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"A big revolution is coming in ultrasound," says Dr. Clement Papadacci from INSERM

**Dr. McDonough:**
What if you could see every blood vessel in a patient's heart, kidney, or liver, down to vessels smaller than a human hair, all in real time?

Welcome to *The Convergence* on ReachMD, where innovators and physicians explore the technology transforming medicine. I'm Dr. Brian McDonough, and today I'm speaking with Dr. Clement Papadacci, who's built an ultrasound probe that does exactly that. Dr. Papadacci is a researcher at Inserm and the Physics for Medicine Institute in Paris.

Dr. Papadacci, thanks for being here.

**Dr. Papadacci:**
Thanks for inviting me, Brian. And hello, everyone. Let's take a big dive into the ultrasound domain.

**Dr. McDonough:**
Let's start with what you've achieved. You recently published in *Nature Communications* showing 4D blood flow mapping entire organs. Can you walk us through what that actually means for someone holding an ultrasound probe?

**Dr. Papadacci:**
Yeah, of course. It's been a very nice journey to end up on this magnificent study. Like you said, we can see the vasculature of a whole organ in 4D. So first, let's define what 4D means. We used to say it's three Ds plus time—the fourth dimension here is time. So what does that mean? It means you can see the three spatial dimensions, like you would see a baby in the belly of their mom, but you add the time dimension, and you see the blood flowing in the veins and the arteries at very slow motion. I would add to that the time dimension is sampled very finely, meaning that you have a lot of details in the time you can see slow motion of the blood, which gives you access to many parameters.

**Dr. McDonough:**
So what do these images look like from your perspective—the colors and those sorts of things?

**Dr. Papadacci:**
It is really fascinating to see them because you can see the true nature. You can see, for instance, the liver, which looks like a tree with the big trunk and the branch that becomes smaller and smaller. So you really have a sense of the beauty of nature. I don't know if you are familiar with the term fractal, which means the division of branches. It's exactly the same for blood vessels.

And so, for instance, you can color the arteries in red and the veins in blue. You can set up the flow velocity. You make it clearer when it's fast and darker when it's slow. And you can see these maps in 3D of the veins and arteries. And if you play the movie, you see this blood moving inside the branches until the very smallest vessel, which can be 100 microns or 50 microns—very small vessels.

**Dr. McDonough:**
You mentioned the liver, and you've tested this in hearts, kidneys, and livers in animal models. What did you see that was impossible to see before?

**Dr. Papadacci:**
What I could see is the different scales of the organ. So what does that mean? I like talking about scale. So let's say the big scale is the whole organ. I can see the entire organ. And it's in animal models, like you said, and porcine models. The interest of using porcine

models is that they have organs of the size of humans. So if it works in porcine models, it's going to work in humans. And so for the first time, we saw the whole organ, and at the micron scale. So you see this difference of scale. The whole organ is about 10 centimeters, and you can see details inside these organs that are about a hundred micrometers.

So in just one look, you have a big overview of what an organ looks like in terms of the vasculature, vessels, artery, and veins until the smallest vessels. And this was impossible before because of the ultrasound technology.

**Dr. McDonough:**
That's a good point. This is completely non-invasive—no contrast agents, no radiation. And as a physician, I'm used to ordering CT angiograms, MRI angiography, that sort of thing. What is different about what your probe shows and the advantages of not having to deal with those things?

**Dr. Papadacci:**
So we do need an injection of microbubbles, which are used in the clinic already in some application of echography. So there are microbubbles of gas that are usually used to enhance the contrast of blood vessels. It's used for cardiac applications. For instance, you're going to inject these microbubbles to see the cavity of the heart filled with the microbubbles. There are some applications on the carotid. You're going to inject the microbubbles to see the blood in the carotid and do some quantification. It's also used in the brain to see better the Circle of Willis.

Microbubbles are available in clinics in the US and in Europe, so there's no big issue about that. Clinicians are used to injecting these microbubbles. And the specificity of our work is that we're going to inject a diluted solution of microbubbles—so less microbubbles because what you want at the end is to follow and track them individually.

