Wake Forest University
School of Medicine

Medical Imaging with Dr. Kiran K. Solingapuram Sai

Making the invisible visible: How can positron emission tomography shine a light on the early stages of disease?

Making the invisible visible: How can positron emission tomography shine a light on the early stages of disease?

Conditions such as cardiovascular disease, Alzheimer's disease, and Parkinson's disease can have devastating impacts on the lives of patients and their families. Unfortunately, they are often not diagnosed until far too late. That is why **Dr. Kiran K. Solingapuram Sai** at **Wake Forest University School of Medicine** in the US is using positron emission tomography (PET) to improve early detection rates, support the development of new treatments, and change patients' lives.

Dr. Kiran K. Solingapuram Sai

Professor, Department of Radiology,
Wake Forest University School of Medicine,
USA

Field of research
Medical imaging

Research project
Imaging new markers for early detection of Alzheimer's disease

Funder
US National Institutes of Health (NIH)

doi: 10.33424/FUTURUM721

PROFILE

Talk like a ... medical imager

Alzheimer's disease – a progressive brain disorder causing memory loss, cognitive decline, and changes in behavior as brain cells become damaged and die

Cardiometabolic disease – a group of interconnected conditions that significantly heighten the risk of heart attacks and strokes

Cardiovascular imaging – a variety of non-invasive and minimally invasive tests, such as PET, used to capture detailed pictures of the heart and blood vessels

Diabetes – a long-term condition where the body cannot properly regulate sugar levels

Microtubules – microscopic protein structures within cells that provide support, help maintain cell shape, and transport materials throughout the cell

Neurodegeneration – the gradual loss of structure or function of nerve cells in the brain and nervous system

Parkinson's disease – a progressive neurological disorder caused by the loss of dopamine-producing brain cells

Positron emission tomography (PET) – a medical imaging technique that uses radiotracers to visualize biological activity within the body

Radiotracers – molecules labeled with a radioactive substance that is detectable by a PET scanner, allowing scientists and doctors to study specific biological processes in the body

Medical imaging techniques such as X-ray and magnetic resonance imaging (MRI) have revolutionized medicine, allowing us to see inside the body and identify problems such as fractures, tumors, and organ abnormalities. Positron emission tomography (PET) goes one step further, enabling us to visualize the biological activity of diseases before they cause any visible structural change.

"Disease often changes how the body functions long before it changes how it looks," says Dr. Kiran K. Solingapuram Sai from Wake Forest University School of Medicine. "PET is a powerful technique that allows us to see what is happening inside the body at a molecular level." PET is now a standard clinical tool used in oncology (the study of cancer), neurology, cardiology, and the prevention of cardiometabolic disorders. For example, in cardiology, PET can measure blood flow to the heart muscle, detect inflammation, and assess viability of heart tissue after a heart attack.

The process is relatively simple. "A patient is injected with a tiny amount of a radioactive molecule, called a radiotracer, that travels through the bloodstream to specific areas of interest," explains Kiran. "A PET scanner captures signals from the radiotracer and converts them into

Kiran reviewing MRI sequencing with Imaging manager, Ms. Lena Moretz. © Wake Forest University

three-dimensional images, allowing us to determine where the radiotracer has accumulated in the body. The result is a detailed map of biological activity." In other words, PET lets us see biology in action.

How are radiotracers developed?

"Radiotracers are specially designed molecules that target a specific biological process in the body," says Kiran. "They are like 'tracking devices' that bind to a particular protein, receptor, or metabolic pathway."

The observation of different biological activities requires different radiotracers as a PET scan can only show the specific biological process or molecule that its radiotracer is designed to detect. For example, a radiotracer designed to measure how cells use glucose cannot be used to reveal cancer-related proteins. "Developing new radiotracers is critical because the targets we want to image keep changing," says Kiran. "Each new radiotracer unlocks a new door."

Kiran creates radiotracers using a long, iterative process, bringing together specialists in bioinformatics, chemistry, and biology. Once a biological target is chosen, such as a protein linked to a specific disease, Kiran designs molecules that bind to it and chooses the most effective one. "After choosing molecules, we attach a radioactive label to them," says Kiran. "We then test them in cells and animal models to confirm they are reaching the target and staying there long enough to image. If the results are promising, we move towards testing them in monkeys followed by human trials."

