OREGON HEALTH & SCIENCE UNIVERSITY ORAL HISTORY PROGRAM

a project of OHSU's Historical Collections & Archives

an interview with:

David Huang, M.D., Ph.D.

interview conducted on: May 1, 2023

by: Yali Jia, Ph.D.

OHSU

Interviewee: David Huang
Interviewer: Yali Jia
Date: May 1, 2023
Transcribed by: Teresa Bergen

My name is Yali Jia, a professor of ophthalmology and biomedical engineer. The first mentee of Dr. David Huang at OHSU. I'm very thrilled to interview Dr. Huang for OHSU Oral History Program. Today is May 1, 2023. We are at BICC Library at OHSU campus. Dr. David Huang, renowned ophthalmologist and a scientist known for his pioneering work, optical coherence tomography as a professor of ophthalmology at OHSU Casey Eye Institute. Dr. Huang has dedicated his career to advancing the field of ophthalmology and has made significant contributions to the diagnosis and the management of eye diseases through his development of OCT technology. So, before we delve into your groundbreaking work, OCT, we would love to learn a little bit more about your background and what led you to pursue a career in ophthalmology. Can you tell us where you grew up and what initially sparked your interest in science and medicine?

Huang: Well, thank you, Yali. And thank you for taking the time to do this interview. So, to start from the beginning, I grew up in Taiwan. And moved to the United States when I was thirteen. And my father was a physician. He practiced family medicine. And so that's always a role model for me to think about medicine.

And in high school, I went to a rural high school in upstate New York. So there were actually very few people who went into science, technology or medicine. But I was very fortunate to have a chemistry teacher, Dr. Terry Peard, who really mentored me and took me around to various universities. And that's probably the reason I applied to many of the top universities that I otherwise wouldn't have thought I could get in. And that's when I went to MIT.

And once I went to MIT, of course I got a very good education in engineering. Was exposed to a lot of different disciplines. And I think I first thought I was going to go into computer science until I had a real programming job and found that it was kind of—I was under stimulated coding on a computer all day long. And I thought I should do something where I would deal with people on a more regular basis, like going into medicine. So that's why, majored in bioelectric engineering and applied to medical school.

And once I got into medical school, I actually missed the quantitative aspect of engineering. Although the program I was in has a lot of kind of physics and engineering aspect. I was in the health science technology program at Harvard/MIT. And one of the professors was Dr. Raphael Lee, who encouraged me to join his lab to do research in tissue engineering. And he said he would pay for medical school. (laughs) So that kind of cinched the deal, since I was kind of missing engineering.

And so once I was back in the electrical engineering department at MIT looking at different labs, I kind of fell in love with the optics group, the ultrafast optics group that dealt with femtosecond lasers because the technology's just fascinating. And optics and lasers, it's a lot more interesting than computer science. To me, anyway. And that's how I got back into engineering.

And as far as ophthalmology, that really grew out of my PhD thesis project in optical coherence tomography, where we work with ophthalmologists to find its first applications.

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Jia: Yes, that's what I want to ask you what inspired you into the ophthalmology already. That and how did you become really interested in developing OCT technology in Dr. Fujimoto's lab? And can you describe some of the challenges when you faced during the development of this technology and how you overcame them and how has your background in electrical engineering influenced in this development?

Huang: Yeah, I think it was really a lot of chance occurrences. Unpredictable events that steered me toward developing OCT. I had several projects in Professor Fujimoto's laboratory at MIT. First I was tasked to build a femtosecond laser system to do tissue cutting in the eye. And unfortunately, I never got enough pulse energy to achieve any significant cutting. So the project, that project wasn't successful. And I had other projects which I actually took the initiative to develop some variations of femtosecond laser, using self focusing. Like we developed this thing called a microdot mode-locked laser that did work, but didn't produce as short a pulse as was later shown to be possible. There was a race to generate a shortest femtosecond laser pulses during that time that was very active and interesting, but had nothing to do with medicine.

So I got another side project where we were using femtosecond lasers to do ranging measurements or distance thickness measurements in tissue, including in the eye. And we explored a variation where we used interferometry and we measured the cornea and retina. It's really when I saw the reflection from retinal samples, which were very complex, that I realized that the natural way to probe the retina would be to produce an image. And then it hit me that what this could be a new imaging modality that would have advantages in having very high resolution.

And I remember then going to Professor Fujimoto to get some funding to buy visualization software and scanning hardware to produce images. And in typical fashion, he says that he'd raise a lot of difficulties and objections. But that was kind of his style, to challenge us to overcome these problems.

But it worked. We were able to get interpretable images where you can see retinal layers. And then we scanned other tissues and could see histology, like patterns. And that was the start of OCT as an imaging modality.

And there were technical difficulties. But I had a secret weapon. And that was Eric Swanson at MIT, Lincoln Laboratories, which made progress very rapid. For example, we did not get enough signal to noise ratio in the beginning and it was too slow to form images in a reasonable time. But Eric designed these balanced detectors that were extremely well-balanced to get rid of excess noise from the light source, as you well know. And that improved the signal to noise ratio so that it was really easy to get images. At least from in vitro samples. And later on, from live animals and clinical human images.

Another difficulty I had was initially we had this free space OCT system where matching the mode, spatial mode of the sample reflection with the reference reflection was difficult. And so that the signal you get is, it's not that reliable. We solved that by going to fiber optics. Which guaranteed that the mode from the sample reflection and the reference arm would be matched.

And I remember doing that at the Lincoln Lab to build the first fiberoptics interferometer for OCT. The first result we got, resolution was very poor. Instead of having 10 micron resolution, we got 100 micron resolution. And that kind of stymied us for about 20 minutes.

Then we figured out it was the mismatch in fiber length in dispersion. And we fixed that in like an hour or so. The progress was just very fast with Eric Swanson. Because he and I could just solve problems in minutes or hours. And he could get his technician to make things in hours. (laughs) So it was incredibly heady time with very rapid progress. That's how we, I think, even though we started later than several other groups, we were able to be the first to demonstrate OCT imaging.