So this is the key invention in this work. It's called ULM, or ultrasound localization microscopy. This technique was invented 10 years ago. It was pioneered in the lab.

So I come from this culture of ULM, and this enables you to see this different scale of vasculature from the big vessel to the smallest vessels. But the field of view was really limited. First, it was developed, of course, for 2D images. So the first application of this technique was performed on the rat brain. It was just a slice of the rat brain, and you could see very well the vessels, the neocortex, the nucleus, and more deep in the brain. And then it has been extended to 3D. And people were very interested in 3D because, of course, all these vasculatures are three-dimensional and they are very complex in the brain, the heart, and the coronaries.

So it's work that I also did with Mathieu Pernot and Mickael Tanter. It was to see the coronaries in a rat heart. So the coronaries—there are veins and arteries that feed the heart muscle because the heart needs nutrients like any other muscles. But there was a problem in extending the field of view and applying it to a human organ. This is really the key of this invention. We invented this probe of the future that is able to see a whole organ of the size of a human and to see the microvasculature. And it comes really from scaling up these probe technologies to a big probe that can see large organs.

**Dr. McDonough:**
You did your dual bachelor's degree in physics and cinema. When I was in school, it was English and biology. And I know in my life, the English major part has revealed itself through broadcast journalism, writing, and those things. And clearly, you have physics and cinema. How does that creative background influence how you approach medical imaging research? Because you obviously must have the ability to visualize things that most of us can't.

**Dr. Papadacci:**
Yeah. It's a very good point. I was passionate about cinema from very young, and because I had some ability in mathematics and physics, my dad, who's very rooted and feet on the ground, told me, "Okay, you can do cinema, but why won't you continue physics at the same time?" So, because I liked challenges, I kept the two. What I was passionate about with cinema was what you were telling with visualization and the beauty of images—but also telling stories. And the third thing that I was very attracted to with cinema is the creativity that you can get there.

And then, when I continued, I left and studied physics at Oxford University. I could not continue at the time—it was just one year abroad. And I really discovered what physics could do. And when I continued in the internship, I was very passionate about applications of physics, especially in the medical field. And when I started to work on imaging, I could see that images and cinema were very close because the way you're going to represent your data is not that obvious. You need to choose the color of the arteries. You need to choose the color of the paints. You need to choose the frame rate. You're going to show the results. So there is a big part of visualization. And now that my research really focuses on 3D and 4D, it becomes even more true.

To give you a story in the lab, we have an engineer, Alexandre Dizeux, who specializes in visualization and helps us do this beautiful movie for people to understand what we do. And it's using software that's from the cinema. It's called Houdini software, and they use it for explosions and special effects, but it's also very powerful for scientific data, especially 4D, because how can you represent 4D there? Our eye can see only in 2D, and to get the sensation of 3D, you need to move around. And it's exactly the same when you represent 3D and 4D data—you need to move around. You need to cut inside. You need to choose the plane of view to represent what you want to show.

So I think it's a very similar approach to cinema. Of course, I don't tell a fantasy story. I want to tell a true story—I am in science. But there's also this choice of what I'm going to show and how I'm going to show it. And, of course, physicians are very important for that. They help us and guide us. They tell us what they want to see, and sometimes they don't know how they want to see, and we need to give them tools and visualization for them to understand the images.

**Dr. McDonough:**
Things have come so far. Early in my career—obviously, I'm a lot older—we used that concept of 24 frames per second, and you could do stop action and educate people by having the stop-action movement, which is so old. But at the time, you were able to educate by giving people those images. And it's so exciting that you can do that now for education and treatment.

So let's bring it back to the real world. Let's say I'm an emergency room physician, and a patient comes in with some sort of acute kidney injury. How would the technology that you have help in ways that a current ultrasound can't?