PET and neurodegenerative disease

PET plays a vital role in the detection and treatment of neurological disorders, such as Alzheimer's disease, Parkinson's disease, and stroke. "These diseases begin at the molecular level long before symptoms appear," says Kiran. "If we can design tracers that detect these early changes, we can diagnose diseases earlier and track treatment responses more accurately."

"Neurodegeneration is a slow, devastating process, and for too long we have been diagnosing diseases only after significant damage has already occurred," continues Kiran. "But now we can image important proteins of Alzheimer's disease, detect dopamine deficits in Parkinson's disease, and assess brain metabolism after stroke or traumatic injury."

An early feature of both Alzheimer's disease and Parkinson's disease is the degradation of microtubules – hollow structures that maintain the shape of cells, transport nutrients, and support communication between cells. "Our lab developed the first PET radiotracer that can enter the brain and track microtubule integrity in living animals and humans," says Kiran. "We are investigating additional applications for it in Alzheimer's patients."

Kiran and his team have also developed a PET radiotracer for a receptor that is disrupted during Alzheimer's disease. "Being able to image this receptor gives us an entirely new way to understand neurological disorders and allows us to test whether new drugs that target this receptor are working," says Kiran.

PET and cardiometabolic diseases

Kiran is also developing new ways for PET to contribute to the treatment of chronic cardiometabolic diseases such as diabetes, which can lead to heart disease. "Type 2 diabetes damages blood vessels and the heart over time, which can lead to heart failure in diabetic patients," says Kiran. "With PET, we can detect inflammatory processes developing in blood vessels and organs like the lungs and joints, often before conventional tests would raise any alarm."

Kiran has developed a new radiotracer for a receptor that is found in the pancreas, gut, and liver and is important in the regulation of blood glucose and insulin release, called GPR119. "Pharmaceutical companies have been actively trying to develop drugs that reach and activate this receptor to treat diabetes," says Kiran. "Our radiotracer allows us to directly evaluate how the activity of this receptor changes with diabetic conditions and, more importantly, how well potential drugs engage with it."

Imaging impact

Ultimately, Kiran's goal is to improve patients' lives by finding new ways to detect diseases at earlier stages and by helping doctors choose treatments that are tailored to each individual. "If we can detect Alzheimer's disease five or ten years before symptoms appear, that changes everything for patients and families," explains Kiran. The same principle applies to diseases such as Parkinson's, diabetes, and cancer, where earlier detection can lead to better outcomes. "The work we are doing is opening up entirely new biological windows," continues Kiran. "We are developing new radiotracers for neurological diseases, such as Alzheimer's disease and alcohol use disorder, and for cardiovascular diseases. We are developing new molecular imaging tools to make the invisible visible."

About *medical imaging*

Medical imaging allows us to see inside the body, helping doctors diagnose disease, monitor treatment, and understand how our bodies work. As an area of medicine, it offers a huge range of opportunities, from developing new radiotracers and treatments to improving the sensitivity of scanners and building innovative AI tools to support the interpretation of images.

"What makes this field exciting is that it sits at the intersection of chemistry, physics, biology, medicine, engineering, and technology," says Kiran. "No matter where your strengths lie, whether you love working with patients, writing code, managing teams, or discovering new science, there is a meaningful place for you here."

The main challenge for Kiran is the length of time it takes to get new radiotracers from the laboratory to the patients. "You can develop a beautiful molecule that works perfectly in rodents and then spend years navigating the regulatory and manufacturing hurdles required to use it in humans," explains Kiran. "Science often moves faster than the systems built to verify and translate it. That tension between scientific possibility and practical translation is the challenge I grapple with most."

However, the reward of seeing a new radiotracer work for the first time makes it all worthwhile. "After months or years of chemistry and preclinical testing, that moment is electrifying," says Kiran. "There is nothing quite like seeing science work. But the deepest reward is knowing that this work is helping patients. When I think about the patients and families affected by chronic disorders such as cardiometabolic diseases and Alzheimer's disease, I think about what earlier, more accurate diagnosis could mean for them. That is what keeps pushing me every day – I am contributing to making the world a better place!"

