February Podcast

Hi. This is Dr. David Bluemke in Madison, Wisconsin. I’m the Editor of the journal Radiology. This is part one of our February, 2020 podcast. The goal of these podcasts is to present a brief summary of key research in our field to keep you up-to-date. Today four topics.

Google gets into radiology, type B aortic dissection and effect on the kidneys, an AI to simulate a gadolinium MRI from noncontrast MRI, and gadolinium all over the brain not just in the deep cortex. Now, onto our first topic for February.


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Our first article for today. This could be either the single most important paper of the last ten years or it’s just another MeToo paper. I’ll let you decide and ask you again at the end. The title “Chest Radiograph Interpretation with Deep Learning Models: Assessment with Radiologist-adjudicated Reference Standards and Population-adjusted Evaluation.” Next the authorship, a first from Google Health. The first author Dr. Anna Majkowska. The senior author Dr. Shravya Shetty. Background: I started with perhaps an absurd statement that this could be one of the most important papers of the last ten years. Why? Factually my statement does not add up. Here’s why. Point one: The authors. Fourteen authors. Zero publishing experience in clinical radiology. A few authors worked on a prior paper about dermatology and skin lesions. Several published a scientific letter, a brief report. Point two: Nearly all of the authors are computer scientists from Google Health. The head of Google Health is Dr. David Feinberg, a child psychiatrist. That’s pretty interesting by itself. What else is Google Health doing? Point three: Google is getting into healthcare. The former head of Google Health Group: Diabetic retinopathy, disease detection, life-style management, heart monitoring, a smart syringe, Parkinson’s disease, and on, and on. Google Health is all over the place. In the words of one business analyst, “Google is working on so many initiatives, focused on so many different facets of healthcare, across so many areas of the company that the chances of failure are high but so is potential for success.” Now with their publication in Radiology Google Health is officially entering the radiology business. Let’s see what happens. Purpose: Develop a deep learning model for chest x-rays. Methods: Computer scientists wrote this paper. They’re figuring out the business of radiology. They see a lot of opportunity for improvement. Why? The introduction is trivial to radiologists. In essence, the authors state that reading a chest x-ray has a lot of variability. Some radiologists see the findings, some do not. And those findings might not really even be there at all. If you’re a computer scientist it might not make any sense. Do you mean to say that in radiology I can’t get a team of expert radiologists together decide unequivocally if the chest x-ray shows a nodule or not? That’s right. You cannot. We know that. To a radiologist it’s certainly not new news. But you can imagine a PhD computer scientist their experience is going to the doctor’s office. They hear remarkable things about CTs and MRIs. The chest x-ray is just a screening examination, not the answer. How does the Google team make an AI for radiology? The answer: Big. Prior to this, the largest AI paper we published used 30,000 x-rays. But the Stanford team had a bigger collection, 200,000 chest x-rays. The Google team had an disadvantage compared to Stanford. They started with nothing. They need a lot of data to train the AI. How do you quickly get a lot of data? Go to a big country. In this case, India, 1.4 billion people. In 2016 in JAMA Google published groundbreaking work on AI for diabetic retinopathy. They also used hospitals in India. About 130,000 images of the retina. For chest x-rays they go back to India. They collected more than 750,000 x-rays from India, another 100,000 from the United States. Together more than four times as large as the largest other study in our field. And yes, this is their first try. Next, there are about 40 different findings on a chest x-ray. How many did Google try to detect? Four. They wanted to detect pneumothorax, nodule, fracture, and infiltrate. The process goes like this: Thousands of thousands of chest x-rays with labels. Feed those images to the AI. Train the AI exhaustively on the first 650,000 chest x-rays. The next step: Test the AI. Give the AI x-rays that it’s never seen before. Again, a large test set, 3,000 new chest x-rays. I could mention more details. For example, the Google team started with an AI that was already trained to recognize common images. It can recognize a pencil. It can recognize a dog, and a cat, a fish. Exception was the AI trained on 300 million non-medical
images. The Google team then trained the AI to read the chest x-ray. Results: How do the computer folks decide on the performance of an AI? They look at the one number, the area under the receiving operating curve. The AUC value, 0.5 is chance, 1.0 is perfect agreement. This AUC number is great for research, not nearly as helpful for radiologists. Let’s start with the research. The AUC for the Google AI was quite high, 0.91. Not the highest or best-performing AI ever. The record right now according to Stanford is 0.93. But AUC by itself doesn’t really mean much to you or me in the clinic. So indeed what does the Google AUC of 0.91 mean? The AUC curve gives you every possible combination of sensitivity and specificity. For example, if the sensitivity of the machine is set to 80 percent the specificity was also about 80 percent. But if you go ahead and try to detect nearly everything, sensitivity 95 percent, then the specificity is only about 50 percent, a lot of false-positives. Conclusion: Google Health now doing radiology more seriously than any other Silicon Valley company. Their report card: Perhaps not the best ever recorded AI for a chest x-ray but very, very good. In that particular number the AUC value is not the main take-home point. Let’s look at what else happened here. First, in its first major effort in radiology the Google team amassed more than four times as much training data as anyone before them. For AI it’s all about the data. Second, they learned that radiologists get it wrong so they figured out other ways to navigate uncertainty in reading the chest x-ray. They did rigorous testing of their AI on 3,000 new x-rays. That’s a large number. A large number of test cases means the Google team has a much better concept of how they’re doing relative to their competitors. Now I’m at the end, and I need to go back to the beginning. Google technology is pervasive. There are 3.5 billion searches on Google each day, a 300 billion dollar company. The largest healthcare system about ten times less, 30 billion. I don’t know anyone whose life is not touched by Google. They provide incredible value and sort of for free. Just to do the research for this segment of our podcast, I did more than 100 Google searches in fractions of a second. Google provides information at the tip of our fingers. Their resources are relatively unlimited relative to any university or private company. So I’ll end with my first question. Does it matter if Google is trying to become a radiologist?