**Dr. Papadacci:**
Yeah, it's a very good question. It's very linked to all the diseases that are linked to microcirculation. When you talk to a physician, and you are one, obviously, they are fascinated by it because they can't see it. It's important in so many diseases, and they get the feeling that when the diagnosis is complicated, the microcirculation is involved.

Actually, everything has to be discovered on this point because you need to show them for the first time how microcirculation gets altered in some pathologies.

So, of course, we have ideas. You mentioned the kidney. We are going to work on nephrosclerosis, which is a pathology in the kidney that affects arterioles and big vessels, and also glomeruli. Glomeruli is a big goal in the imaging of the kidney. So if one day, you offer a clinician a way to see them and quantify them and tell it's abnormal because the density of glomeruli in this patient is too low compared to what we know from healthy volunteers, then you really would make a difference in the kidney world.

So I'm hoping that with this kind of technology, I will be able to build some device and put it in the hands of physicians who have ideas on their pathologies and think that microcirculation is involved for them to characterize their pathology and to understand how microcirculation plays a role here. And I think it's key in many pathologies.

**Dr. McDonough:**
Many of my colleagues and I learned ultrasound on conventional machines, and now we're talking about a golden age of ultrasound thanks to ultrafast imaging, which was pioneered 20 years ago. At your institute, what is that like—conventional versus ultrafast? What is the difference?

**Dr. Papadacci:**
So ultrasound is a beautiful modality for sure because it's real time, portable, and easy to use. Of course, you need to get some training. But when you have it in your unit, it becomes an essential tool for many organs—for instance, the heart. You can see it moving in real time and play with the parameters. And then you get the Doppler. So you have many good parameters and good imaging techniques that are able to screen some patients.

That being said, since it was invented and clinically applied 40 years ago, the main goal of the ultrasonic device manufacturers was to enhance the imaging quality. The resolution means the details that you're going see. The contrast is how dark what you want to see is dark and how bright what you want to see is bright. So with these two parameters, they wanted to announce it, and it was the only research that that was done, basically.

And what ultrafast imaging permitted—so just a brief explanation of what it is—ultrafast imaging is looking inside the body at ultrafast frame rate. What I mean by a frame rate is it's the speed you see the image for. For instance, your eye is seeing basically 50 images or 60 images per second. This is real time. This is what enables you to see reality and things moving around you. Ultrafast imaging can go 1,000 or 10,000 images per second. So what you can see is completely different.

For instance, I'm going to give you an example of what you can see in the human body. When you feel your wrist, you feel your pulse

wave. This pulse wave is basically a shear wave that propagates inside your arteries. And if you film it with ultrafast imaging, you see this shear wave in red and blue moving around your artery. Another example is the valve closure inside your heart—when the aortic valve or the mitral valve closes, they send a little earthquake inside the heart, and you can see the propagation of this shear wave all around your heart. And this is only possible with ultrafast imaging because these waves are too fast. We are talking about order of magnitude of a meter per second. So to see them, you need a very high frame rate.

And then, like we said earlier, with slow motion, you can see very slowly this wave propagating all around. And you're going to ask me, "What is it for, and why do you need that?" It's because this shear wave has the magic property of being directly related to stiffness inside the body. So if you can measure the speed, you can measure stiffness. And it's actually the first big application that occurred with this technology of ultrafast imaging. It was generating a shear wave and creating a map of stiffness where you generated the shear wave. It was applied, for instance, on breast cancer, where sometimes, you want to know if the carcinoma is in remission. So instead of doing a biopsy, you can make a stiffness map and see if the stiffness decreases—it means that the carcinoma is in remission.

So just as a summary, this golden age comes from this ultrafast imaging. I quoted just one application, but there are many.

**Dr. McDonough:**
I was thinking about here in the United States—it's probably not as big a problem in Paris—we have a lot of people with metabolic syndrome because of diet and other things and fatty liver. FibroScan is something many US physicians order for liver fibrosis staging to see if fatty liver is getting worse, and that uses shear wave elastography from ultrafast ultrasound. So can you walk us through how that works and why it's replacing liver biopsies in many cases?