Jia: Yeah. That's incredible, your electrical engineering background, how you were to boost the signal to noise ratio with Eric Swanson. How about, you mentioned there's a software that could generate 2D frame.

12:52

Huang: Mm hmm. Yeah.

Jia: Did you evolve the software development? Or you improved the software? Or that's the commercial software?

Huang: Oh, yeah. There was a commercial software to make images called SpyGlass at that time. That was many decades ago—(laughs)

Jia: Yeah. That's very fancy at that time.

Huang: Many decades ago. Like 1990. And yeah, I tweaked the color scale so that different layers of the retina would show up. And that was used for—it's still used. The extended pseudocolor imaging scale. Even though people later found that it could produce artificial boundaries in retinal layers, and it's better to show them in gray scale. So that kind of probably held up progress because I chose to show color scale - in terms of accurate interpretation. But it was actually a selling point in the beginning. Because people look at that flashy color and they think it's really fancy and new and attractive. So it helped the initial popularization of the new imaging technology.

Jia: Yeah, I agree. That's a turning point to show what the OCT looked like in the first stage.

Huang: Yeah. It increased the contrast for layers.

Jia: I want to move to your OHSU work a little bit. Because although I know you since I was a student in the Biomedical Engineering Department in Dr. Ricky Wang's group, I read all of the paper with your name in the citation. But I started to know you when you joined OHSU. You became my postdoc advisor. That was thirteen years ago. (laughs) It's quite long time ago. Could you describe why you came to OHSU? I think I am really curious to know why you moved from USC, University South California, to OHSU. Still staying on the west coast. But what's the reason, the initiative?

Huang: Well, I was at University of Southern California. About 2010, there were some upheaval in the medical school and ophthalmology department there. So that prompted me to think about moving elsewhere.

And I came to OHSU primarily because Dr. Dave Wilson recruited me. I already had a moderate-sized research group, laboratory. And he promised to build a space so that that whole group could work together with three faculty members together. Now, of course, we have six and a much larger group, including technicians and trainees. But Dr. Wilson promising the space to grow and also finding a faculty position in the School of Management for my wife then. This made it possible, make it very easy for us to come here.

And also, there were a couple of people here that I wanted to work with. One is your PhD supervisor, Dr. Ricky Wang, who was working on OCT angiography. It's an area I thought had a lot of potential. And I wanted to move into in terms of clinical translation. Another is Steve Jacques, who I actually briefly worked with him at MIT, who's well-known in laser-tissue interaction. He was very encouraging and friendly. And so they helped persuade me to move here.

And once I got here, I found that Dr. Wilson did everything he'd promised. Built a space, helped me recruit. Gave startup funds. So, it was, it's actually rare to find an academic leader who kept all their promises. And is actually more than generous and always supportive. I think he's definitely a wonderful role model as a leader.

And Ricky Wang, as you know, he moved away to University of Washington half a year after I moved here. So that was kind of a disappointment. But it was also fortuitous because it inspired me to come up with my own scheme for OCT angiography. And I was very fortunate that you were available to join our group and work on OCT angiography. And of course you made it a huge success. And now a widely used imaging modality. So I was also very fortunate to have you join a group and become the most productive young faculty that I've ever known.

19:20

Jia: That's some story I really know well. Let me go back a little bit. Because I just realized USC is not your first place you started your faculty career. Actually, you start from—

Huang: Cleveland Clinic.

Jia: Cleveland Clinic, right?

Huang: Yeah.

Jia: Tell me a little bit about your first position. Even including your residency, fellowship. Because I rarely hear about that part. After you graduated from MIT Harvard, how you start your career. And what inspired you to move to the ophthalmology, started from your residency, fellowship. I want to hear those stories back to twenty years.

Huang: Yeah. So, I worked with a number of ophthalmologists doing the initial clinical translation of OCT. People at Harvard and Tufts. And that inspired me to go into ophthalmology myself. Because I liked the surgeries in ophthalmology and I liked the applications of OCT, the potential applications. And so when I applied for ophthalmology residency, I interviewed all over the country. And I liked USC in particular. Again, because of the personal charm of the leaders, Steve Ryan and Ron Smith were running USC's Department of Ophthalmology at Doheny Eye Institute. And I really liked the fact that the residents seemed all very confident and were basically running the LA County Eye Clinic. There's a lot of camaraderie and hard work. And they were also recruiting a lot of new faculties who all seemed to be very innovative and energetic. That's why I did my residency there.

And then I did a cornea fellowship at Emory. Because I was very interested in corneal laser surgeries. Refractive surgier then was just on the upswing, was very hot then.

Jia: Why cornea and not retina? Just because you like optics?

Huang: You may not remember, but retina then was kind of a dismal subspeciality where you just watched patients go blind. That was before AMD was treatable. And when diabetic retinopathy was treated with primarily laser photo coagulation, which just killed a lot of retina. So most patients had bad outcomes.

Unlike cornea and refractive surgery, where when you do those surgeries—

Jia: you are pretty certain on the outcomes (laughs)

Huang: --you have wonderful outcomes and happy patients. Of course now there's a lot of new therapies in retina that was developed with the help of OCT that are very effective now in restoring vision or saving vision. So, that's why I liked practicing cornea, because of the great visual outcome we can achieve. But—

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Jia: So, one-year fellowship at Emory?

Huang: One-year fellowship at Emory. Then I went to Cleveland Clinic. Which at that time was run by Hilel Lewis, who was in a big expansion mode, hiring new faculty and building new buildings and being very successful. Also, a feeling of it's a time of growth. A lot of creative young faculty there. and also, I was very fortunate that Joe Izatt—

Jia: Oh, he was at the same institute

Huang: He was at Case Western Reserve University. And I knew him from MIT. Because he was a postdoctoral research fellow that took over the OCT project when I left, when I finished my PhD.

Jia: Did you have an overlap at MIT?

Huang: Yeah, we overlapped a couple of years. I think my PhD thesis borrows some of the clinical images that he really was primarily responsible for. Because I think that the last couple of years I was there, I was mainly doing clinical rotations. So Joe was—

Jia: carrying out the research?

