancy.\(^4,4\) Teratomas may be discovered incidentally, but can present with acute pain. Teratomas have classic imaging features including macroscopic fat, soft tissue components, cystic attenuation, and possibly calcifications.

Ovarian torsion may occur de novo or may be due to a lead point, such as a teratoma or enlarged adnexal cyst. CT demonstrates several findings including an enlarged ovary (> 5 cm), wall thickening or target-like appearance of the fallopian tube between the uterus and enlarged adnexa, medial or contralateral displacement of the adnexa, whirlpool sign of torsed adnexal vessels, ascites, and uterine deviation toward the affected side.\(^4,5,47\) This emergent diagnosis requires prompt surgical intervention to restore blood flow to the affected ovary.

In the infected patient, tubo-ovarian abscess may demonstrate complex fluid collections with thickened and irregularly enhancing walls, thickening of the uterosacral ligaments, parapelvic fat stranding, and anterior displacement of the broad ligament (Figure 11).\(^4,4,48\) IV antibiotics are the treatment of choice in the presence of tubo-ovarian abscess, although if large enough, or if patients fail to adequately respond to antibiotics, percutaneous drainage may be required.

Pelvic pain originating from the uterus is less common. Degenerating fibroids can cause pelvic pain in up to 30% of patients.\(^4,4\) CT may demonstrate a low-attenuation uterine mass with peripheral enhancement and a necrotic center. Uncommonly, migration of an intruterine device, as demonstrated by mal-positioning of the device into or through the myometrium, may cause pain.\(^4,9\) Hemorrhage and free fluid may accompany these findings, particularly in the presence of perforation. Gynecologic referral for device removal should accompany these findings, particularly in the presence of perforation. Gynecologic referral for device removal should be recommended when these findings are encountered.

In general, pelvic pathology found at CT will often require confirmation via pelvic ultrasound given its increased sensitivity and better depiction of anatomic structures.

**Conclusion**

Acute abdominal pain is a common presenting symptom in the emergency department and has a wide variety of causes. CT provides rapid and accurate assessment to narrow the differential and aid in the diagnosis of both surgical and non-surgical causes of pain.

**References**

Chemoembolization via intrahepatic collateral arteries

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Case Summary
A 53-year-old man with chronic hepatitis B presented with elevated transaminases while taking herbal supplements, but was otherwise asymptomatic, Child-Pugh A5 and ECOG performance status 0. Workup included nonreactive hepatitis B surface antigen, negative hepatitis C antibody, negative colonoscopy except for small hemorrhoids, negative antinuclear antibody, negative alpha-1 antitrypsin and ceruloplasmin tests. He transferred his care to a second hospital and underwent hepatic ultrasonography, revealing a 16 cm mass, confirmed on multiphasic CT scan to be a hepatocellular carcinoma (Figure 1). He then transferred his care to a tertiary care hospital, where he underwent a trisegmentectomy.

One year after “curative” resection, follow-up imaging revealed a hypervascular lesion in segment 3 measuring 2.1 cm, indicative of recurrence (Figure 2). A second possible lesion in the fissure of the ligamentum venosum was measured at 0.8 cm, and was felt to be inaccessible for ablation (Figure 2). The patient’s liver function remained Child-Pugh A5, but his performance status had deteriorated mildly to status 1 after surgery. He was referred for hepatic angiography and chemoembolization.

Imaging Findings
Initial hepatic angiography revealed postsurgical distortion of the arterial anatomy, with proximal occlusion of the segment 2 and segment 3 arteries with distal reconstitution from intrahepatic collateral vessels (Figure 3). Parenchymal phase imaging confirmed two hypervascular lesions (Figure 3).

Although the collateral vessels appeared too small in diameter and too tortuous to accommodate standard microcatheters, treatment was attempted using a Fathom 0.014” guidewire (Boston Scientific, Marlborough, MA) and a 2.8-Fr SeQure® microcatheter (Guerbet, Roissy CdG, France). (At the time, smaller-diameter SeQure® microcatheters had not yet been released).

The submillimeter branch supplying the falciform cleft was successfully selected, and the lesion treated with doxorubicin-loaded LC beads 100-300 µm (BTG, London, England) until stasis of the tumor-feeding branch (Figure 4) was achieved. Likewise, the tortuous intrahepatic collateral vessel to segment 3 was selected and the segment 3 lesion was also treated with drug-eluting LC beads (Figure 4). Completion angiography confirmed disappearance of tumor blushes but maintenance of flow in nontarget vessels (Figure 5), and unenhanced cone-beam CT confirmed retention of contrast medium in the treated lesions (Figure 5).