**Dr. Papadacci:**
Yeah, of course. It's a great example of how shear wave elastography made a difference in the clinics with this device that you mentioned. This was created from the work 20 years ago in the lab by Mickael Tanter and Mathias Fink. They created this technology.

So what they do is they make a little vibration on top of the body of a patient, and it creates this shear wave. And this propagation of this shear wave is really magical and fantastic because the velocity is directly linked to the stiffness. So then you get a detector that's going to measure the velocity of this shear wave at an ultrafast frame rate. And then you're going get the stiffness, and you are able to grade the fibrosis in this patient. And they showed that depending on the stiffness—the shear wave velocity that you measure—they are grade zero to grade four. So it's able to really discriminate the patient and know how bad the disease is. And then you get the therapeutic decision based on that.

**Dr. McDonough:**
Briefly, I just wanted to ask you how ultrafast imaging impacted traditional Doppler studies as well.

**Dr. Papadacci:**
So very briefly, because ultrafast imaging is very fast, you get a lot more temporal information. And because Doppler is studying the motion of the blood, the more temporal information you have, the more sensitive your Doppler is. So some device manufacturers use ultrafast Doppler to increase the sensitivity of their images.

**Dr. McDonough:**
That's why I wanted to bring that up. I want to move on to ultrasound localization microscopy and 4D imaging. Ultrasound localization microscopy is probably new to most physicians. What is it, and why is this such a big deal?

**Dr. Papadacci:**
So I'm going to go back a little bit in the physics there just for you to understand what's limiting the ultrasound to be able to make this microcirculation imaging. So basically, we talked a little bit about the resolution earlier. The resolution tells you what details you can see in your image, and the resolution is directly linked to the wavelengths. The wavelengths are linked to the frequency of your probe. So any sonographers or physicians who have already used ultrasound devices, they're going to choose their probe, and they know this one has five-megahertz frequency, or that one has two-megahertz frequency. For example, three megahertz is for the heart, and five megahertz is going to be for the liver or the kidney, and so on. And this frequency is directly linked to the detail that you can see. And this detail is about one millimeter or five millimeters, and you cannot do anything about that. It comes from physics. It's a barrier that you cannot break.

Ultrasound localization microscopy uses a trick. And the trick is if you inject some microbubbles, you can localize them and track them, and you are not limited by the resolution of the wavelengths. You are limited only to the path that the microbubble's going to take. If the microbubble takes a path in a four-micrometer vessel and you can track it, then you can resolve a four-micrometer vessel. It's as simple as that. You have these microbubbles, and if you can track them individually and follow their path, and they take a path in the smallest

vessel, then you are able to resolve it. And it is as simple as that. But it works.

And, of course, to construct a map of the vasculature from the biggest vessel to the smallest vessel, you need to wait and accumulate the frames, because at each bifurcation, you have the probability that the microbubble will go right or left. So you need to cover all the possibilities to recover the entire map of the vasculature. And when you've done that, you accumulate everything and get a full vessel mapping from the biggest vessel to the smallest.

**Dr. McDonough:**
And that obviously matters a great deal because you now get a greater sense of what's going on, right? You're seeing imaging that that makes real difference.

**Dr. Papadacci:**
Yeah, exactly. What's very strong about that is we don't just localize these microbubbles—we're also following them with the tracking. You get the velocity, and the velocity is so important because it gives you a sense of the function of the organ. It's not just a static image, like many modalities give you; it's also dynamic. So that's why we really want to emphasize the 4D part of this technology.

And then we can retrieve some very interesting index. The flow rate is so important because you, of course, can calculate the ranges of the velocity you can get, so the flow rate of the velocity. That's very important. And so many other parameters that clinicians are interested in—tortuosity—we still have some hidden index, and we need to discover them, and I think it's going to help a great deal.

**Dr. McDonough:**
It's interesting, I read one of the things you have where you said that structure tells you about disease dynamics and function. The function is the key of what we're doing when we're trying to treat patients because that's really how it's revealed to them in one symptom or another. This has to be so helpful.