Huang: He was building the systems for the first clinical imaging. So I knew him since MIT. And he was building a new lab at Case Western then. He was actually in the department of gastroenterology. So his main sponsor was the GI doctor who wanted endoscopic OCT systems. But he was still interested in the eye. And I think the new thing we built then with Yan Li and Maolong Tang, a couple of my students then, was anterior segment OCT to do corneal imaging and anterior chamber and angle imaging. Developed all that. So that was our accomplishment when I was at Cleveland Clinic for five years.

I think the downside of Cleveland Clinic was that I did not feel like I had the research time—

Jia: A lot of corneal stuff

Huang: --that I wanted. I didn't think I had enough support. And also, it was very difficult to work with some of the clinicians there.

Jia: So you left first. And then Joe also left.

Huang: So, yeah. Yeah. I left. And Joe then went to Duke, where he built a big group of actually now several labs. He's in charge of the biophotonics program at Duke. So he's in charge of a huge program. Of course, super accomplished. So I was very fortunate to collaborate with his group that was technically very strong in OCT. Yeah. I was really blessed to work with very talented people like Eric Swanson and Joe Izatt.

Jia: So you left and he lost the best collaborator. Then he went to Duke to build up a larger group, right?

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Huang: Mm hmm. Oh, he found wonderful collaborators there. Cindy Toth. You know, all the other guys.

Jia: Yeah. Do you still collaborate when you moved to the USC?

Huang: When I moved to USC—

Jia: You have a new collaborator.

Huang: No, I did not work with Joe that much when I moved to USC. I actually struck up a collaboration with Professor Jim Fujimoto at MIT again.

Jia: Mm, I see.

Huang: For anterior segment imaging. And for retinal imaging, I started working with a commercial company, Optovue, with Jay Wei, who was the lead engineer at Zeiss, who moved out and founded his own company.

Jia: So is that the time you started to commercialize your software, right?

Huang: Right. Yeah, yeah.

Jia: And then start your retinal project.

Huang: Uh huh.

Jia: That's in USC.

Huang: Yeah. I was probably the main advisor for Optovue clinical translation for a couple of years back in 2005-2006, that timeframe.

Jia: So the majority accomplished at USC is connecting with commercial company like Optovue and another, I think I remember you have a very big grant, AIG.

Huang: Mm hmm. Yeah.

Jia: The Advanced Imaging for Glaucoma grant.

29:08

Huang: Yeah. It was kind of strange that my first NIH grant, which I got towards the end of my Cleveland Clinic stay, was in the area of glaucoma. And it was like a big bioengineering partnership that involved four different institutions and like one or two million dollars a year in budget. And that was my first R01! Most people start small from R21 or training grants. But I started big.

Jia: Bravely start with R01

Huang: But I just started with a multi-institutional partnership. I was, again, very lucky. I started my NIH-funded grant funded research career during the Clinton years. And you know, Clinton then was doubling the budget of NIH over the period of five years. So funding was much easier back then compared to now.

Jia: So that R01 is equal to a couple of R01 today.

Huang: It's equal to three R01s today.

Jia: Three R01s.

Huang: So that's how I got started building a lab. And we had actually a much harder time getting anterior segment OCT grants. We actually have one or two smaller grants for anterior segment. But they were kind of on and off. That was harder to be continuous over a long run. But glaucoma grant I had continuing since 2003.

Jia: Oh, two decades.

Huang: So that's actually one of my most successful research program. At USC, I think the main accomplishment we had was to demonstrate glaucoma evaluation with imaging of the macular ganglion cell.

Jia: Yeah. That has been used for many years

Huang: Now it's widely used to diagnose and, probably more importantly, monitor the progression of glaucoma.

Jia: Yeah. It is quite interesting that you are corneal surgeon but your research was established from glaucoma. (laughs)

Huang: Yeah, in terms of translational research, I'm agnostic on which subspecialty of ophthalmology I work in. I'm a member of the American Glaucoma Society, the Cornea Society, the American Society of Retinal Specialists. Even the pediatric ophthalmology. I went to their meetings for several years.

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Jia: So actually your retina research is probably mainly from OHSU, right? After you joined OHSU.

Huang: Yeah. We, at USC we started working on Doppler OCT and its application to renovascular diseases like diabetic retinopathy. With a number of people that you know. Like Vas Sadda and Amani Fawzi and several other people. And I think I would have moved on to OCT angiography with those guys, anyway.

Jia: Because, yeah.

Huang: Because that's kind of the logical next step to look into ocular circulation, which I saw as being an important application. So I was thinking about all that already at USC, you know, around 2008, 2009, as a new research direction in retina. And I'm still very good friends with Vas and Amani - they're very smart people.

Jia: Yeah. I didn't know you have already started the retina research at USC. That's the first time I know that, you have already thought about the ocular circulation and bear those ideas to OHSU. And initiate--

Huang: That's why I was really interested in working with Ricky.

Jia: Yeah. Angiography. Just describe a little bit of how you continue to innovate at OHSU. Like, give us some specifics, like your involvement, for example, your involvement with the development of OCT angiography. And discuss the potential to revolutionize the diagnosis and the management of retinal vascular diseases. I think that's probably the major accomplishment, I think, you're going to tell us a little bit more about it.

Huang: Yeah. I think these research directions were really inspired by many of the smart people in OCT research. So I started getting interested in ocular circulation when I saw Zhongping Chen's Doppler results at UC Irvine. I visited him a couple of times, this must be fifteen years ago. (laughs) And I saw that he could see larger blood vessels quite well.

Jia: Mm hmm. Yeah, that's true.

Huang: And could possibly measure flow velocity. So I just took it next step in terms of translation into quantification and clinical application. So we developed a method to use that Doppler OCT to measure total retinal blood flow.

Jia: Dual circle. That's quite a smart idea.

Huang: And develop a scan pattern and processing workflow to do that with Tomy Tan.

