Evolution of Computerized ECG Interpretation

Announcer: Welcome to Mayo Clinic's ECG Segment: Making Waves, continuing medical education podcast. Join us every other week for a lively discussion on the latest and greatest in the field of electrocardiography. We'll discuss some of the exciting and innovative work happening at Mayo Clinic and beyond with the most brilliant minds in the space and provide valuable insights that can be directly applied to your practice.

Dr. Kashou: Welcome to Mayo Clinic's ECG Segment: Making Waves. We are so glad you could join us today. Today we have an incredible episode planned for you with a guest that I've been looking forward to speaking with for a while now. We will look at one of the leading computerized ECG interpretation programs that has shaped the ECG criteria used in clinical practice today. We'll be joined by a special guest, the pioneer and the leader himself, to glean some insight into the program's evolution and what the future looks like in the field of computerized electrocardiology. I'm very excited for this discussion so let's waste no more time and get started. The ECG is critical in making timely medical decisions that can save lives. The use of computerized ECG interpretation software was developed to support clinical decision-making and workflow. Early investigative works for the methods to analyze ECGs with automated techniques were started at the University of Glasgow. They began in the 1960s and since that initial decision to develop an ECG analysis program in the late 1970s, and with its refinement over the years, the University of Glasgow ECG interpretation software has represented one of the world's premier resting ECG analysis programs. Apart from accurate rhythm and interpretive analysis in both adult and pediatric patients, it has demonstrated a particular advantage in recognizing ST elevation myocardial infarction, or STEMI. In fact, the algorithm STEMI rule-based criteria based on age, gender and lead variation helped improve the STEMI ECG criteria guidelines used in medical practice. While computerized ECG interpretation takes its share of jabs for its imperfections, its clinical value is undisputed and its importance has only grown in an age of fading ECG literacy amongst medical providers. How did the University of Glasgow's computerized ECG analysis program come about? What did the commercial development and refinement processes look like? What does the future of computerized electrocardiology look like? Well, that brings us to our focus today, the evolution of the University of Glasgow's computerized ECG interpretation program. And there's perhaps no better person to discuss this topic with us than the lead developer himself, Professor Peter Macfarlane. Professor Macfarlane is Emeritus Professor and Honorary Senior Research Fellow at the University of Glasgow. He was Professor in Medical Cardiology from 1991 to 1995 and Professor of electrocardiology from 1995 until 2010. His basic training was in math and natural philosophy and he obtained a Doctor of Science degree in 2000 for a compilation of publications on computerized assisted reporting of electrocardiograms. The work of his team has been adopted commercially and the University of Glasgow ECG interpretation program developed in his laboratory is currently used worldwide. He has a particular interest in the differences in ECG appearances due to age, gender and ethnicity. And as a result, he has influenced international guidelines for the ECG definition of acute myocardial infarction. Professor Macfarlane has also established a central ECG laboratory for handling ECGs recorded national and internationally for clinical trials as well as for epidemiologic studies, including the landmark, West of Scotland Coronary Prevention Study. He has published over 400 scientific papers and 14 books, some of which are conference proceedings. He was also jointly awarded the 1998 Rijlant International

Prize of Electrocardiology by the Belgian Royal Academy of Medicine. And in January 2014, he was awarded the Commander of the Order of the British Empire, or CBE, for his services to healthcare. Professor Macfarlane, what a true honor to have you. Thank you so much for joining us today.

Dr. Macfarlane: Well, thank you very much for your very kind introduction. I'm delighted to be able to join you to what I have been over these past few years.

Dr. Kashou: Yeah, I know. I mean, the intro is easy to write, you know. To be honest, looking at all what you've done, it's been incredible and this is something I've been truly looking forward to. And so, there's so much that we can discuss, but we'll kind of narrow it in and we're gonna probably start from the beginning. Can you take us back to the beginning of the ECG analysis and maybe tell us how it all began in Glasgow?

Dr. Macfarlane: Well, if I'm truly honest, I have to take you back to 1964 when there was an interest in the royal infirmary at Glasgow in looking at automated interpretation of ECGs. Dr. Veitch Lawrie at the time had noticed what was happening in the US and Washington and he put out some soundings to see if anyone would be interested in this project and that's where I came onto the scene. So, mid-summer 1964, I really started off on some PhD work to look at the topic of automated ECG interpretation. Unfortunately, Dr. Lawrie hadn't been able to provide anything in the way of the equipment in those days so I started with a pencil and a paper. That meant that for a couple of years, I had to extensively in electrocardiography, mathematical modeling of the ECG, get engaged in the practical aspects of ECG recording just so that I was fully aware of what it was about. Did that for a while. And then eventually, Dr. Lawrie sent me on a study tour. I went to Washington to see Dr. Pipberger, Dr. Caceres, and believe it or not, I visited the Mayo Clinic in the spring of 1965, but I don't think I saw you around at that point. I may have missed you. But anyway, shortly afterwards, we were able to obtain some funding from the British Heart Foundation and Northfield Provincial Hospital's Trust that enabled us. And we were fortunate that at that time, Digital Equipment Company in Maynard, Massachusettes, had developed a smaller laboratory computer called a PDP-8. We were able to buy a PDP-8 and ECG recording equipment. And that got us started. It did allow us to record the ECG, transfer it to the PDP-8 in analog form, and then there was a process of changing the electrical signal to digital form. That data was written to a small magnetic tape called the deck tape. Unfortunately, the University of Glasgow computer could not read a deck tape. So, what happened was these deck tapes were sent down to Rolls-Royce in Bristol where they were building the Concord and they had equipment that allowed one tape transferred to a much larger tape, which then came back to Glasgow and we could use that in the larger university computers, which were few miles away from the hospital. But that was enough to allow us to record ECGs, transform them to digital form, take them to the university, develop some software, and that allowed us to analyze the ECGs, complete with interpretation. At the time, we looked at two forms of ECG, one was using three leads, the other was using 12 leads. And we showed that there was a very marginal improvement using the 3-lead ECG. And that was basically the start that we made and was really the conclusion of my PhD thesis.