Management of Renal Arteries in Conjunction with Thoracic Endovascular Aortic Repair for Complicated Stanford Type B Aortic Dissection: The Japanese Multicenter Study (J-Predictive Study)

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The second topic. Short title “Management of Renal Arteries in Conjunction with Endovascular Aortic Repair for Type B Aortic Dissection.” The first author Dr. Iwakoshi from the Radiology Department at Nara Medical Center in Nara, Japan. The senior author Dr. Kichikawa. What about Nara and Nara Medical Center? Nara. It’s a prefecture. In the U.S., it’s like one of our states. There are 47 prefectures in Japan that govern the country. The prefectures began from smaller local districts descending from fiefdoms headed by a local warlord or family. At one time there were more than 300 prefectures in Japan. In 1888, this was reduced to 47. The largest prefecture is Tokyo, 13 million people. The average prefecture has 1 to 2 million people. Nara has a population of about 1.3 million. Nara is a landlocked state south of Tokyo, 300 miles or 476 kilometers south. Take the bullet train first from Tokyo to Kyoto, two and a half hours. Then in a little less than an hour to Nara station. The cost of a ticket? One hundred thirty dollars. Why go to Nara? Manufacturing is 20 percent of the economy. But tourism is a big issue. Many Shinto shrines, historical Buddhist temples, national parks, more UNESCO World Heritage Sites than any other prefecture in Japan. In the U.S., we’ve heard more about Kyoto. Nara has a deep history and is more off the beaten path. Background: Aortic dissection. We use the Stanford classification. Stanford type A involves the ascending aorta. The main concern in type A dissection is the dissection flap extending back towards the heart. If the dissection goes back to the heart the dissection flap can occlude the coronary arteries causing death. Equally bad, the dissection can bleed directly into the pericardium. This causes cardiac tamponade, high-pressure fluid around the heart, death. Type A dissection is a surgical emergency. Immediate repair of the ascending aorta with a graft. Type B dissection. This starts at or distal to the takeoff of the left subclavian artery. Here’s the physiology: The pressure in the aorta usually forces the intimal tear to go down the thoracic aorta starting from the point of the tear. Most type B dissections are treated with medical management, antihypertensive medication, and a follow-up CT to rule out rupture. But is it just that easy? Type A dissection, surgery, type B, medical management? No. Not really. The management of type B dissection came up a lot when I was in Baltimore at Johns Hopkins, usually in the emergency room overnight. Type B was an important issue for the residents. In those days obtaining an MRI or CT in the middle of the night was a big deal. The techs in CT were gone after 10 or 11 p.m. A lot of grumpiness if they had to come back to the hospital. The radiology residents had a badge of honor, try to block all of the unnecessary studies. ED staff calls, wants a CT at 4 a.m. Well, how bad is it really? Can we negotiate a little? The
CT tech will be here at 6 a.m. I hate to wake them up earlier. We had an idea about type B dissection. I’m not sure where it came from. The idea was that type B dissections were safe and they never convert to type A dissection. No need for a CT at 4 a.m. Wait a few hours. Here we have a patient with a known history of aortic dissection type B, now comes back to the emergency room in the middle of the night with chest and back pain, hypertension. The ED resident thinks the dissection could have become worse but the prior CT showed it was a type B. Can those wait? Somehow the thinking was that type B did not convert to type A. The force of the blood should push the dissection down the aorta not the reverse course. It should not extend proximally. Wrong. When I began on staff, I then started to see all of the cases, not just a few resident cases from overnight, and now we teach, of course, type B can and does convert to type A dissection. No. You