Jia: it is very practical

36:05

Huang: And Vas Sadda. It worked. But it didn't really take off clinically. I think because blood flow rate is just a number. And so far I've seen it's detailed images that allow more finesse in diagnostic applications. But it's still a very valuable research tool. And I think I will continue to develop that. The problem was also that the accuracy is not sufficient for some clinical applications that I think we want to target. And a time resolution. And all that we're still working on.

And so another related technology is OCT angiography. And was inspired by Ricky Wang and also Ben Vakoc at Massachusetts General Hospital Wellman Lab. It was really visiting Ben Vakoc that he explained the different approaches based on amplitude and phase that I developed a mental picture and physical intuition about how the signal came about. And that's how I got the idea of splitting the spectrum and developing our brand of split-spectrum amplitude-decorrelation to measure blood flow. And it actually worked. (laughs) Surprisingly.

Jia: In the beginning I remember we were still very ambitious. We wanted a map, all the vascular velocity from the map. Then we figure out that's not really, we move to just achieve the first goal. To see the vasculature first. We just want to see the detail first. That's why we generate a new name, OCT angiography. We focus on the angiogram more rather than focus on the velocity.

Huang: Right. At first, we were trying to sum up the flow. And then we decided that it's more reliable and reproducible to just look at the vascular pattern and vascular density. And then we decided more sensitive to look at the hole instead of the donut and look for non-profusion. So our thinking evolved. But I think we were always a little bit ahead of the field in introduce these new concepts to how to translate this basic technology, the ways to detect flow signal, into patterns or parameters that you look at when you want to diagnose disease and make management decisions.

Jia: Yeah. We can always be adaptive to the evolvement of the field. And I think, for the major contribution of OCTA, you lead the field for this technology into the clinic, right?

Huang: Yes.

Jia: So I want to know, could you see the future of the OCT? What's the potential clinical relevance? And how, you know, when that could be really used in everyday practice based on the current development, andf you know, the involvement from the different research groups. And how many years do you foresee that could be the everyday tools?

Huang: Well, OCT's already an everyday tool for, definitely for retina specialists. But also comprehensive ophthalmologist, glaucoma specialists, cornea specialists. And then I'm gratified it's already used almost universally now in ophthalmology. But there's some limitations, of course. It's mostly used to image the posterior pole of the retina. So imaging of the peripheral retina, I think it's a challenge and a new area that we'll really expand its application in the retina field. And there's a vision to use OCT to evaluate neurological diseases and cardiovascular diseases. And I think that that will come to be a feasible application with more research on OCT angiography and how to use it. And OCT and how to use it in those diseases. And then that will bring it into application in primary care. Just medicine in general. So that's another frontier that I think is worth working on.

Another frontier is using OCT in real time to guide surgery or laser treatments. And I think that's on the cusp of something that, one of the research areas for our research group.

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Jia: So that's emerging OCT technology?

Huang: Yeah. And of course, novel contrast. Like optoretinography, looking at photoreceptor activation and nanoparticle contrast. And imaging of mechanical properties and elastography. You know, we are working on all that. I don't know what, how much clinical application these new contrasts will be. But I think some of them will work out to be high impact.

Jia: Potential impact, right?

Huang: Yeah.

Jia: And how do you see the integration of AI, artificial intelligence, impacting OCT technology and also ophthalmic research in the future? Because artificial intelligence already involved. And also helped OCT technology. We saw a lot at the conference.

Huang: Yeah.

Jia: Even in my team, we also start, we're probably the pioneer to start that. Did you envision some very strong potential in the future for AI engagement?

Huang: Well, I think computer technology has always been an enabler for OCT to develop. And so just since the start, it's a digital imaging technology. So without digital signal processing, we would not be able to do OCT imaging at all.

And then as you know, the speed of OCT has been doubling every two or three years since our initial development in 1991. And so the amount of data that's generated is now hundreds of megabytes, every time you scan even a small area of the eye. So without the continuing development of processing speed and memory capacity of computers, we couldn't even accommodate that amount of imaging data.

And now human interpretation of this three-dimensional volumetric gigabytes of data is another bottleneck. And I think that's where artificial intelligence comes in. Because we need to convert these three-dimensional volume information on structure, flow or modulas or any other contrast into disease features. Like two-dimensional maps of disease features. You know, like thickness of layers or whether there's blood profusion, blood flow. Or whether there's some sort of pathological growth of blood vessels or exudation. All that needs artificial intelligence to recognize and reduce to two-dimensional images that humans can easily appreciate and quantify into image-based biomarkers. Numbers that you can base diagnoses.

Jia: Yeah, that's an interesting perspective. I think, yeah, I think, you know, people always think we need automation. We need reliable automation. Then we use AI. But your perspective is we want to generate 2-D map to help people or clinician to better perceive what's going on in this map. Slowly transfer from the conventional fluorescing angiography to the current OCT.

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Huang: Yeah. There are people who do artificial intelligence who believe in a feature-agnostic AI that you just train with a large enough data set that the AI can come up with a diagnosis themselves without going through identifying human recognizable features. But I don't think of it that way (laughs) because I think it's, I think the evolution is limited by how much the clinicians, who are humans, trust the diagnosis or measurements that the AI produces. And it's very helpful to generate features and numbers that the humans can verify, can directly interpret, that would produce a trust for this to be used clinically. Because trust in something new is probably the limiting step here.

And also, limit size of these databases so that if you use imaging features as an intermediate step, you can reduce the amount of imaging data that you need to train artificial intelligence. So it's more practical.

Jia: Yeah, we do have such a project to generate those features to better interpret what's going on inside of AI. Then we can move to the direct diagnosis step. I think you lead the group already focus on this direction. We talked about the AI, kind of computational level. We talked about imaging and clinical application, etc. There is a lot going on inside of, you know, many type of expertise inside our lab. Can you speak the importance of collaboration and interdisciplinary research advancing the field of ophthalmology and medical technology development? The importance of the collaboration.

Huang: Mm hmm. Well, I think collaboration has really enabled the development of OCT at every stage. And certainly every stage of my career from collaboration between engineers. You know, my initial work with Professor Fujimoto, Eric Swanson and Joe Izatt. And then collaboration with clinicians to translate the technology. And that's really probably the major bottleneck. It's hard to find clinicians who are interested in research rather than just generating a lot of clinical income, who put in the time to understand the technology and form a relationship with the scientists or engineers. So as you know, we really treasure them and cultivate these relationships because it's important.