**Dr. Papadacci:**
Yeah. I agree completely. There are many ways to see the function of the organ, but in many diseases, it's indirect. You cannot really see deep in the organ and how the function is. So, for instance, to evaluate coronary function, you can inject vasodilators to see the reserve of the coronaries, but you do it only for big vessels. Here, you can imagine doing it also for the smallest vessels. You can do the same kind of stuff, for instance, to see the reserve of the Circle of Willis, to see if these arteries still have reserve. You ask the patient to hold their breath to create a vasodilation, and with this, you can see it and follow it with this technique.

**Dr. McDonough:**
I understand the concept, and I think a lot of our listeners and those viewing do, of going from 2D to 3D to 4D for entire organs. And it's one thing understanding it, but it's another thing looking at the conceptual and technological challenges that you faced. What were some of those things as you were moving? I'm sure that wasn't easy.

**Dr. Papadacci:**
No, that was not easy. We needed to go back to the physics, and I'm going to explain why. The current technology is based on piezoelectricity, which is the way to emit ultrasound in the body. It was discovered a hundred years ago, and it's really the basis of ultrasound. And these probes that are able to do 3D, they are matrix. It means they're squared. And this square is cut in many pieces, and current matrix arrays have thousands of these pieces. We call them elements. And these thousand elements—the specificity of ultrafast imaging is the need to be connected to a channel.

So what's the channel? It can be seen as an oscilloscope—this device to be able to measure, an electric signal. We can imagine that these matrix probes need to be connected to thousand oscilloscopes. So on an oscilloscope, you see it's the size of a computer. Imagine a thousand of them. It makes a big machine. This is the current state of the art. And this big technology is only to make an image of one centimeter by one centimeter. So if you want to extend this to human organ, which is 10 centimeters by 10 centimeters at least, then you're going to need to multiply this device by a hundred or thousand. A hundred thousand oscilloscopes stacked together is going to be bigger than an MRI and even more expensive.

So this is, for now, impossible, and no one has been crazy to do it. That was the starting point. This is not doable. We need to find a way to reduce this number of channels to reduce the number of stacked oscilloscopes. So how can you do it? You need less elements in your matrix, but if you do that, then you have less energy. We said, “We want less elements, but we want them big to cover a big surface of a probe.” But if you do only that, because your elements are big, they're not able to work together, they're going to stay alone. And in a matrix probe, they need to work as a team. Like every work in life, you need to work as a team. Nothing can be done alone. It's the same for a probe. And so they need to see each other. If they are big, they cannot see each other. They can see only in front of them.

So the trick here, and it's really the key invention, is to put an individual lens for these big elements to be able to see each other and to see on the side. And by doing that, they can work together. They can make an image. They recover their nature of being able to work together and make a beautiful image. It can be compared to an optical lens, something that you put on your eye to see.

We do that exactly the same for the elements of the matrix probe. We put an acoustic lens for them to see again and to be able to work together. We want this on every side. The size of our probe is huge—10 centimeters by 10 centimeters. No one has ever been able to do that. With such a big ultrasound probe, the number of elements is low—about 200. We were talking about 100,000 earlier, and there's only 200 in this probe. And they have this acoustic lens that can restore good imaging quality. And I could apply it to see all the vessels that we talked about earlier.

**Dr. McDonough:**
You're listening to *The Convergence* on ReachMD. I'm Dr. Brian McDonough, and my guest is Dr. Clement Papadacci. We're talking about 4D ultrasound—the technology and practical uses.

I want to move onto some clinical uses. So to help me visualize this, and for those who've been listening to this, you're a physician at a bedside with the probe. What is my workflow? How long would a scan take, and what would I be seeing on this screen?

**Dr. Papadacci:**
That's a good question, and we are still working on that for sure. But I have a very good sense of how it works. As you may know, we are moving to clinical trials very soon. We have already done some human volunteers, and we are very near the clinic. So we have a very good sense of how it works now.