cannot turn down the CT in the middle of the night just because it’s a type B. New or recurrent chest pain for a patient with a prior dissection is not good, very concerning. Do the CT as soon as possible. I’m now in Madison at the University of Wisconsin. We have a remarkably high rate of severe vascular disease. I’m not sure of the cause. Such a healthy city. People jogging, biking, outdoors all the time, riding bikes with fat tires in the middle of the winter. However, there’s a lot of vascular disease in our area. I’m not sure why but I’m suspicious of all the beer and cheese. Wisconsin is the leading cheese producer in the United States, 3 billion pounds of cheese per year. Our surgeons at Wisconsin publish their experience with retrograde extension of type B tears, aortic tears that extend backwards to the aortic root, starting as type B and becoming type A, cases of retrograde aortic dissection. How often do you think that happens? The Wisconsin experience. Eleven percent of all type A’s were retrograde extension of type B dissections. When you interpret the CT scan focus on the location of the intimal tear. If the tear starts in the distal arch, most tears go distally down the aorta but some also extend proximally to the ascending aorta. Find the start of the tear. The further down the aorta for the origin of the tear the less likely to extend retrograde back towards the heart. There are two risk factors for retrograde extension. Number one: A larger aneurysm in the arch. Number two: Thrombosis of the false lumen. If the false lumen is thrombosed, all of that pressure in the aorta cannot push the dissection down the aorta. In those cases, the dissection may extend in the reverse direction more proximally. So now we’ve covered the proximal complications of type B dissection. Let’s see what happens distally. Purpose: Determine what happens to the abdominal aorta in type B dissection. What is the effect on the kidneys? Methods: Two hundred nine patients, average age 66, cases gathered over five years from 20 different medical centers. Patients who have a complex type B dissection were treated with thoracic endovascular aortic repair. The abbreviation, TEVAR, T-E-V-A-R. What’s the definition of complex type B dissection? Aortic rupture, severe pain, uncontrolled hypertension, rapid increase in aortic size, or lack of perfusion to the distal organs. Surgery used as a last resort when a graft is not possible. Patients’ survival is better with TEVAR and medical therapy compared to surgery for type B dissection. The graft is made of plastic, a combination of different types of Teflon wrapped around a complex wire mesh made of an alloy nickel titanium. The proximal portions of the graft cover the proximal tear in the aorta. That keeps blood from going to the false lumen. But the dissection flap can extend into the renal arteries as well. The kidney may be supplied by the false lumen or the true lumen. After type B dissection with TEVAR, the authors looked at kidney size and function over time. Results: Main points. Number one: If the kidney is supplied by the true lumen about 60 percent of those dissections to the kidney healed without further treatment. If only the false lumen supplied the kidney, only 6 percent of those dissections healed at follow-up CT. Number two: If the kidney had blood supply from the true lumen but the dissection narrowed the renal artery those patients did worse. The kidney got smaller. Kidney function decreased. Number three: If the main blood supply to the kidney was from the false lumen, those kidneys had worse function over time and decreased renal size. Conclusion: In type B dissection look carefully at the renal artery. If blood flow is from the false lumen, make sure you report that. The perfusion to the organ may appear to be fine, the kidney enhances, but blood flow in the false lumen is not normal. When there is end organ supplied by the false lumen blood flow is compromised. For the kidney this means worse renal function and a smaller kidney. The treatment may be to stent those kidneys to preserve renal function.