And academic-industry collaboration is also very important. Because they're really complementary. In academia, we can explore things that are years ahead of commercialization. So the companies really couldn't justify doing it themselves. But in industry, they have much larger teams that can produce refined products that allow easy, you know, larger clinical studies where you really develop, understand how to use it and produce the workflow of image processing tools that allow clinicians to actually use it in a large scale. So I also spend a lot of time cultivating relationships with industry, which has been really important. And you know, you spend a lot of time doing that, also.

And then collaboration between universities, also very important. Like the advance imaging and glaucoma study where I was able to get four institutions to work together to generate the necessary clinical data to validate using OCT in monitoring glaucoma progression. For example, it's very difficult to do within a single institution. To have all the clinical resources, and statistical and scientific, engineering resources. So I also spend a lot of time knowing people at other universities.

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Jia: Yeah. That's a good point. Company, they have all the expertise in one place. But with other university faculty, we have to cultivate the collaboration, right? Yeah.

Huang: Right. Yeah, yeah, yeah. We don't want barriers like they do in industry. That's another limitation of industry is that they are by necessity siloed into different companies that try not to transfer any know-how between them. Whereas in academia, we want to do the opposite. To share knowledge.

Jia: Yeah. Besides your success in the research, I want to emphasize a little bit on your leadership at OHSU. You direct Center for Ophthalmic Optics and Lasers, COOL Lab. Can you describe the mentorship you provide in the lab and what's the opportunity and the challenges for the junior faculties in the lab?

Huang: Yeah, I've been fortunate to be able to recruit now we have six faculty members in our group, the Center for Ophthalmic Optics and Lasers. And my approach is to recruit young faculty and then support them in building their research program in terms of having them be the principal investigator on grants and helping them set up collaboration with clinicians. Introduce them to commercial industry collaborations so that they can develop research program and make an impact. And I also I think set a tone in that I don't want to develop technology for its own sake. Don't want to just break some world record, the fastest imaging system or the highest resolution or—there's no need to spend a lot of effort just to generate news. I think we want to do things that make the biggest clinical impact in the long run. And there's plenty of work to do just focusing on that. So we tend to do things that's commercialized. Like if we develop this technology, we can anticipate in five years like the components will be there. It will be economical enough for a lot of clinicians to use it. So.

Jia: That's what I learned from you. Very critical point, I think I make some tools, technologies, clinically-orientatated. I think that's really attractive point, you pointed to other faculties. I'm the first one, probably you trained at OHSU. (laughs)

Huang: Yes.

Jia: I think that's also very important, the things we can attract other talent from other universities to join us. That's very important that people not just think about okay, let's get published on *Nature*, on *Science*. But we want to do something clinically useful.

Huang: Yeah. We get a lot of citations in clinical journals. And technical journals for technology that a lot of people then go on to use for clinical research. And, you know.

Jia: Yeah, in term of the publication, you have published more than 300 peer-reviewed articles. With citation, probably more than 40,000. (laughs) Nobody can reach this number. At least so far what I know. Which paper or which research project is your favorite, you think, is your top, number one, you know, this article? Besides your *Science* article. I know that generate 40,000 citations already. Beside that. I just want to say the recent, which publication is your—

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Huang: Well, I think the *Science* paper of course is my number one paper. That was kind of very fortuitous in that that was actually my second publication ever. And I just knew that *Science* is the top journal and it's very difficult to get in. But I have something brand new that's a new imaging modality. So that was a huge coup. And sort of gave me confidence to submit papers to prestigious journals and work on something very new.

And then I think the notable papers after that include a paper with Michael Hee to introduce polarization-sensitive OCT. I'm proud of that in that it's just, the concept just kind of came out of nowhere. (laughs) And that it actually worked.

Jia: But you didn't continue doing PS-OCT.

Huang: But I did not, yeah, because I couldn't figure out how to make it really clinically useful. A lot of people are working on it. It's actually a very difficult technical challenge. And a lot of people like that. But I couldn't see it being widely used because it's difficult and expensive. But I liked it anyway because it's kind of a brainchild. And I'm proud of just coming up with it.

Jia: But the many other research group are still doing it, right?

Huang: Right.

Jia: Like Yasuno's Japanese group. And a couple of other groups from Vancouver and yeah, Vienna group, they're still working on PS-OCT

Huang: And then I think with my initial work with Joe Izatt, I think what came out of it was corneal imaging and imaging of the angle for angle closure glaucoma assessment. For angle assessment, I'm also very proud of writing the initial paper on it. Although we haven't worked on it for a long time because it's not a common disease here. But it's taken off in Asian countries. So I'm happy to see that. And we did go on to work on corneal mapping. And we're still, initial papers on mapping corneal thickness and epithelial thickness, I think has made an impact. And it hasn't grown as quickly as retinal imaging or OCT angiography. But I think eventually it would replace the Scheimpflug camera-based technologies or Placido ring technologies for corneal imaging.

Jia: Has it already been commonly used?

Huang: It is commonly used. But not as commonly as Scheimpflug technology, which is dominant now. I think the past twenty years has kind of, where Placido technology is phasing out and Scheimpflug technology is coming in. And then I think the next twenty years—

Jia: Will be OCT.

Huang: OCT will take over for corneal imaging. So, things take a long time. Fortunately, you know, I started young. (laughs) So I can see all these evolving over decades.

Jia: Yeah. Glad that you have Yan still continue the project.

Huang: Yeah, that's right. And then it, USC years, looking at macular ganglion cells, it's probably the biggest accomplishment. And that's with Tomy Tan. And initially we had a lot of resistance. The first paper we tried to publish, people think, they said it was not important, has no use. It was rejected from *Ophthalmology*. I had to appeal to the editor-in-chief. And now it's one of the most cited papers in *Ophthalmology*.

Jia: For diagnosing glaucoma, that's a very significant one.