Follow-up MR imaging at 3 months revealed complete response of the ligamentum venosum lesion and partial response of the segment 3 lesion. Residual disease was treated with percutaneous microwave ablation.
Discussion

Microcatheter design must balance the demands of: 1) adequate lumen to accommodate viscous or particle-containing injected fluids; 2) flexibility to navigate tortuosities without causing vessel injury; and 3) longitudinal stiffness to allow pushability. Additional features may include shaped tips, torqueability, and characteristics that help reduce reflux.

Conclusion

Selectivity of catheterization and treatment has substantial impact on outcomes of transarterial chemoembolization. Navigation of small, tortuous vessels is possible using the SeQure® microcatheter, even using the large 2.8-Fr version. Although this case cannot demonstrate the reflux reduction features of the SeQure® microcatheter, it demonstrates the flexibility and pushability that allowed selection of small, tortuous vessels. Future studies using radiopaque microspheres may be performed to test the controlled reflux feature.

Suggested Reading

The market for applications based on artificial intelligence (AI) is heating up throughout health care, with an ever-growing number of offerings for diagnostic imaging. Numerous products have received FDA marketing clearance and CE marking in recent years. Many, if not all, to date are for narrow indications and, from the perspective of a clinical manager, are best described as features rather than products.

While the much-heralded ability to assess pediatric bone age from skeletal radiographs, for example, could be marketable as a free-standing product, the targeted market is small. Imagen has received FDA approval for wrist fracture, but the company won’t have a genuinely marketable product until it transfers learning and gains approval for broader, full skeletal applications.

Mammography, with its ever increasing study volume and complexity, as well as a shortage of qualified readers, represents a huge opportunity for AI. Curemetrix has regulatory approval for CMAssist, which can discern positive cases from a stack of screening mammography studies, but on its own, the practical impact of this capability is small. Again, the company will not have a truly complete offering until it gains approval for the full and functional computer-aided detection (CAD) capabilities that published research suggests can improve breast cancer diagnosis and clinical workflow, owing to fewer flagged false positives compared to conventional mammography offerings.

Many companies are attempting AI-based identification in chest X-rays of what computer scientists call anomalies, such as pneumothorax, pneumonia, and misplaced lines and tubes. Multiple triage-based CT tools (some of which are still under development) detect hemorrhage and stroke (eg, products from AIDOC, MaxQ-AI, Viz AI), spine fractures, intra-abdominal free air, and pulmonary embolism (AIDOC). To achieve broad relevance and adoption, however, these offerings must expand to encompass the full spectrum of entities that radiologists are required to identify or exclude—all perceptible imaging findings—and assess their pertinence to the patient’s condition and clinical concern.

The capabilities of all-encompassing stroke-based products must include detecting large-vessel occlusion, assigning ASPECTS scores, identifying bleeding, and mobilizing the treatment team via secure text or email.
A complete product would further leverage the ability of machine language (ML) to synthesize multimodal information, including advanced studies like CT angiography and perfusion imaging, with patient phenotype, and to suggest the next treatment step based on predicted outcome. Once validated, the complete offering would be essential for suspected stroke patient studies. Individual features that don’t meet full exam requirements could still find a home consolidated into another product, or perhaps on the imaging device itself; eg, a portable X-ray unit could possess the embedded capability of notifying the technologist immediately of a misplaced tube, and a CT scanner could alert the technologist to urgent findings before the patient leaves the imaging suite.

A product that could set aside, or identify, “normal” findings on X-ray or CT exams would have immediate and universal appeal. A product that could set aside, or identify, “normal” findings on X-ray or CT exams would have immediate and universal appeal, especially in regions where personnel shortages prevent timely interpretation, and could serve to redirect resources to exams with a likelihood of positive findings.

Machine learning lies behind the enhancements in commercial offerings for quantitative MR- and CT-based neuroimaging. Initial products attacked the diagnosis of dementia (Coretechs’ NeuroQuant) and demyelinating disease (icometrix’s icoMS), an important but narrow range of diseases. Diversification was inevitable; both tools now cover both conditions and incorporate features to assess epilepsy and traumatic brain injury. Ultimately, to meet the requirements of a full neuro suite and attract customers, these companies will likely need to expand and diversify their products to encompass the range of neuroimaging analysis, including perfusion, and perhaps fMRI via organic development or alliances with other companies.