Pathway from school to *medical imaging*

Studying chemistry, biology, and physics at school and beyond will build a valuable foundation. "Never lose sight of biology," says Kiran. "Understanding how the body works and how disease begins at the cellular level – that's what gives the science its purpose. The best people I've worked with are the ones who can think like a chemist and a biologist at the same time. You need both."

"At university, chemistry, biochemistry, pharmacology, biomedical engineering, and physics are all great pathways into the field," says Kiran. "I'd also strongly encourage students to explore computer science or data science. AI is changing how we read and interpret imaging data, and that's only going to grow."

"Medical imaging is not a single discipline; it's chemistry, physics, biology, and data all talking to each other," says Kiran. "The more 'languages' you speak, the further you'll go."

Explore careers in *medical imaging*

"My first advice is simple: find a lab and get involved," says Kiran. "Reading about science is one thing – doing it is something else entirely. The moment you pipette your first compound, run your first scan, or see a PET image light up a region of the brain, something clicks. That experience is irreplaceable."

"In my lab at Wake Forest, we actively welcome motivated high school students and undergraduates for summer volunteering," says Kiran. "Students get to work alongside our team on real neuroscience. Some students who began with us as summer volunteers have gone on to medical schools and graduate programs at some of the country's finest institutions."

"The Society of Nuclear Medicine and Molecular Imaging (**snmmi.org**) and the World Molecular Imaging Society (**wmis.org**) are the leading professional organizations in our field," says Kiran. "They offer educational resources and host annual meetings bringing together researchers, clinicians, and students worldwide."

Kiran working on autoradiography with post-mortem brain tissue analyses. © Wake Forest University

Meet *Kiran*

I grew up in India in a lower middle-class family. Every step of the way, I depended on the generosity of people around me — family, friends, neighbors, teachers, community programs, and strangers who believed in a kid they barely knew. It taught me that where you start does not determine where you finish, and that nobody gets anywhere alone.

I lost my grandmother to dementia when she was only 64. It came on fast and it was devastating – we lost her within two months of her diagnosis. Through all of it, there were no tools to catch it early, no way to see what was happening inside her brain, and, where we lived in India, no real access to specialized care even if those tools had existed. That experience never left me. Every PET tracer we develop, every image we generate, every earlier detection we inch toward – it is for her. It is for every family sitting where my family sat, watching someone they love slip away while medicine looks on without the tools to intervene.

Every radiotracer we develop starts with a biological question and then becomes an enormous, multi-layered puzzle. It takes collaboration across chemistry, biology, physics, and clinical medicine to develop them. Some of the best ideas in my lab have come from conversations between a chemist and a clinician who are both looking at the same image and asking completely different questions. That collision of perspectives is where the science gets exciting.

I genuinely believe that curiosity about the world makes you a better scientist. When you sit with people whose lives look nothing like yours, you come back to the lab with a broader sense of what matters and who you are ultimately doing this work for.