Huang: It's very common when you try to write about a new approach. The first paper, people say either how can you be sure you're seeing ganglion cells? How do you validate it if this is a first paper? So you cannot prove this is what you're seeing. So they wouldn't allow it to see the light of day. Or they say, "Oh, it's not useful. We can already measure other things. So why do you need this new thing?" And almost invariably, ten years later, these first of a kind papers are highly cited and have huge impact. But reviewers from journals to grants find it hard to really accept innovation for some reason. And they're probably one of the bigger impediments. But I'm proud of being able to get that paper published and have that kind of widely used, and having several other groups having that as their research emphasis.

Jia: Yeah. That paper actually proved the concept. We don't have to see the single ganglion cells.

Huang: Right. Yeah. We don't have single ganglion cells. We see the complex. Yeah.

Jia: Exactly.

1:05:25

Huang: And a lot of people still don't believe it. They like to see single cells, even though that would be extraordinarily expensive. So we're developing optoretinography. Siyu is working on that. You're working on that. And again, I think people will object that our approach, even though it's much simpler, don't see single cells. And they don't believe it. But eventually, because it's cheaper, more reliable and simpler, it will be widely used. And it would be high impact.

Jia: You always do that.

Huang: The same thing happens every time. You try an effective approach that eventually would have high impact. And people don't believe it because they don't see something directly.

Jia: So my paper not on the top five? (laughs) You already discussed four or five papers. How about our split-spectrum amplitude-decorrelation angiography paper?

Huang: Oh, of course.

Jia: It's on your top five?

Huang: Yeah, that's, yeah, other than the *Science* paper, that's probably my most cited paper.

Jia: Number two? Oh,

Huang: Your most cited paper. Yeah. Yeah, that was pretty amazing. One, that it worked. And two that it got commercialized and it beat out other competition as the first commercialized approach for OCT angiography. And it's approach that, the split-spectrum approach could be extended to other OCT contrasts.

And then, you know, along the OCT angiography line, you and I made several other kind of landmark papers, right? I think kind of—

Jia: PNAS?

Huang: --delineating the limitations in measuring flow is one. That's not cited as much, but I think it's really fundamental to our understanding. And then our paper in the *Proceedings of National Academy of Science*, which is, I think, your initiative to write it. And it's very widely cited and started a lot of concepts in applying it to retinal diseases. And then the projection resolved OCT angiography and the delineation of retinal vascular anatomy, the different plexuses based on that. We had a series of papers. Also very widely cited. And that's still playing out. People still think that retina has two plexuses. I think half of the publications still just have that, whereas, but I think because of our review papers and the book we wrote, our definition of retinal circulation with four plexuses and separate measurements, that's beginning to take hold. There are some papers that use our new system. And again, it's going to take probably a decade for that to play out. It's actually pretty amazing that science doesn't move faster. But it takes a long time for things to disseminate, both scientifically and clinically.

Jia: This paper, I think has been widely used. Not just the research group, right? Also, widely adopted by OCTA companies. This time we went to a New Orleans ARVO conference, I saw the use those slab definitions. Most companies adopted the definition of OCT angiogram.

Huang: Yeah.

Jia: And most of them have already used the projection-resolved method. Whether they see our paper or copy our technology. I'm very glad that it has been commercially adopted.

Huang: Yeah. People copy us without paying us royalties.

Jia: I know. (laughs)

Huang: Which actually is not that important. I think it's important that people are adapting our approach and definitions, whether they're in China or Japan or Europe. You know, they are adopting our standards. And that's a big compliment to us.

Jia: Just the feel of this adoption process is super slow. We published this paper kind of ten years ago, right? They just started to realize it okay, I need to follow—

Huang: Just eight years. It was 2015, right?

1:10:51

Jia: Oh, yeah. Eight years. Almost a decade. I just, we think we have to be patient. If we think something useful, we have to be patient.

Huang: Yeah. It's actually right on time. It takes about ten years.

Jia: Yeah. Initially we feel oh, we really feel alone. We talk about this. We try to set our standards and criteria. But people discuss different things, you know. They came out a lot of FAZ, different sides of FAZ. They didn't listen But times proved our concept, our criterias have been used.

Huang: Yeah. I think you're going to be very successful. You'll see even more citations of these kind of first of a kind papers you've written.

Jia: Yeah. SSADA is my favorite, number one.

Huang: It was great that you published them so quickly. (Jia laughs) To define all the approach and terminology.

Jia: Yeah. We have to move efficiently. Anyway, as like a, you direct COOL Lab. That's a thirty-person lab. But you also serve as a director of research at Casey Eye Institute. I think you must stay up to date with the latest research and the technological advances in your field, right? How do you do, and what resources do you recommend for others to do the same? Because you know, as a director of research, you have to know all the latest advances in your field in the ophthalmology and research. What do you do to keep everything up to date? That's how you direct the research faculty team in the entire department. I feel that's a very challenging job.

1:13:01

Huang: Yeah. Based on my own experience, what I try to bring is synergy between clinicians, basic scientists and the clinician scientists. I think the most productive advances are in the intersection between new science or new technology and changing clinical practice. So that's what we try to do in recruitment is we try to have a balance of clinician scientist and productive clinicians who are interested in clinical research, and basic scientists in the areas that are really rapidly progressing. Not just in our area of imaging, but in fields like artificial intelligence, informatics and genetics. I think it's because I took on this research director position that now I even go to the gene therapy summit.

Jia: Right. (laughs) The conference.

Huang: Because I have to understand things outside of my small personal research area. So that I could not really understand the science, but at least understand which areas are making advances and who are the key players and how Casey Eye Institute can make contribution. And really continue our dominance, for example, in genetics, gene therapy clinical trials. And upcoming areas. Like stem cell research. I think we've been very successful in recruiting new members to the faculty and continuing to support our existing faculties. And I try to have these research retreats, you know, for everyone to meet so people know—

Jia: That's really a great idea.

Huang: So people know what each other are doing, so we don't miss collaborative opportunities. Which is sometime a limiting factor.