Fledgling companies and investors in the AI space should keep these concepts in mind. Just as a feature does not make a product, a narrow application doesn’t make a company. Those who eventually provide a suite of applications that can fulfill most, if not all, of the requirements of end users (broad triage of urgent findings on a class of exams, disease-based synthesis of multimodal information, and full indication-based assisted diagnosis) have the best chance of thriving in this rapidly evolving field.
CASE SUMMARY
A 30-year-old man from Southern California with no significant medical history presented to the emergency room with a one-month history of progressive right elbow pain. He denied trauma, repetitive arm activity, interaction with pets, gardening, fevers, weight loss, or other joint pain. On physical exam, patient was afebrile with normal vital signs. A 4 × 4 cm mildly tender nodule with minimal erythema and warmth was palpated in the medial aspect of right elbow.

IMAGING FINDINGS
An X-ray of the right elbow showed soft-tissue edema surrounding calcification adjacent to the right medial epicondyle, likely within the common flexor tendon and concerning for epicondylitis (Figure 1). Ultrasound of the right elbow demonstrated a prominent lymph node with hyper-vascularity consistent with a reactive lymph node (Figure 2).

An MRI scan was obtained to further characterize the suspected mass. The images demonstrated abnormal hypointense signal in the medial epicondyle on T1-weighted MR imaging (Figure 3). A postcontrast T1-weighted MR image with fat saturation showed enhancement in the medial epicondyle and the adjacent soft tissue, concerning for osteomyelitis or primary bone lesion. There was also a fluid collection with peripheral enhancement within the enhancing soft tissue, suggestive of an abscess (Figure 3).

Histological diagnosis was subsequently pursued. Since a primary bone tumor was in the differential, an ultrasound-guided biopsy of the enlarged lymph node (Figure 2) was performed to avoid altering the bony lesion. It showed a granulomatous inflammation with spherules, consistent with coccidioidomycosis.

A CT scan of the thorax was performed to evaluate for asymptomatic pulmonary lesions; it showed a focal consolidation in the inferior right middle lobe and a small focus of peribronchial opacity in the peripheral-inferior lingula.

DIAGNOSIS
Coccidioidomycosis with musculoskeletal involvement. Differential diagnosis includes primary bone malignancy, septic joint, osteomyelitis, and tuberculosis/other granulomatous disease.

DISCUSSION
Coccidioidomycosis is caused by inhalation of the spores of two genetically distinct but morphologically identical species of fungus, Coccidioides immitis and Coccidioides posadasii. It has worldwide distribution but is most prevalent in southwestern United States, Mexico, and South America.1,2

Coccidioidomycosis is diagnosed by clinical symptoms, serology, culture, and/or tissue biopsy. Nonspecific flu-like symptoms develop in 40% of affected patients and the rest are asymptomatic. Coccidioidomycosis most often manifests as pulmonary illness. In 75% of cases, it is seen as solitary or multi-segmental or lobar consolidation on CT chest, and up to 15-20% develop pleural effusion.3

Approximately 1% of cases result in disseminated disease,4 with asymptomatic patients being particularly at risk. This leads further to delays in diagnosis and treatment.1,2 Most commonly affected extra-pulmonary sites include bone, joints, skin, soft tissue, and meninges.5 Musculoskeletal involvement occurs in 10-50% of patients with disseminated disease.5 The most common patterns seen on radiography are punched-out lytic lesions with circumscribed margins, permeative destruction with periosteal reaction, and soft tissue disease. On CT, the lesions are hypodense. The most sensitive, although relatively nonspecific, modality for detecting early disease is MR imaging, which shows T1-hypointense and T2-hyperintense...
lesions. Serology tests can be helpful in suspected cases. A coccidioides complement fixation titer that is high, particularly greater than 1:16, may indicate disease disseminated to the bone. Culture or tissue biopsy provides definitive diagnosis when endospore-containing spherules are observed. The initial treatment of coccidioidomycosis is oral fluconazole or itraconazole.

Our patient had asymptomatic pulmonary coccidioidomycosis (as proven on post-biopsy CT), which spread to involve his right elbow. Given his lack of pulmonary symptoms and immunocompetence, primary bone malignancy was high on the differential diagnosis for his painful bony mass. Soft
tissue infection and osteomyelitis were of concern, particularly given the MRI findings; however, the normal ESR and CRP were more suggestive of other etiologies. Ultimately, tissue biopsy revealed granulomatous inflammation with spherules consistent with coccidioidomycosis. His coccidioides complement fixation titer was elevated (1:32), corroborating the diagnosis of disseminated disease. Our case illustrates how granulomatous diseases such as coccidioidomycosis can mimic malignancy. Obtaining a good clinical history and maintaining a high suspicion for asymptomatic or disseminated coccidioidomycosis is important in patients who have resided or traveled in endemic areas.

