Hi everyone. This is Dr. David Bluemke in Madison, Wisconsin. This is the part 2 of the March 2019 issue.

For the first topic today, I wanted to make sure you were aware of a new consensus statement. The title is, “Imaging of Kidney Cysts and Cystic Kidney Diseases in Children: An International Working Group Consensus Statement.” The first author is Charlotte Gimpel from Freiburg, Germany.

This article has the highest number of downloads for March, more than 2,000 at this point. The consensus statement also serves as a nice review article regarding pediatric cystic renal disease. Great images of major diseases are included with key findings. I will summarize just key points so you get an idea of the article context. The statement has been endorsed by three major European radiology and pediatric societies.

First: what's covered here? The topics of the consensus statement range from simple cysts, multicystic dysplastic kidneys, cystic dysplasia, and both autosomal dominant and recessive renal disease.

Some key points.

#1: Ultrasound should be used as the major initial imaging examination. CT and MRI are not recommended for routine evaluation. Contrast enhanced ultrasound is not recommended due to insufficient information.

Regarding cyst description, the recommendation is to state either 1 cyst, 2-5, 6-10 cysts, or more than 10. Indicate if they are unilateral or bilateral. Indicate the maximum diameter of the largest cyst.

#2: Simple cysts. Unlike adults, simple renal cysts are rare in children. A cyst may be an early indication of a cystic disorder or genetic condition. The recommendation is any cyst should have at least one follow-up ultrasound evaluation to check for cyst size and any additional cysts. For follow up, MRI and CT are not recommended, nor is contrast enhanced ultrasound.

#3: Multicystic dysplastic kidney: this is characterized by replacement of the whole kidney with multiple disorganized cysts. There is lack of any normal surrounding renal parenchyma. Remember about 30% of patients with multicystic dysplastic kidney have an abnormal contralateral kidney. About 1 in 3 children with these dysplastic kidneys have associated GU tract anomalies. When I trained, it was not common to determine renal function with nuclear imaging. This statement indicates renal function testing with DMSA or DTPA nuclear tests is not recommended – especially if the contralateral kidney is normal. There is no increased risk of malignancy in this condition.

#4: Next a condition is recently described. Renal disease associated with mutations in the HNF1B gene. This is a rare genetic cause of maturity onset diabetes of the young: affected patients have early onset of diabetes before 25 years, pancreatic beta cell dysfunction. In 2001, the disease was known as renal cyst and diabetes syndrome.

Interesting pearl: HNF1B nephropathy is the most common cause of echogenic kidneys at prenatal US and of kidney cysts in older children. It can mimic adult recessive polycystic kidney disease. There may be uterine abnormalities and abnormalities of serum uric acid and magnesium. Genetic testing is required if this condition is suspected. It is autosomal dominant.

#5: Also, perhaps less familiar: Nephronophthisis (nephron noph thisis). This is an autosomal recessive cystic kidney condition that progresses to end stage renal disease typically before 20 years of age. It is disease of the cilia, a ciliopathy, like Meckel-Gruber syndrome and Adult polycystic renal disease. The kidneys are small to normal. There is bilateral increased echogenicity. Cysts at the corticomedullary junction are suggestive but obvious cysts not always present. Patients suspected of this condition should undergo abdominal ultrasound to assess for liver fibrosis.

Just 2 more diseases, perhaps back to the familiar:

Point #6: Autosomal recessive polycystic kidney disease: key feature here, the salt and pepper pattern of renal disease – due to tiny renal cysts. Kidneys are enlarged. Key association: Caroli syndrome. Caroli syndrome is hepatic fibrosis associated with bizarre and irregular bile duct dilatation, usually associated with kidney cysts. You were probably quizzed on this during your residency training. You could hit a home run by finding the combination of bilateral renal cystic disease and liver and biliary disease.

Last one: #7: Autosomal dominant polycystic kidney disease. Diagnosis: if more than 15 years old: 3 or more bilateral cysts are required for diagnosis.

If the patient is less than 15 years, positive family history and only 1 or more cyst is highly suggestive.

I will stop there, reminding us of the 2 newer pediatric renal diseases: “Nephron-nophthisis”, small to normal echogenic kidneys with cysts, progressing to end stage renal disease. And renal disease associated with HNF1B gene mutations. It can mimic autosomal recessive polycystic renal disease.