Jia: I think that is a really effective event for us to know each other and improve our collaboration between each other. I think that's something new compared to multiple years ago, you know. We barely knew BRB [Biomedical Research Building] basic research [people and] what they do, right?

Huang: Yeah.

Jia: But now we frequently interact with each other.

Huang: Right. The fact that Casey Eye Institute, even on campus, is split into three different buildings. And Covid19. All these are impediments for people to get to know each other and collaborate. So we try to, I think try to break the barriers is important.

Jia: Yeah. Your retreat idea is really, you know, got very good feedback from all those faculties. Really brilliant the idea. And also anyway, you also brought a lot of research results to support the research team, you know Give us some flexibility to use some capital equipment resource and some resources for the publication. I think that that's really generated the positive feedback. I think you took off your leadership in that department. Really good start. And besides research and your leadership, you also a successful entrepreneur. At least in my point of view. And you are the founder of GoCheck, maker of the smartphone app that provides early vision screening for children, right? And could you describe your experience as an entrepreneur? And what inspired you to pursue this project? And there are definitely some challenges and rewards in this venture. So I want to hear a little bit about that. Because we frequently discuss the research project at that time. I never heard you talk about your business.

1:18:09

Huang: I think that it stemmed from a desire to make an impact in eye diseases. It was really inspired by Dr. Linn Murphree who worked on retinoblastoma. When he came to give a guest lecture, he talked about how often retinoblastoma is missed in young children, and often discovered by chance smartphone photographs. And that's really where I got that idea initially.

And you know, mobile phone with cameras and interactive screens, it's a new technology that developed in the past twenty years. And Hiroshi Ishikawa and I often talked about how to capitalize on this technology to make a bigger impact. And this was the most concrete ideas that we thought could be easily realized. And it's a unique niche, because other people are not doing it. So that's why I started the company with Hiroshi and other cofounders.

And we were able, we entered this particular area of preschool vision screening or photo screening for refractive errors and emperipolesis factors because there's reimbursement for it. And that has allowed us to raise venture capital. So it's now a five-million-dollar-a-year company. And we've screened more than five million preschool children. And it's still growing. The reimbursement for this is not high, though. So we're still struggling to make profit. But it's making a big impact, which is all that matters for me.

Jia: Preschoolers, they don't need to pay, right? It's just the reimbursement. So you hold the patent?

Huang: OHSU has the patent based on our initial invention disclosure. And OHSU is a partner in this company.

Jia: But you told me you got the idea from a guest lecturer, right?

Huang: Uh huh. Yeah.

Jia: Isn't smartphone photography already being used?

Huang: No. People were using dedicated cameras and devices. But we came up with a way to use the smartphone for it. Which make it more economical and actually more reliable. Because smartphone technology is pretty robust.

Jia: Isn't Hiroshi also a cofounder in this?

Huang: Yeah. Hiroshi is also a cofounder. And I hope to do other things with Hiroshi as well.

Jia: Yeah, he quite smart. Yeah, I think you also have your, you continue to commercialization idea. Recently you founded another small company?

Huang: Right. Yeah. So, I have another startup with Steve Pflugfelder at Baylor Medical College in Texas, and Scott Prahl who's in Oregon Institute of Technology, to develop laser thermal conjunctivoplasty. Which is an under-appreciated condition that most older people have. That's kind of loose folds of conjunctiva on the surface of the eye that cause irritation and dry eye symptoms. We have a device that's going to make treatment of that very simply so that it can be treated more easily in the office, and probably relieve a lot of dry eye symptoms.

Jia: What's the stage of this startup?

Huang: It's preclinical prototyping. And we have good results in animal eyes ex vivo and also in the live animal eyes.

Jia: So you already got some capital, venture capital?

Huang: No. We are going to get as much work done as possible with nondilutive funding first, before we raise venture money. This is what I learned from my last round. That once you raise capital, venture capital, you are on the clock for rapid clinical translation. And it becomes more difficult to refine your technology the way you want to.

1:23:39

Jia: I see.

Huang: So we want to iterate the technology to a form that we like before we raise money to push it into clinical practice.

Jia: So once you on the VC collection phase, you want to move so fast on the market, right?

Huang: Right.

Jia: You have very little chance to revise or to change anything.

Huang: It's exciting but actually not that much fun. At that stage you want to really, I would want to hand it off to other people.

Jia: So do you think this would be as successful as your last round? As “GoCheck”

Huang: Well, of course, I don't know. I hope it will be more successful in that it’s a therapeutic device. It’s probably easier to generate revenue than a diagnostic device.

Jia: Nice. That’s a different way. The first round is for diagnosis. This one’s therapeutic.

Huang: Yeah. That’s why I’m also thinking the idea of the image-guided therapeutics as a potential commercialization.

Jia: Yeah, your first one is completely independent from your lab research.

Huang: Mm hmm.

Jia: The second one, a little bit associated? Or fully independent? The second, you know, the second technology is associated with your lab research a little bit?

Huang: It’s not in the COOL Lab right now. Although I think in the next stage of the device development, I might bring it in our lab at some point.

Jia: I see. Okay.

1:25:39

Huang: We also have to manage conflict of interest, of course, in that that gets things, gets complicated.

Jia: That’s true. Okay. I also impressed by your leadership in our International Ocular Circulation Society (IOCS). You were the founding president. And can you tell us a little bit about this society and its mission? And what inspired you to take on this leadership? And another question is, how has the society contributed to our understanding of the ocular circulation and its relevance to the clinical practice?

Huang: I was really inspired by an Association for Ocular Circulation meeting that I went to.

Jia: Oh, AOC. Yeah.

Huang: AOC. This was more than a decade ago. When I was still mainly working on Doppler OCT before I came to OHSU. And I was particularly inspired by all the talk on systemic [applications], how ocular circulation can be a window into systemic diseases. And also by a lot of basic physiology of the ocular circulation that people talk about. And so I created this new society because that old society was kind of, not very active. And I thought it would be important to tie our new technologies, such as OCT angiography and Doppler OCT to applications in basic research to get to know people who really study the basic science of ocular circulation for decades, so that we borrow from their knowledge and so that what we do have a sound scientific basis. And also to bring in clinicians so that we can make a clinical impact.