CONCLUSION

Musculoskeletal coccidioidomycosis is extremely rare but can occur in 10-50% of patients with disseminated disease and could be mistaken for a neoplasm. Diagnosis and treatment of disseminated coccidioidomycosis are usually delayed in patients without pulmonary symptoms. It is important for clinicians to obtain good clinical history and have high suspicion for coccidioidomycosis for patients who have resided in or traveled to endemic areas.

REFERENCES


Prepared by Dr. Liu and Dr. Johnston while practicing as radiology residents at Harbor-UCLA Medical Center, Torrance, CA; Ms. Lee while a fourth-year medical student at Ross University School of Medicine, Miramar, FL; and Dr. Varma while a faculty radiologist and Division Chief of Musculoskeletal Imaging at Harbor-UCLA Medical Center, Torrance, CA.
The Extravasation Detection Accessory (EDA™) is an optional accessory and is indicated for the detection of extravasations and is not intended as a substitute for proper patient monitoring and good clinical practice.

**NEXO Contrast Management System**

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This device is intended for retrospective and statistical data management and visualization. It is not intended for real-time data visualization, diagnostic applications or for any other use for which the device is not indicated. This device is only to be operated by and under quasi-continuous supervision of qualified and trained staff in an appropriate licensed health care facility.

The NEXO Contrast Management System is compatible with the EmpowerCTA Injector System version 8.0, and EmpowerCTA®- Injector System version 9.0 and higher.

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CASE SUMMARY
A 4-year-old female without significant medical history presented for evaluation of possible seizures. The patient’s mother stated her daughter had a 5- to 6-week history of strange, increasingly frequent movements. Each event lasted for 15-90 seconds and was associated with head slumping, hand clenching, arm stiffening, and unusual repetitive movements, such as turning in circles, repeating short phrases, or grasping at imaginary objects. The spells varied, occurring during the night or day. When each episode concluded, the child became angry, fearful, or affectionate.

IMAGING FINDINGS
An axial noncontrast CT scan (Figure 1) revealed wedge-shaped hypodense lesion in the left frontal lobe (Figure 1), while an axial T2-weighted image (Figure 2) demonstrated a heterogeneous, T2 hyperintense lesion involving the left frontal cortex and extending into the subjacent white matter. There were areas of peripheral cystic appearance. No significant mass effect or adjacent edema was identified. Finally, axial fused PET/CT images demonstrated hypometabolism within the left frontal lobe lesion.

DIAGNOSIS
Dysembryoplastic neuroepithelial tumor (DNET). Differential diagnostic considerations included cortical dysplasia, ganglioglioma, or other low-grade neoplasm.

DISCUSSION
Dysembryoplastic neuroepithelial tumors (DNET) typically present in childhood or in young adults (mean age at onset 10 years) and can account for 20% of medically refractory epilepsy.\(^1,2\) Diagnostic criteria include partial seizure disorder that begins before age 20, no neurological deficits, and a cortically based tumor. The most common location for a DNET is the medial temporal lobe (50-80%). However, 15-25% of DNETs are found in the frontal lobe, as in this case.\(^2\) The unusual seizure manifestations in this case may have been reflected by the tumor location. Additional locations include the occipital and parietal lobes, deep cerebral nuclei (particularly caudate nuclei), cerebellum, and brainstem.

The overall appearance of DNETs varies. The tumor usually is circumscribed, wedge-shaped or cystic. On CT, DNET can demonstrate wedge-shaped cortical hypoattenuation and mimic ischemia or infection (Figure 1). The cystic (“bubbly”) appearance can help to differentiate the lesion from other tumors. The MRI appearance is T2/FLAIR hyperintensity with corresponding T1 hypointensity (Figure 2). There can be adjacent regions of cortical dysplasia. The tumor will have slow to no growth over years and can remodel the adjacent calvarium. Intratumoral calcifications may be seen in one-third of cases and peritu-
moral edema is exceedingly rare. The tumor can demonstrate faint nodular or patchy enhancement in 20% to 40% of cases.\(^1\) PET FDG-18 imaging will demonstrate hypometabolism within the tumor (Figure 3).