Dr. Kashou: And so that all began, you were saying in 1964. What was your, I guess, experience up until that point? You know, it seems like you went pen to paper to start it. Did you already

have some background or was this something of interest to you that you wanted to take on? And who else was in that space at the time? Was there much others?

Dr. Macfarlane: Dr. Caceres was looking at the 12-lead ECG in Washington, and also in Washington, Hubert Pipberger in the VA hospital was looking at the 3-lead approach. Three leads recorded simultaneously, known as the orthogonal leads. So these were the other folks. There were a few groups in Europe thinking of doing this, particularly one in Rotterdam. They were looking at ECG analysis in around about 1967, if I remember correctly. But there weren't very many people at that time engaged in this. Having said that, I know that Dr. Smith in the Mayo Clinic was very interested. He was working with IBM at the time to develop software for ECG interpretation.

Dr. Kashou: Interesting. So, you know, there weren't many people out there doing much things similar. I guess one of the things we think about is the computer, we get this interpretation it provides, or we get the recording, get an interpretation, and these labels that come out out, and there's multiple, probably at least close to a hundred, if not more of those labels. For instance, sinus rhythm. How do you, let's just take that label for instance, how do you make maybe the criteria for it to recognize sinus rhythm? What are some of the key features that you have to think about as you program this?

Dr. Macfarlane: Well, first of all, we obviously have to detect every heartbeat, every QRS complex. Then we have to look and see if all of these heartbeats have the same morphology, same share. Having done that, we're looking next at the regularity of the heartbeats and so on. For sinus rhythm, we would also be looking for a P-wave before the QRS complex. But that would be done by what we call wave typing. We would collect all those heartbeats of the same morphology and then within that average beat, we would then be looking for a single wave prior to the QRS complex. Of course, in the rhythm interpretation as a whole. We may be looking for more than P-wave, et cetera, et cetera.

Dr. Kashou: Amazing.

Dr. Macfarlane: Maybe I'm getting too detailed.

Dr. Kashou: Very complicated. Because you're asking a machine to detect all these, the physiology of the underlying cardiac bio signal. I guess the next step, you know, as it evolved and you had this program, it then got commercially developed. What does that process look like? How does it start and proceed? Did it start with a full comprehensive interpretation software or did it? How did that look?

Dr. Macfarlane: Well, I left off really, 1970, we had each interpretation based on the university computer. We got the data from the hospital, took it to university and analyzed it. So the other part of the 70s, we had to bring that inside the hospital. Got it all running on a PDP-8, and therefore we think we had the world's first hospital-based mini computer system running a routine ECG interpretation service. That ran right through until the end of the 70s. And that point, our source of funding held a meeting, an international meeting, which it was stated that for any further developments, you must use 12-lead ECG. So that set us off purely on the 12-lead

ECG analysis. Now, by complete chance, I knew we were opening an extension to the Royal Infirmary and we were looking for a supply for cath lab. And a representative from Siemens Zilina came from Stockholm and visited the hospital to talk about the Siemens offering in terms of cath labs. And he saw what we were doing about ECG interpretation. And immediately he said, "We want that software." And that's pure serendipity, but that's how it happened. At that time, the university did not have anybody who knew anything about commercial developments, believe it or not, but we're going back to 1980. And so we had some consultancy help to the university, went to Stockholm, agreed a contract with Siemens Zilina. And that was the start of the commercial development. Took off from there. By mid 1980s, Siemens had a product. They called it the Medgo REC. We didn't like REC. It was spelled R-E-C, but we thought it might be misinterpreted as W-R-E-C-K. But nevertheless, we had to accept the name of Medgo REC. We obtained many of these machines and we used them within the hospital to have a more routine 12-lead ECG reputation service. Siemens then bought Burdick in Milton and Wisconsin. They transferred to Deerfield in Wisconsin. But our software then made its way into the Burdick range of products. The name was used very widely in North America, particularly in family practice. Then there was a management buyout at Burdick. It's a long story, but a management buyout And they'd gotten to other the with space labs and so on. And a lot of all of these space labs renegotiated agreements. And they said, "We don't want the solo right to the software." And that then was agreed and it free us up to license the software to any other company that wanted to use it. And I think very quickly on the scene, we worked with Physio-Control, now Stryker in Seattle, who had a long association with that company. And so, for many years we've been working with the industry, different countries all around the world.