Overall, the consensus statement indicates heavy reliance on ultrasound, MRI as a backup, and CT only when MRI cannot be tolerated. The images in the article and descriptions serve as an excellent review of renal cystic disease in the child.

Next, onto our March research articles.

Perinodular and Intranodular Radiomic Features on Lung CT Images Distinguish Adenocarcinomas from Granulomas

Niha Beig, MS • Mohanmadhadi Khorrami, MS • Mehdi Alilou, PhD • Prateek Prasanna, PhD • Nathaniel Braman, BS • Mahdi Orooji, PhD • Sagar Rakshit, MD • Kaustav Bera, MD • Prabhakar Rajiah, MD • Jennifer Ginsberg, MS • Christopher Donatelli, MD • Rajaat Thawani, MD • Michael Yang, MD • Frank Jacono, MD • Pallavi Tiwari, PhD • Vamsidhar Velcheti, MD • Robert Gilkeson, MD • Philip Linden, MD • Anant Madabhushi, PhD

Our first article for March is one of the most thoughtful articles so far this year. The topic is how radiomics might work and why. The title is, “Perinodular and Intranodular Radiomic Features on Lung CT Images Distinguish Adenocarcinomas from Granulomas.” The first author is Niha Beig, the senior author is Dr. Anant Madabhushi. The study is from Case Western Reserve University with authors from the Cleveland Clinic.

One quick story. At the University of Wisconsin I read mostly cardiovascular studies. But this week, a new set of images popped up along with the standard lung and soft tissue windows on the chest CT. The new images had all of the lung vessels and bronchi removed, and simply showed only the left over lung nodules. This is a new AI software tool. I had not seen it before, so I asked my excellent resident, what was going on. And, did he think that maybe the 15 mm nodule on these new images should perhaps be mentioned.
in the CT report? It was impressive: the nodule was quite central, large, but still hidden on the conventional images. A nice demonstration of a new AI tool in the clinic. Unfortunately, the AI found at least a dozen other possible nodules, nearly all of which were false positives. It took quite a while.

Back to our research article on chest CT.

Background: The authors started with a good topic, an unresolved problem. How accurately can a radiologist determine if a small nodule is an adenocarcinoma or a granuloma on a CT scan? Will you give you the answer upfront based on data in this paper: diagnostic performance of a radiology test is defined by the area under the receiver operating characteristic curve.

The maximum value is 1.0. 0.5 is a toss of a coin. For lung nodules, the AUC of the expert radiologist in this study was barely better than a toss of a coin, 0.61. The AUC of the expert pulmonologist was about the same, 0.60. For the first 20 lesions, the radiologist and pulmonologist had the same diagnosis on 16. But when they did agree, their consensus diagnosis was wrong 50% of the time.

Why not just get a PET scan? Prior data indicates that most small granulomas can be PET avid with FDG during the acute phase of infection. Many times PET can help, but granulomas can be hot on PET. Plus, getting a PET later does not help you interpret the CT scan now.

So, we have a pretty good problem. Use a computer to see if we can get a better indication of lung adenocarcinoma versus granuloma.

The second element of a good paper: a good hypothesis. The authors suggested that two different categories CT features could be important. The CT features of the nodule itself, and the features of the lung tissue around the nodule: the peri-nodular features. OK, what do we know about nodule shape? If the lung nodule is lobulated, cancer or granuloma? We teach the residents its more likely cancer. But 25% of benign nodules can also have a lobulated shape.

What do we know about peri-nodular tissue? Sometimes there is a hazy border around the malignant nodule. The border for malignant nodules has a different histology: the peritumoral region has tumor infiltrating lymphocytes and tumor associated stromal macrophages. Those cells change the texture of the lung around the malignant nodule, but are not present with a granuloma.

Finally, a good method: we have this wonderful set of new tools called radiomics. Radiomics is better than we are: we can describe the tumor as lobulated or round. But radiomics gives a number as to how lobulated the tumor is. We can describe nodule border as speculated but I cannot give you a number. Radiomics is able to assign a number. Finally, for the hazy perinodular texture around the malignant tumor, radiomics gives a number for that feature as well. In total, the authors evaluated more than 1500 radiomics features to search for the best parameters.