DNETs are WHO grade 1 lesions, and specific glioneuronal elements should be present on pathology that are characterized as axon columns lined by uniform oligodendroglioma-like cells with intervening floating neurons.\(^3,4\) Histology is differentiated by the subtypes, including simple (only glioneuronal elements), complex (associated with cortical dysplasia), and nonspecific (resemble low-grade glioma with no specific glioneuronal elements).\(^3\) In this case the pathology was a low-grade glioneoplastic neoplasm most consistent with complex dysembryoplastic neuroepithelial tumor.

As performed in this case, gross total resection of the DNET and adjacent cortical dysplasia, if present, is the treatment of choice in DNET. Recurrence is rare, although follow-up imaging is recommended. In this case, there was no recurrence on follow-up and the patient’s symptoms improved. Tumors that recur are usually low grade; transformation into malignancy is very rare.

**CONCLUSION**

Dysembryoplastic neuroepithelial tumors are rare, low-grade brain tumors, with the majority presenting in individuals younger than 20 years. Imaging always plays a role in the work-up of seizures. Individuals with seizures may have normal imaging. In this case, the child’s strange behavior was secondary to the DNET. Considering an anatomic cause is important when a child presents with seizure-like symptoms. Children with a normal neurologic examination and a cortically based lesion with T2 hyperintensity and minimal mass effect should raise the possibility of a DNET.

**REFERENCES**


Prepared by Dr. Moore while practicing at Barrow Neurological Institute, Phoenix, AZ; and Dr. Cornejo, Dr. Jorgensen, and Dr. Towbin while practicing at Phoenix Children’s Hospital, Phoenix, AZ.
CASE SUMMARY

A 28-year-old female with no significant medical history presented with abdominal pain, nausea, and vomiting, along with left-sided abdominal mass of approximately 6 months’ duration with progressive enlargement. The patient denied any loss of appetite, weight loss, cough, chest pain, shortness of breath, or urinary or bowel symptoms. Physical exam revealed a firm, palpable mass in the left hemi-abdomen. No direct or rebound tenderness was appreciated. Laboratory evaluation showed mild iron deficiency anemia.

IMAGING FINDINGS

A CT scan of the abdomen demonstrated a 9.3 × 8.2 × 17.5 cm heterogeneously enhancing left renal mass, with significant mass effect and displacement of adjacent structures. The left renal vein and inferior vena cava were patent without evidence of intraluminal filling defect or tumor thrombus. Left para-aortic lymphadenopathy was also noted, with the largest lymph node measuring 2.2 × 1.8 cm (Figure 1). Retroperitoneal ultrasound showed a large heterogeneous solid mass with increased color Doppler flow. There was calyceal dilation noted with a rind of renal cortical tissue along the superior aspect of the mass (Figure 2). A CT-guided biopsy of the renal mass lesion was subsequently performed by interventional radiology.

Pathology sections from the left kidney demonstrated a lesion composed predominantly of histiocytes with admixed plasma cells and lymphocytes and focal evidence of emperiploesis. Immuno-stains showed histiocytes to be CD68 positive and negative for CD1A. S-100 showed diffuse positivity in the histiocytes. Cytokeratin was negative and PAX-8 highlighted background lymphocytes. The presence of emperiploesis and S-100 immunostaining are most consistent with extranodal Rosai-Dorfman disease (Figure 3).

Patient was referred to to surgery for left radical nephrectomy via a sub-costal incision. Intra-operative findings demonstrated a bulky renal mass, which was removed en bloc.

DIAGNOSIS

Extranodal Rosai-Dorfman disease

DISCUSSION

Rosai-Dorfman disease (RDD), also referred to as sinus histiocytosis with massive lymphadenopathy (SHML), is a rare, benign proliferative histiocytic disorder first described in 1969 by Rosai and Dorfman.1,2 The most common presentation of Rosai-Dorfman disease is painless lymphadenopathy; about 43% of patients the disease may also arise in extranodal sites and almost any organ can be involved.3

The imaging findings of RDD are very nonspecific, with a wide differential diagnosis which includes benign and malignant neoplasm, infection and other mass lesion etiologies. As such, diagnosis depends on tissue sampling and pathology demonstrating diffuse histiocytosis with presence of emperiploesis and S-100 immunostaining.4

Genitourinary, specifically renal involvement has been rarely described. A case of an adult female with a retroperitoneal pelvic mass causing urinary obstruction was described by Leiva, et al.5