Deep Learning for Predicting Enhancing Lesions in Multiple Sclerosis from Noncontrast MRI
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Next a neuro article and a nice idea. The title “Deep Learning for Predicting Enhancing Lesions in Multiple Sclerosis from Noncontrast MRI.” The first author Dr. Narayana, the senior author Dr. Gabr. The authors are from Diagnostic Imaging at the University of Texas Health Science Center in Houston, Texas. Background: Multiple sclerosis or MS, always a hot topic for radiologists. In May of 2019, we discussed if gadolinium was always needed for these patients. MS lesions that enhance after gadolinium have active inflammation due to a disrupted local brain barrier. Lesions that enhance after gadolinium indicate active disease in multiple sclerosis. Patients who have clinical relapses are more likely to have enhancing lesions. Gadolinium MRI is useful for guiding therapy. Comments from a world authority on MS. Some of their patients in MS clinical trials have received more than 100 doses of gadolinium during the course of their disease. That’s 2 liters of gad contrast. Now, if brain deposition of gad was going to cause neurologic symptoms you might think that 2 liters of gad might be enough to do it. The problem is that MS patients who progress will have cognitive impairment. Any cognitive change due to gad would be confounded by the progression of MS disease. The conclusion from research done in Munich: A large cohort, 500 patients, have had progression of disease. There were about 2,000 new MS lesions. Of those, only nine lesions were not seen on noncontrast images. Literally, all of the approximately 250 patients who progressed were
Nonhomogeneous Gadolinium Retention in the Cerebral Cortex after Intravenous Administration of Gadolinium-based Contrast Agent in Rats and Humans

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Our last topic for today. Quick update on new knowledge about gadolinium. The short title “Gadolinium Retention in the Cerebral Cortex after IV Administration of a Gad-based Contrast Agent.” The first author Dr. Olga Minaeva, the senior author Dr. Lee Goldstein. The study was done at the Radiology Department, Boston University School of Medicine. Background: We keep learning more and more about brain gad but the big picture is relatively easy to remember. I previously gave you four easy facts to remember about brain gad. I’ll summarize those points. Number one: On MRI, brain changes are seen in some patients who have six or more doses of gad. Most reports are with the linear contrast agents, Magnevist, Omniscan, and OptiMARK. Number two: At autopsy, atoms of gadolinium can be detected in the brain. The technique using mass spectrometry. It’s atomically accurate but we see only the atom not the gadolinium chelate. Number three: We don’t know if the brain gad is permanent. One report showed decreased T1 brain signal over time. Number four: Nearly all studies evaluate brain gadolinium by looking at the ratio of MRI signal in one brain area compared to another brain region. Unlike CT, the signal on MRI has no units. On MRI, the signal from water can measure 1,000, or it can measure 20, or anything. So we measure the ratio of one bright signal region to another more normal region. Here’s a thought experiment: Increase the signal intensity of the entire brain by 10 percent. Will you see any change on the MRI scan? The answer, no. We only see relative differences comparing one area of the brain to another. After multiple gad exposures to linear contrast agents the ratio of signal in the globus pallidus to the thalamus ratio is elevated, also the ratio of the dentate nucleus to the pons. Purpose: Use the best available techniques in the lab to map the entire brain for gadolinium. Rather than just looking at areas that are visibly bright on T1 images, look at the entire brain. Look for atoms of gad using mass spectrometry. Methods: The researchers gave Magnevist, the linear contrast agent, to rats. They also looked at the entire brains of two patients who had died. One patient with a brain tumor, a GBM, had 15 doses of gad. The other patient had brain trauma and had 3 doses of gad before he died. Both had Magnevist. Results: In the animal model, surprising results. Number one: The amount of gad in the cortex of the brain was elevated. The brain cortex had the same relative amount of gad as regions that are already known to accumulate gad, the globus pallidus, the caudate, and the putamen. Number two: In the brain cortex, the brain deposition was not uniform. In humans there are six layers of neurons in the cortex but gadolinium was found only in certain neuronal layers of the brain. If gadolinium causes neurotoxicity, it seems only those cells from certain brain layers will be affected. Those cells from certain layers of the brain could be tested in cell culture. Number three: Regions of the brain that accumulate gad were the same regions that accumulate iron. It’s possible that the same transporters for iron also distribute brain gad. Number four: The prior points were in the rat model. But what about humans? In patients who received gad just before they died, similar findings. Gadolinium was found in specific layers of the brain cortex not just...
the basal ganglia as previously reported. Conclusion: We continue
to understand more and more about gad in the brain. Results of this
study suggest that the entire brain may act as a reservoir of gado-
linium, not just the deep nuclei. Brain gad tends to accumulate in
the same areas as brain iron. Another piece of the puzzle. Perhaps
what we really need to know are the neurons in the brain damaged
by accumulation of gadolinium? So far, the answer is no. Let’s hope
that continues to be the case.

That concludes this week’s articles. 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.