Jia: Yeah. Stimulate some new ideas.

Huang: Although there are a lot of retina conferences and imaging conferences, there's really no other society that's focused on ocular circulation. And because we want to make imaging of ocular circulation a major focus in our lab, I invested a lot of time to found this society, or cofound it with you and Hao and all the other trustees to stimulate this exchange. We're kind of in the middle, actually. We're the technologists. And on the one hand, there's the basic scientists who teach us about what we're seeing in terms of the retina plexus, for example. And on the other hand, the clinicians can tell us how to use our technology.

Jia: Yeah. I think your vision has broadened with the time. Before that, do you remember we had OCT angiography summit, right? At OHSU campus. Probably twice.

Huang: Yeah. Right.

Jia: We focused on how to translate OCTA in the clinic. And your vision has broadened by oh, why not bring in the basic researchers. Then we can learn each other. Yeah.

Huang: Right. Yeah. That OCT Angiography Summit was really—

Jia: That was successful, too. Yeah.

Huang: --trying to educate the clinicians about this new technology. And I think it was regional. So I found it easier to do that clinician outreach at the American Academy of Ophthalmology meeting. To develop a course on OCT angiography.

1:30:22

Jia: Mm hmm. Still continue it.

Huang: Yeah. So we're still continuing to do that.

Jia: Simple version.

Huang: Yeah. It's at a stage now where I think that can be handed off to mainly clinicians who are already actively using OCT angiography at this stage.

Jia: Yeah. But a couple of years ago, it's very important to have the OCTA Summit, right? There is a lot of interest in going along. People want to learn OCTA. So we kind of serve as a hub of the OCTA.

Huang: Yeah. That's to attract the—

Jia: Attract international—

Huang: --the first adopters. The initial group of clinicians who are willing to learn of this strange new technology.

Jia: You always adapted to what's going on right now and what we should do next. I think we can dive into the last section. I want you to talk about, you recently have been elected to the National Academy of Engineers. Congratulations. It's the highest professional distinction for engineers. And before that, you also received the -

Huang: Champalimaud.

Jia: Champalimaud Award. That's the largest prize, right, for ophthalmic research. And numerous achievement awards. We want to know what the recognition means to you, and how you consider this recognition in those societies passed to you? What did you feel about those recognition in the recent few years? There are a lot of awards that you received.

1:32:29

Huang: They're wonderful confirmations, of course, that I have accomplished something that made an impact and that the basic approach is bearing fruit. And I think these recognitions or awards were based on the impact that OCT has had in ophthalmology and a few other medical fields. So the approach I've taken of working on areas, clinical areas and technologies that could have clinical impact, a lot of people would use, that would be useful in major blinding diseases, that has paid off. And so it certainly helps to continue to motivate me to work hard on these areas. You know, it's hard to get positive feedback. When we apply for grants and write papers, the reviewers are sometimes very discouraging in what they don't understand sort of don't think is significant. But people citing our work or using our technology or copying us or these awards, those are kind of the main positive feedback or rewards for working.

Jia: Yeah. Yeah. Also these awards did not come suddenly, right? They recognize you, I think for the National Academy of Engineers, they recognized you a few years ago. You received Russ Prize?

Huang: Right. That's a prize from the National Academy of Engineering.

Jia: Yeah. You were adopted as a senior member, then as a fellow. I think gradually people recognize the impact of OCT. Then those awards. Not just highlight yourself, also highlight the OCT impacting the whole field of, it's good news for all the imaging researchers. And at the end, can you share some tips or advice for young researchers or clinicians interested in the ophthalmic imaging or they want to make impact on all the medical technology, they want to make impact some of young clinicians, they still maybe struggling in the lab. The young researchers. They have those ambitious ideas they want to achieve. They consider you as a role model. That's probably the moment you want to give some tips or advice to them.

Huang: Well, my advice include having an inquisitive mind and seeking out collaborators or mentors, or just talking to smart people in adjacent areas so you can more broadly recognize opportunities for new research areas and intersections between technology and clinical practice where impact can be made.

Another thing that's important is to be collegial and share credit and really build relationships with collaborators. Especially people who are complementary, who are creative, who are trustworthy. These partners are very difficult to find. So when you find them, you have to treasure them. And often I have had projects where the idea was there for many years, but can't get done until I meet enough people who can advise me and help me form a team to really get things off the ground. So I think finding your partner is probably something that is worth devoting a lot of time.

Jia: Always evaluate whether this is the right timing, right?

Huang: Right.

Jia: For certain projects,I think you did very well on this. I always appreciate that you always can find a good timing for the right project,you know who you want to collaborate, and if this is the right time to do the right thing.

Huang: Yeah. Often, it's hard to put everything together. Either you don't have the right people or the technology is not ready yet.

Jia: Exactly. Yeah. Yeah.

Huang: It could be too early. Or you don't have the funding. But you have to kind of just be patient and put all those things together. And sometimes things just come up fortuitously. For example, the reason OCT got used so commonly in ophthalmology was the development of anti-vascular endothelial growth factor therapy for wet AMD. And I could not have anticipated that would occur and that OCT would be very important in providing the endpoint for that treatment, which anti-VEGF therapy to be developed and used. So those two became like the biggest developments in ophthalmology in the last couple of decades synergistically. And I certainly could not have predicted that. And so opportunity come up, you have to grab it.

Jia: All right. Well I think it has been an absolute pleasure speaking with you today. Your contribution to OCT and your leadership in our understanding the ocular circulation is really remarkable. I also really appreciate you, my first postdoc mentor. You know, you guide my entire career. And many faculty members like me, we are so lucky to have you be our mentor and career sponsor. And OHSU, such lucky to have you to continue your innovation. And, well, I also want to thank OHSU Oral History Program for giving this opportunity to interview, you know, have this chance to interview. Dr. David Huang. Thank you very much.

Huang: Well, thank you, Yali, for being a great partner and for this conversation.

1:40:36
[End Interview.]