Manifestations of extranodal RDD have been treated with surgical resection, medical/chemotherapy and radiation therapy; however surgical therapy has been the most successful and definitive treatment.5,6 The most commonly reported sites of extranodal involvement are the skin and soft tissue; this usually presents as well-defined papules to palpable masses, with or without satellite lesions.7

Our patient presented with a slowly growing left sided abdominal mass over a period of 6 months. Emergency presentation was precipitated by sudden pain over the left side of the abdomen. During initial clinical evaluation, there were no systemic constitutional symptoms described or lymphadenopathy other than a palpable left sided abdominal mass. A CT scan of the abdomen did demonstrate a large left renal mass and multiple enlarged para-aortic lymph nodes measuring up to 1.8 cm in short axis.

Our case demonstrated classic histological features suggestive of RDD, which included emperiploesis (presence of an intact cell within the cytoplasm of another cell) and diffuse positivity for S-100 immuno-stains. Surgical resection was chosen due to the size of the mass and associated symptomatic mass effect.

CONCLUSION

Extranodal Rosai-Dorfman syndrome accounts for almost half of all clinical presentations; however, renal involvement has been very rarely reported. We
present a case of extranodal RDD as a renal mass in a young female patient, with imaging findings and pathologic-diagnosis correlation.

REFERENCE


Prepared by Dr. Tesfay and Dr. Bashiti while at the Department of Diagnostic Radiology; Dr. Greenlee and Dr. Hurley while at the Department of Urology; and Dr. Lincoln while at the Department of Interventional Radiology; and Dr. Govil while at the Department of Pathology; Michigan State University-College of Human Medicine, Southeast Michigan Campus, Providence Hospital, Southfield, MI.
CASE SUMMARY
A 28-year-old woman presented to our hospital with a three-month history of vague upper abdominal pain for which she had been taking NSAIDS. The pain was insidious in onset and non-progressive. On physical examination, the abdomen was soft and non-tender.

IMAGING FINDINGS
A contrast-enhanced CT scan of the upper abdomen was performed. The CECT revealed the left kidney measuring 10.1 × 5.1 cm with non-obstructive calculus measuring 4.5 mm in the upper interpolar region, and a calculus of about 2-3 mm in the upper and mid poles. The vascular supply was via a single renal artery and renal vein showing no anatomical variation.

On the right side, meanwhile, the scan revealed two fused kidneys, with the cranially located kidney measuring 8.3 × 3.7 cm, and the caudally located kidney measuring 8.0 × 3.5 cm. These kidneys were partially fused and demonstrated a small parenchymal bridge between them. Two distinct main renal arteries supplied the fused left kidneys. The cranially placed kidney received its arterial supply from a branch of the abdominal aorta. The caudally placed kidney received its arterial supply from a branch of the left common iliac artery (Figure 1). Both the cephalic and caudally placed kidneys drained via renal veins draining separately into the IVC (Figure 2).

The excretory system was normal on left side. However, on right side the renal pelvis of the cranially placed kidney was directed medially, whereas the caudally placed kidney was malrotated with the pelvis directed laterally. Both kidneys on right side were drained by a bifid ureter (Figure 2).

DIAGNOSIS
Supranumerary fused kidneys on right side with tiny renal calculi on left side. Differential diagnosis is duplex kidney.

DISCUSSION:
Supernumerary kidneys are said to be present when the total number of kidneys exceeds two; therefore, supernumerary kidneys can be defined by either the presence of more than two separate kidneys or the observation of an extra kidney coexisting with a horseshoe kidney. A supernumerary kidney can develop from secondary outpouching of the wolffian duct or from branching from the initial ureteral bud; both means of development induce growth of the metanephric anlage, even though the kidneys have separated entirely.

The supernumerary kidney needs to be differentiated from the more commonly occurring duplex kidney, which is defined as having two pelvicalyceal systems associated with a single ureter or with double ureters. The supernumerary kidney, in contrast, is thought to be an accessory organ with a separate arterial supply, venous drainage, collecting system, and distinct encapsulated tissue. It may be either totally separate from the normal kidney or connected to it by loose areolar tissue acting as a bridge between the two kidneys. Two types of supernumerary kidney exist: one is drained by a bifid ureter and the other is drained by
a separate ureter. When a bifid system is present, the supernumerary kidney lies caudally; however, when a separate ureter is seen, the supernumerary kidney is located cranially in relation to the normal kidney.4