As with any echographic system, you need some gels. You need to put some gels on top of the probe for the ultrasound to be able to pass. So this is not different—maybe the difference is because the probe is so big, you're going to need a big amount of gels. So maybe that's something that you need. When I go to the hospital, it's always funny because the tubes of echographic gels are always empty. You're running in every room to try to find one that's full. So maybe you need to take that into account and get one near you.

And then you position it on the patient, and on the screen, you have a b-mode image, which is a real-time image of what's going on inside. But, of course, you won't see the beautiful image as you will see in the video because this takes time and post-processing. So you won't see that in real time. In real time, it will only tell you you're in front of the organ of interest, so you're good to go. So when you're good to go, you start injecting some microbubbles. In regulations, you are able to inject one dose, which is five milliliters. My advice would be don't inject everything at the same time; inject little by little. You can do boluses of one milliliter every minute.

And then you start the acquisition. So basically, the acquisition will start at five minutes, and every minute, you inject a bolus of microbubbles of one milliliter, and then everything is stored on the machine. We have tools to see if the data are correct and the positioning is definitely good. So you have a pre-processing tool to not be completely blind, and then you do the post-processing offline for now, and you get the beautiful image in 10 or 15 minutes, and you can already see some of the results.

**Dr. McDonough:**
You mentioned that you're heading into human clinical trials. What are the first clinical applications that you're targeting at this time?

**Dr. Papadacci:**
So we are targeting an application for atherosclerosis patients—the patient who has plaques all around their body—to see how it impacts the vasculature. And we are targeting two organs—the heart to see if we can already detect some blockage in the coronary, and also the brain because we want to see the Circle of Willis and how it could affect the distribution of the blood. This patient has big plaques in the carotid, and they will undergo surgery, and physicians want to know how the Circle of Willis will be able to redistribute the blood during the surgery because it's a very heavy surgery. You need to clamp the carotid, so you stop the blood. And so, the Circle of Willis, as you know, redistributes the blood through the carotid arteries, but if it's incomplete, then there is a risk of stroke in the patient.

So they have tools that they use—MRI angiography, CT angiography—to look at the Circle of Willis. But sometimes there is some shadowing. You are not sure if the communicating arteries are really functional. And we are very confident that with this technology we developed, we'll be able to quantify the communicating arteries and the way they work. We have very nice work that's finished and that we're going to be publishing very soon on primates, where we could very finely characterize the Circle of Willis and its ability to redistribute the blood inside the main cerebral arteries. So that's basically the application that we are targeting.

So it's a complex clinical trial because we are going to try on the heart, on the brain, and on the same patients. And we think we can make a difference in the decision afterwards for surgery.

**Dr. McDonough:**

In cardiology, for instance, patients can have angina, yet they'll have normal coronary angiograms, so the imaging we have can be a source of frustration for the cardiologist trying to figure things out. What would your probe show that might change management as you begin the testing and you're seeing what's happening?

**Dr. Papadacci:**
This is an interesting application. You referenced this big family of pathology—coronary microcirculation dysfunction. The decision tree is very complex in this pathology. Anyone who's listening to us who's been confronted with this kind of patient having angina and a normal coronary angiogram, they pass so many tests before concluding it must be a CMD. Being able to visualize microcirculation right away could save time for this patient, and also, diagnosing very early is important for sure, but also, to develop new therapeutic strategies—it's very difficult for companies to develop therapeutic strategies when they can't see the effect directly on what they're targeting.

So I think it's both to diagnose, but also, on the therapeutic follow up, it's very interesting. As you know, ultrasound is non-ionizing, so you can use it as many times as you want. I think it could make a big difference in this kind of pathology.

**Dr. McDonough:**
Another thing that I'm thinking of—we talked about it before—is how metabolic syndrome can lead to liver fibrosis through fatty liver changes. One of the other things we're seeing, obviously, is it increases the number of people with type two diabetes and people who might develop diabetic nephropathy. Your tool could really help by looking at the entire kidney microcirculation in a 4D approach. With so many people battling this, it would seem like the uses are almost endless for perfusion defects and responses to treatment and those sorts of things.