To summarize: a good question was addressed: lung granuloma vs adenocarcinoma. A good hypothesis: look at the texture and shape of the lung nodule itself. And, look at the texture around the lung nodule. Finally, a good tool: radiomics.

Purpose: Use radiomics features to classify small lung nodules as granulomas or adenocarcinomas.
nondiagnostic results. Nondiagnostic results are defined as pathology results that were nonspecific. Nonspecific path results include cases where tissue is nondiagnostic. Nonspecific results are obtained as a result of nondiagnostic biopsy, which is defined as percutaneous transthoracic needle biopsy of lung lesions. A nondiagnostic biopsy was defined as pathology results that were nonspecific. Nonspecific results include cases where tissue is nondiagnostic. Nondiagnostic results are defined as pathology results that were nonspecific. Nonspecific results include cases where tissue is nondiagnostic.

A final brief article on lung biopsy - how effective is a lung biopsy for diagnosing cancer? The title is, “Nondiagnostic Percutaneous Transthoracic Needle Biopsy of Lung Lesions: A Multicenter Study of Malignancy Risk.”

Background: We say that the accuracy of percutaneous lung biopsy is very high. For example, cone beam CT was reported to have 97% sensitivity and 100% specificity for biopsy. But those numbers pertain to success of obtaining tissue, not obtaining a specific diagnosis. Many times the lung biopsy tissue is nondiagnostic.

Purpose: Determine the rate of nondiagnostic percutaneous transthoracic needle biopsy of lung lesions. A nondiagnostic biopsy was defined as pathology results that were nonspecific. Nonspecific path results included inflammatory cells or atypical cells that were not specific for malignancy.

A good resident quiz question: two tumors: one is a solid nodule, long axis size is 1 cm. Another case is a part solid nodule – the solid portion is also 1 cm. The same T stage. Which patient has worse survival? Answer: the solid nodule, much worse, about 2 times worse disease free survival.
national health care system, analysis of digital mammo in the UK is possible. Concerns from prior studies are that recall rates are increased. A study in 2013 of 6 million screens with digital mammography showed a 25% greater recall rate than with film mammography.

Purpose: Determine the impact of switching from film mammography to digital mammography.

Methods: Evaluation of 11.3 million annual breast cancer screening examinations in the United Kingdom.

From 2009 to 2011, two-thirds of breast cancer screening was done with conventional film, and one-third was digital. A middle period was 81% digital, the last interval from 2014 to 2016 was 98% digital mammography.

Since there were 3 time periods, statisticians could estimate cancer detection rates inferring 100% conventional film 100% digital mammography.

Results: The rate of breast cancer detection was 14% greater for digital versus film. Fairly impressive. But what type of cancers were found? Where they all low grade lesions, unlikely to cause problems? That was not the case. Invasive tumor detection increased by 10%.

The DMIST United States study showed digital was beneficial only for younger women, due to greater density of breast tissue. DMIST evaluated 50,000 women. The current study from the UK evaluated 11 million women in a clinical practice setting. In this UK study, cancer rates with digital mammography were improved in both young and older women.

In several other international trials about digital mammography, the recall rates for digital were 20 to 30% greater than for film mammography. In the UK with the double reading approach, recall rates were not changed. More cancers but not greater recall. That’s ideal.

Conclusion: Overall excellent real world data from 11 million women in the UK health system. The overall impact is greater than expected from the DMIST trial, a very well controlled experimental trial in the U.S. Two points:

#1: in nationalized healthcare systems, radiology technology can be evaluated on a nationwide basis. We think better technology improves health. Increasingly, we will know for sure.

#2: this interesting study gives an example of technology impact in a huge clinical practice setting, rather than a carefully designed clinical trial. Most often, results from the clinical trial are less impactful when generalized to the population. Not in this case. Perhaps better technology is more impactful for the general physician or general radiologist, compared to the academic who can focus on only 1 small area of specialization.