A supernumerary kidney is a rare congenital anomaly of the urinary tract, with fewer than 100 cases documented in the literature, with no difference between the genders and preferential occurrence on the left side. Because of its rarity, the condition typically goes undiagnosed until the fourth decade of life.1,5 Symptoms have been noted in about two-thirds of cases.6 The most commonly associated pathologies include hydronephrosis, pyelonephritis, pyonephrosis, renal and ureteral calculi, carcinoma, papillary cystadenoma, and Wilm’s tumors.7,8

CONCLUSION

Although the patient in this case presented with vague pain, most cases of supernumerary kidneys present with renal symptoms urging prompt medical and surgical attention. As a rare entity, showing variable anatomical features, the condition must be differentiated from the more commonly occurring duplex kidney using imaging findings. Proper description of the number, size, position, orientation, vascular supply, and excretory system of the kidneys should be given, in the event surgery is required to address complications like hydronephrosis, pyelonephritis, pyonephrosis, renal and ureteral calculi, etc.

REFERENCES

Prepared by Dr. Arora while a DNB Resident; Dr. Mishra while a Consultant Radiologist, Vardhman Diagnostic Centre, and Dr. Purohit, while Department Head of Radiology, all at SDM Hospital, Jaipur, Rajasthan, India.
A 29-year-old male with a history of recently diagnosed systemic lupus erythematosus presented to the ED with a 3-day history of hemoptysis and dyspnea. He also complained of weakness and bleeding gums. On physical exam the patient was in no acute distress with a soft, non-tender abdomen. He had normal pulses with 2+ bilateral lower extremity pitting edema. Hemoglobin at time of admission was 6.6 g/dL. The patient had a known history of lupus nephritis and was on hemodialysis for renal failure.

A portable chest radiograph at the time of presentation demonstrated mild cardiomegaly with diffuse interstitial opacities throughout both lungs suspicious for pulmonary edema (Figure 1).

A CT of the chest was subsequently performed secondary to the patient’s hemoptysis. Given the patient’s history of SLE and anemia, there was concern for diffuse alveolar hemorrhage. CT showed diffuse mixed interstitial and alveolar opacities with diffuse interlobular septal thickening throughout both lungs (Figures 2, 3). The partial view of the abdomen demonstrated abdominal ascites and diffuse soft tissue anasarca consistent with the patient’s known history of lupus nephritis and renal failure.

Diffuse alveolar hemorrhage (DAH) is a clinicopathologic syndrome characterized by the accumulation of red blood cells within the alveoli arising from the alveolar capillaries. The syndrome is an often fatal, dreaded complication of systemic lupus erythematosus (SLE) with a median age at diagnosis of 27 years. It can be acute or subacute, occurring over hours to several days. The clinical syndrome usually includes hemoptysis, dyspnea, anemia, hypoxemic respiratory failure and anemia, with dyspnea being the most common presenting factor occurring in 74-100% of patients. DAH is frequently associated with SLE and has been reported to occur in 2-5% of all cases. It also has a strong association with lupus nephritis with evidence of active kidney disease in 64-100% of patients with lupus related DAH. Diffuse alveolar hemorrhage is typically defined by three major components: signs (blood on bronchoscopy) or symptoms (cough, hemoptysis, and dyspnea); a new drop in hemoglobin; new, diffuse infiltrates on imaging.

Diffuse alveolar hemorrhage occurs in three distinct but overlapping histologic patterns: pulmonary capillaritis, bland pulmonary hemorrhage, and diffuse alveolar damage. Pulmonary capillaritis consists of neutrophilic infiltration of the alveolar interstitium with fibrinoid necrosis of the alveolar and capillary walls. Nuclear debris accumulates within the interstitium with subsequent loss of the alveolar-capillary basement membrane which results in alveolar accumulation of red blood cells. Bland pulmonary hemorrhage presents with accumulation of fibrin and erythrocytes within the alveolar spaces with sparing of the alveolar structures. Lastly, diffuse alveolar damage consists of alveolar septal edema with formation of hyaline membranes. The predominate pattern seen in SLE is that of pulmonary capillaritis.

Mortality is reported to be as high as 50% but is declining with increasing awareness and aggressive treatment. Mortality is mainly attributable to respiratory complications. There are multiple treatment options available as appropriate treatment protocols have yet to be established due to the lack of prospective studies. Corticosteroids are the main-
stay of therapy, but there are no reported guidelines for the dose or duration of therapy. The use of cyclophosphamide is controversial and has been linked to both increased survival as well as increased mortality rates. Plasmapheresis is commonly used for other autoimmune related causes of vasculitis related pulmonary bleeding but has not been proven effective for DAH associated with SLE. B-cell depletion has shown promising results but the available data is limited. One study of 6 patients with bronchoscopically confirmed DAH treated with activated recombinant factor VII showed decreased oxygen requirements and sustained hemostasis after treatment. The evidence to support any particular therapy is, therefore, limited.