**Dr. Papadacci:**
Yeah, exactly. The same as for CMDs, in this pathology that's difficult to diagnose, it's also difficult to make groups. We have so many pathologies that we put all the patients in the same groups because they just don't respond to other markers and well-known biomarkers. So by creating new biomarkers, like microcirculation and function, it could really help clinicians to say, "This pathology can be divided in two or in three, and in this first group, we can give this kind of medication, and in this second group, another kind, and I can follow up on what's going on in the microcirculation part."

I think this gives a lot of hope in these pathologies. The decision tree is very complex, and it's often called diagnosis by exclusion. You exclude every other cause, and afterwards, when you have excluded everything, you say, "Okay, it must be that." And I'm sure that seeing the microcirculation, visualizing it, quantifying the function, and comparing it to what's normal and what's expected would save a lot of time for the clinician and for the patient that is suffering from that.

**Dr. McDonough:**
This is portable. I was thinking about my experience with point-of-care ultrasound and how we're using it now in offices, the ED, and the ICU, and where I saw challenges was getting the results into the electronic medical record so that people could use it and see it. That was a very simple problem to have, although very difficult to deal with. This is portable, and you mentioned connecting to small equipment. So how do you see point-of-care applications working, and could we use this technology in places such as the ED, the ICU, or even outpatient clinics?

**Dr. Papadacci:**
Yeah, that would be really the dream—to make it easily transportable to anyone who wants to see more and know more about microcirculation. And as you mentioned, because it can be connected to any ultrasound device, it'll be in the clinic from a small company we may start or a big company that wants to integrate the technology into the ultrasound system. So I'm really hoping that it gets into the hands of any practitioner that feels it has a use.

And I think another part of your question is how easy the biomarker will be to interpret. Will it be easy for anyone to read images? And this is the work that we are doing now—making the ultrasound images visualizable, but also working with clinicians who tell us what they want to see. Sometimes, you make big 4D images, but the clinician in the specialty only wants to see one part of it, and you can only select what you want to see if you have seen it all.

And this is my big trust in 3D and 4D imaging—it's to get simple, you first need to get complicated because you don't know what you want to see. So seeing it all makes you then select the part that you want to see and the biomarkers that you want to see. And maybe for some applications and some clinicians, they will want to see just one value or just one piece of the image. It's fine.

And this is what we want. We need to work with a physician now for them to tell us what is important in their world and in their application.

**Dr. McDonough:**
You alluded to the use of microbubbles. Certainly, that contrast agent use is something that is necessary for the probe. What can't your probe do yet? What are some of the limitations physicians should understand about this?

**Dr. Papadacci:**
For now, we have developed it really for the application of ultrasound localization microscopy. We can't expect for now to have, for instance, beautiful b-mode images. In real time b-mode images in 3D, you would see the baby in the belly of their mom. This is not doable for now because the probe has not been done for that. And I think all the devices do it very well. I think the sonographer and the clinician are fine with switching probes for different applications, so I don't see that to be an issue. But, of course, because we want it all, we'll try to improve on that.

**Dr. McDonough:**
One of my favorite parts of *The Convergence* is talking about the future because it's already exciting, and then you start to think of where we go next. What is the timeline moving forward? Here in the United States, when will physicians actually be able to order a study and use a probe, from a realistic standpoint?

**Dr. Papadacci:**
I think that's what's also fascinating with this project—it goes very fast. Three years ago, I had the idea of these lenses, and we were doing a simulation, and I remember the first time I sent the publication to my peers to be peer reviewed. The researcher did not believe it could work because we were only doing simulation, and they were saying, "No, it won't work because of this kind of probe does bad imaging, and this just can't work." And it was very difficult to get the first paper published three years ago. It was published in 2022. So you see, from three years ago, it's really fascinating to see how fast we went from this little idea, this little simulation made with the team, but we just needed a computer. And three years ago, we moved on and did whole organ animals. We already did porcine models. It's published. Primates are about to be published. And we are moving next year to clinical trials.