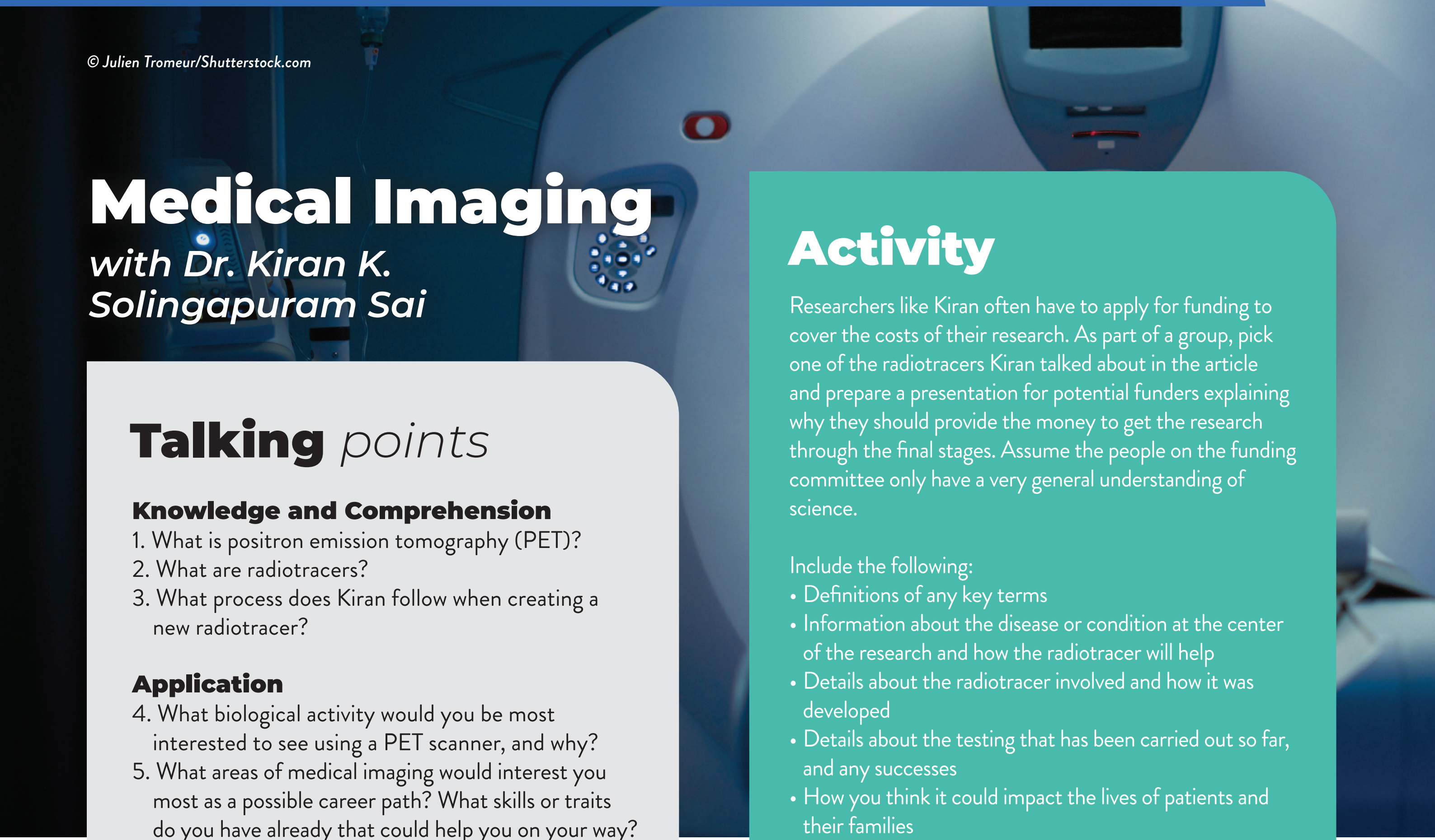
Spending time with my family is what truly recharges me. My beautiful wife, Mohini, and my two cute daughters, Kiara and Kiona, have a way of pulling me completely into the present moment – and that is something no amount of data or grant writing can replicate.

Dance genuinely lights me up. I have been learning Bharatanatyam, one of the oldest and most beautiful classical dance forms from India, and it has become something I deeply treasure – the discipline, the storytelling, the way every movement carries meaning. In many ways, it reminds me of science. Both require patience, precision, and a willingness to keep practicing long before mastery arrives.

Kiran's *top tips*

1. Get comfortable with failure. The scientists who make the biggest contributions are the ones who have the resilience to keep going when things don't work, and the wisdom to learn something useful from every failure.
2. Find mentors who believe in you and push you. I have been fortunate throughout my career to work with scientists who challenged me to think bigger and to not be satisfied with easy answers.
3. Remember why you started. The reason for pursuing this kind of science is the impact it can have on real people's lives. On the days when experiments fail, holding on to that purpose makes all the difference.