A Grading System for the Assessment of Risk of Extraprostatic Extension of Prostate Cancer at Multiparametric MRI

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Sherif Mehraliand, MD • Joanna H. Shih, PhD • Stephanie Harmon, PhD • Clayton Smith, BA • Jonathan Bloom, MD • Marcin Czarniecki, MD • Samuel Gold, BS • Graham Hale, BS • Kareem Rayn, BS • Maria J. Merino, MD • Bradford J. Wood, MD • Peter A. Pinto, MD • Peter L. Choyke, MD • Baris Turkbey, MD

The last study was about the leading cause of cancer in women. Lung and prostate cancer are the leading cause of cancer deaths in men. The title is, “A Grading System for the Assessment of Risk of Extraprostatic Extension of Prostate Cancer at Multiparametric MRI.” The senior author is Dr. Baris Turkbey, the study is from the National Institutes of Health in Bethesda, MD. In the U.S., certainly the NIH is one of the top sites for prostate cancer research. Lots of resources, large patient population. Let’s see what they say.

Background: for patients who have surgery, the presence of extraprostatic extension of prostate cancer at pathology is bad news. Survival is worse. If there is surgery, the excision requires larger margins with more complications from surgery.

The best noninvasive test to determine extraprostatic tumor extension, or EPE, is MRI. If you read prostate MRI, you must state if EPE as present or absent. However, the MRI is not often definitive; instead of present or absent, you might often like to say “maybe.”

Purpose: develop a grading system to predict EPE, or extraprostatic extension of prostate cancer.

Methods: The authors developed and tested a simple grading system based on 3 factors.

#1: the tumor abuts the capsule of the prostate gland. Is the distance of contact between tumor and capsule greater or less than 1.5 cm?

Factor 2: is the prostate capsule smooth, or irregular with a bulge in the capsule due to tumor?

Factor 3: Do you think the MRI shows a frank breach of the prostate capsule by the tumor. Do you think its invading the seminal vessels or adjacent structures?

The system was designed to be simple. You may not remember these 3 factors from a podcast, but you could look at Figure 3 in the paper and remember these points in about 60 seconds.

Results: The MRI’s were graded, the reference standard was pathology. If there was grade 1 or the lowest grade of EPE, 24% of patients actually had EPE at pathology. Grade 2 was correct 38% of the time. The highest grade 3 is the radiologist saying there is definite breach of the prostate cancer by tumor. But even for these grade 3 cases, EPE was present at pathology only 66% of the time.

Conclusion:

#1: Don’t be too overconfident based on the MRI. Even when it appeared there was frank breach or disruption of the prostate capsule, only two-thirds of cases were positive at pathology.

#2: the authors combined MRI with clinical grading taking PSA, prostate specific antigen, into account. Then, overall prediction of EPE improved a bit. The AUC value was 0.81, out of maximum of 1.0.

Summary: you read prostate MRI, you use PI-RADS. Very useful, but PI-RADS just helps you state the likelihood of a tumor present or not. PI-RADS is not about prostate staging.

Right now, the prostate report mandates that you also state EPE present or absent. But very often, you want a probability of extraprostatic tumor extension, you want to say “maybe.” This approach from the NIH presents a nice grading system that could be useful for standardized reporting of prostate cancer.
That concludes this week’s articles.

It occurred to me we covered a lot of ground today. If you are jogging or watching TV while listening, it’s hard to keep all of this in mind. Let’s summarize:

First article: remember there are new consensus guidelines for pediatric renal cysts. CT is almost never recommended. A cyst in a pediatric patient is unusual, and needs to be worked up.

Lung nodules, 3 points from 3 articles.
#1 Excellent progress on radiomics of lung nodules: computer verification that about 25% of the prognostic information is in the perinodular tissue adjacent to the nodule. Nodule shape is important to us as humans, lobulated shape suggests malignancy. But lobulated or round shape was not important in the computer analysis.

#2 Lung staging: only the long axis of the nodule dimension that is used for staging. Patients with solid nodules do about two times worse than patients with part solid nodules – even though the solid component is the same size.

#3 Lung biopsy: nondiagnostic needle biopsies 28% of the time.

Next, digital mammography: convincing evidence in the UK of the benefit of this technology, 14% more breast cancers identified.

#5: Prostate cancer: how accurate are you, when stating that the prostate cancer extends beyond the capsule of the prostate? An easy-to-use grading system from the NIH provides a logic to describing MRI findings about extraprostatic tumor beyond the prostate capsule.

I hope these podcasts were helpful to you. Until next time, this is Dr. David Bluemke for the journal Radiology. I hope you have a good rest of your week.