I think that's the magic of this project—it's moving very fast. And after that, we want to do other clinical trials on different organs. We are thinking now of maybe launching a company, like I was telling you, but we're also very open to working with big companies.

We really think this device and this technology should spread as fast as it can because it can make a difference. And there are still many things to discover, and physicians are the right tool for that because they have many ideas. They are very creative. They have patience. They know what they want, and some of them really want to do research. So that's the next step. And I think it'll go fast.

**Dr. McDonough:**
With your background in cinema, you know the great producers, directors, and writers all have tremendous imaginations and vision going forward. If you could wave a magic wand—I'm sure you've thought about having this technology everywhere—let's say in 10-year period, what do you think would change in how we practice medicine if this tool becomes a tool that we start using?

**Dr. Papadacci:**
It's a nice question. I've always been fascinated because I'm from ultrasound. I see the x-ray that's being performed every day in the clinics when technicians come and take your hand and look at the broken hand and see the bones, and the images goes to the radiologist who analyzes it, and it's done. It's so easy, and technicians can perform the act. And then the physician analyzes the image, and the diagnosis goes with the current flow. It's easy. It's fast.

And I think this probe could be like that because you don't need a big specialist to position the probe. You can make a big probe that you're sure will cover the organ, and then you make this big image of the entire volume, and the radiologist or the specialist of the domain can interpret it and give you the diagnosis fast.

I think I'm dreaming, as a physicist working in the medical field, of making a difference in the world of the clinic and that some patients get a bit of what I do. I think my biggest dream is to be able to make a difference for patients.

**Dr. McDonough:**
That's a wonderful dream. And this technology grew out of your work in Paris and your research. For physicians watching and listening all over the country, how do you stay connected to emerging technologies that could transform our practices? Do you have any advice where people should look or read? These things just don't pop into the journals all the time. Any ways you suggest we could get more engaged or learn if we're interested?

**Dr. Papadacci:**
I think the key is to stay really open-minded and try to find researchers around this kind of technology who want to apply it in the medical field. We are very interested in physicians' input. I get fed by that. I'm a physicist, but I learned to talk with physicians because it's really

key for us to be able to understand each other and interact. Sometimes, we have a new tool, and we go to see a physician and ask them, “How can it serve you?” And sometimes, it’s the other way around. Physicians come and they say, “I really want to see this part. I really want to quantify this part. Do you have a tool for me?” And we cannot grow if we don't have this exchange. And finding a physician we can talk with is of great value.

So my advice would be stay open-minded. Everything doesn't work the first time. Sometimes, you have some development to do together. So don't expect that you’ll press a button and it works. Sometimes, it's like that when we work together. But it's a great adventure, and I recommend it to any physicians that are listening to us today.

**Dr. McDonough:**
Dr. Papadacci, what would be one message you want every physician listening to remember about ultrasound's potential? And maybe we’ll leave this conversation with that thought.

**Dr. Papadacci:**
I think a big revolution is coming in ultrasound, and the new tools are going to help their lives, I hope, and the lives of their patients.

**Dr. McDonough:**
Well, it was our honor to have you, Dr. Clement Papadacci. I want to thank you very much for taking the time to join us.

**Dr. Papadacci:**
Thank you so much for inviting me, Brian.

I would like to thank the team—it was a great job that everyone performed. I want to thank my student, Nabil Haidour—a really good part of the project. And I would also like to thank the physicians listening to us because, like I mentioned earlier, they are really the input that enables us to do all this beautiful work.

**Dr. McDonough:**
You've been listening to *The Convergence* on ReachMD, where innovators and physicians explore the technology transforming medicine to hear about other technological advances shaping the future of healthcare, visit *The Convergence* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for listening, and we'll see you next time.