Let us know what you think of this educational and career resource. To provide input, simply scan the QR code or use this link: **redcap.school.wakehealth.edu/surveys/?s=NPK347RYHCR3FNDC**



© Julien Tromeur/Shutterstock.com

Medical Imaging

with Dr. Kiran K. Solingapuram Sai

Talking *points*

Knowledge and Comprehension

1. What is positron emission tomography (PET)?
2. What are radiotracers?
3. What process does Kiran follow when creating a new radiotracer?

Application

4. What biological activity would you be most interested to see using a PET scanner, and why?
5. What areas of medical imaging would interest you most as a possible career path? What skills or traits do you have already that could help you on your way?

Analysis

6. How does PET compare to other methods such as X-ray or magnetic resonance imaging (MRI)?
7. What are the advantages of developing imaging techniques that are able to investigate and diagnose conditions of the heart and brain?

Evaluation

8. Developing a new radiotracer can take many years and cost a lot of money. To what extent do you think the potential benefits justify the investment?
9. Kiran tests his radiotracers using animals and humans. What do you think are the advantages, disadvantages, and ethical considerations of medical research tests in animals and in humans?
10. Kiran talks about the importance of multidisciplinary work in medical imaging. Why do you think working with professionals who have different specialties is valuable, and what do you think the challenges could be? How good are you at working with others?

Activity

Researchers like Kiran often have to apply for funding to cover the costs of their research. As part of a group, pick one of the radiotracers Kiran talked about in the article and prepare a presentation for potential funders explaining why they should provide the money to get the research through the final stages. Assume the people on the funding committee only have a very general understanding of science.

Include the following:

- Definitions of any key terms
- Information about the disease or condition at the center of the research and how the radiotracer will help
- Details about the radiotracer involved and how it was developed
- Details about the testing that has been carried out so far, and any successes
- How you think it could impact the lives of patients and their families
- What further research could also be carried out in the future

Think about how you will make your presentation engaging, interesting, and convincing while keeping it clear, accurate, and factual. Share your presentation with your fellow students, and watch theirs.

Reflection questions

- How well do you think each of the presentations a) explained the science and b) provided convincing reasons for funding?
- Did you enjoy creating your presentation? What did you find challenging? What would you do differently in the future?
- How would the style, tone, and approach of your presentation change if the aim was to educate other medical professionals about your new radiotracer? Or if it was to explain to a patient how the PET scan works?

More *resources*

- Visit Kiran's Futurum webpage to read his article in Spanish and to find an animation, podcast, and PowerPoint about his work: **futurumcareers.com/medical-imaging-with-dr-kiran-k-solingapuram-sai**
- Watch this series of TED Talks to explore different ideas and research on the topic of medical imaging: **ted.com/topics/medical+imaging**
- This video from Cancer Research UK shows what it is like to have a PET scan: **youtube.com/watch?v=lk-VzATcv4M**
- To learn more about guidelines for medical research in humans, visit the NIH considerations for human subjects research website (**grants.nih.gov/policy-and-compliance/policy-topics/human-subjects**) and read the Belmont Report (**hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html**).
- To learn more about guidelines for medical research in animals, visit the Office of Laboratory Animal Welfare (OLAW) (**grants.nih.gov/policy-and-compliance/policy-topics/animal-welfare**) and Animals in NIH Research (**grants.nih.gov/policy-and-compliance/policy-topics/air**)

Photo *montage*

Top: *Kiran working with senior postdoctoral fellow, Dr. Bhuvanachandra Bhoopal, on cell culture.*

Middle row: Left: *Kiran discussing radiochemistry with radiochemist Dr. Ryan Fitzgerald.*

Center: *Kiran writing a program for a new radiotracer production.*

Right: *Kiran reviewing MRI sequencing with Imaging manager, Ms. Lena Moretz.*

Bottom: *Kiran working on autoradiography with post-mortem brain tissue analyses.*

+44 117 909 9150
info@futurumcareers.com
www.futurumcareers.com

futurum

This educational material has been produced by Wake Forest University School of Medicine in partnership with Futurum and with grant support from The Duke Endowment. The Duke Endowment is a private foundation that strengthens communities in North Carolina and South Carolina by nurturing children, promoting health, educating minds and enriching spirits.

Wake Forest University
School of Medicine

THE DUKE ENDOWMENT