CONCLUSION
DAH is a potentially deadly complication of SLE that needs timely diagnosis for early management. DAH should remain in the differential for patients with diffuse alveolar opacities, interlobular septal thickening, and a history of SLE, especially those with a history of hemoptysis and new onset anemia.

REFERENCES

FIGURE 1. AP Portable chest radiograph shows mild cardiomegaly with diffuse interstitial opacities most suggestive of interstitial pulmonary edema.

FIGURE 2. Coronal contrast-enhanced CT of the chest in lung windows demonstrates diffuse alveolar opacities mixed with interlobular septal thickening.

FIGURE 3. Axial contrast-enhanced CT in lung windows demonstrate diffuse interlobular septal thickening with left lower lobe areas of focal consolidation.

Prepared by Dr. Kliewer and Dr. Hull while PGY-4 Diagnostic Radiology residents, and Dr. Yasmer while serving as Assistant Program Director of Diagnostic Radiology, Hemet Valley Medical Center, Hemet, CA.
I love technology (kind of)

C. Douglas Phillips, MD, FACR

“Technology is, of course, a double-edged sword. Fire can cook our food but also burn us.”
—Jason Silva

We had some friends visit us at the Jersey shore a while back, and while we were sitting at a nice seaside café, having a drink and watching the waves break, their 18-month-old was playing with their cell phone. That might not seem all that odd, but on further observation, it took my breath away:

An 18-month-old—a toddler—was swiping through videos, finding the ones she wanted to watch, and starting them! After watching a video through and laughing, she swiped through to the next one. Wow. I’ve just figured out a lot of that stuff myself, and here was a toddler already smart enough to use a smartphone. At her age I was playing with blocks.

It got me thinking about where our technology is, where we are likely headed, and what it is going to mean. Conversely, I also started thinking about the old days. Perhaps I’m feeling old again, or maybe just getting realistic about life, and wondering about where our field will go, but it is reasonable to think about the past from time to time.

We already are in the midst of training a generation of colleagues who have never used a typewriter (well, except for the hipsters, who have for some unknown reason embraced them). They have never used a rotary phone. They see one on an old TV show, or in a period movie, and they ask you, “Hey, did you ever use one of those?”

Well, yes, I did.

So, imagine how old you feel, how creaky and decrepit you imagine yourself, when you relate your best roller scope/alternator story. Generation gap. Remember when an alternator would jump a panel? Life came to a halt. Perhaps some daring soul would stick their arm down between the panels to grasp an emergent study you needed, but, otherwise, it was downtime of the highest order. Get a coffee. Read a book. Wait for the engineers to come and fix it.

My favorite was when you were able to keep the roller scope functioning, but it would bang incessantly as the panels moved. It became a disaster about to happen. You knew at some point the thing was going to jam, but you took some kind of demented pleasure in continuing to use it, letting it bang away. The best was when clinicians were in the room and you looked like a daredevil. They would move away, wondering when the thing was going to seize up, or maybe even blow up.

Then there was the hot light. Have you ever described a hot light to one of the juniors? Man, that is one tough concept to get across. Kind of a window/level adjust for a prior era. The hot light had to have an amazing bulb in it—it kind of like a supernova bulb. A good one was way too bright to look at. One of my older colleagues would take out bulbs with too little wattage to be effective and throw them in the trash: “Bring us a proper bulb for this, please?”

This, of course, was a really great idea for people who rely on their eyes. “Here, look at this film, and take care you don’t blind yourself.” If you didn’t have the film well situated over the hot light before you hit the switch, you weren’t much good for the next hour or so.

And, the heat they generated was freakishly unbelievable. Potential major hazard here—getting the film too close could melt it, or even start a fire. No better way to show you’re a rookie than melting a valuable (and one-of-a-kind) radiograph. That impresses the techs, for sure. “Yeah, Dr. Phillips melted the lateral swimmer’s view on that trauma. You’ll have to repeat it.”

We all bitch and scream about our current technology. Yeah, yeah, I know. I do it, too. It has quirks and limitations, no doubt, but it also has removed us from a whole host of other things that weren’t necessarily our friends.

Keep doing that good work. Mahalo.
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