Dr. Kashou: It is really amazing. You call it serendipity, but you know, the process and the work you'd had been doing all around and it's that golden moment, you know, it's not waiting around, but you were kind of spearheading it and so it's amazing how all the stars align. As you started to commercial this and get this out, were any studies or trials that you tried to use to maybe validate some of the work or?

Dr. Macfarlane: Yeah. Yes, that's a good question. One of the clinical trials which you did actually mention in your introduction was the West of Scotland Coronary Prevention Study. I thought that was a great study. Never been replicated since in our part of the world. Sorry, I should say. We had ECG machines that have been built by Mortara for Siemens. And we used these machines in various health centers around the west of Scotland for five years. The study had recruited 6,595 men, hypercholesterolemia, 45 to 75, and ultimately showed that there was 31% relative reduction in a non fatal and fatal myocardial infarction for those who took statin versus the placebo group. But one of the things about that study was the relationship between the participants in the trial and those running the trial. We used to have meetings in community centers around the west to Scotland and encourage the wives of the participants to come along and somebody would present the best diet that they could possibly have to reduce the cholesterol levels and so on and so forth. And it was just one of the situations where everybody was involved; the participants and the trialist the study directors themselves. It was excellent. And at the end of it all, the results were with American Heart in Los Angeles in 1995. And after that, some of us were very lucky to be traveling here, there and everywhere. And moments was just to give a chat about the benefits of statin. So, I always remember was, of course, it has been a great trial from that point of view. The other study that I can think of was so-called CSE study. I had

done a short tour of Europe, sponsored by European Union in 1974, looking at those who were working in the area at that time and suggested there should be some variation. So European Union in 1976 funded this CSE, common standards for quantitative electrocardiology. And about 40 people got involved from various centers in Europe and North America. And for 15 years, everybody worked together. It was a steering committee of which I was lucky enough to be a member. And we met almost quarterly for 15 years. Major developments out of that were twofold. One was a publication on the standards for which measurements or ECG analysis. And the second complication related to a database that was established, where patients were classified from the basis of the clinical information. And that has been used as a yardstick ever since 1991 for software evaluation. We still, when we're submitting data to the FDA, for example, we use these 1,220 ECGs to evaluate the software. So these two studies stand out to me quite significantly.

Dr. Kashou: Yeah, and I think some of the best studies that have been put together, you don't really see many of them like that today. You know, another specific interest just from looking at your work was the influence of age, sex, race and ethnicity on the ECG, I guess. What prompted your initial and now continued interest with those set of factors?

Dr. Macfarlane: Well, during the 1980s, we recorded ECGs from an apparently healthy group of individuals living in and around Glasgow, around 1500 individuals. And from some of the very basic findings or statistics, we saw very clearly that there were differences between males and females. For example, if I talked to you or any cardiologist what their criteria were for left ventricular hypertrophy or the nonclinical folks enlargement of the heart you would probably say Sokolow, often Lyon. Most physicians would. And they'll say, "Yes, this measurement and that measurement, "add them together and they're greater than a threshold." But that's not with any relation to age. It's not with any relation to sex. And when you look at the normal limits for males and females, young men have a very significantly higher upper limit of normal voltage than young ladies. And young men have higher voltage than old guys like me. So you have to tailor your criteria to fit the age and gender of the patient whose ECG is examined. So that very basic study of one simple measurement certainly got me interested in looking at age and sex. The next thing of significance in this respect was really a public in 2000 by European Society of Cardiology and American College of Cardiology. And they put forward criteria for STEMI that we mentioned earlier, from of heart attack as the way it shows up in the ECG. And again, there was nothing about age or gender there. They grouped three leads together, I have to say V1, V2 and V3. They grouped them together and every other lead was then separate. So they had criteria for the three and the criteria for the nine leads. In other words, two thresholds. One for the three leads, one for these remaining nine leads. Again, two problems with that. V1, V2 and V3 do not have the same upper limits of normal. V1 is very different from V2 and V3. And then age, again, ST thresholds. But that part of the segment of the ECG has a higher limit of quality in males than in females. So that led us to change these criteria. We did a lot of work with nice big database at that time that allowed us to do that. So the need of there about. The next set of guidelines that come in, I'd taken V1 away from V2 and V3. And that was the beginning, and we also separated male and female and moved on a little bit to later on when we brought age-related criteria into it just to handle a little bit to it. So that was the way that we helped these criteria to evolve. I think you also mentioned race there. And again, interest there rose from the fact that we had a young physician from Taiwan, from Taipei, who came to work in the department in the early 1980s.

And we became a good friends and I ultimately went to Taiwan a couple of times. But we thought it'd be good to compare these from Taiwan, look at the Chinese ECG versus the Western Caucasian ECG. And we managed to ship. One of these Mengo RECs survived. It wasn't a wreck. It survived the journey to Taipei. And recorded 500 ECGs in the Veterans General Hospital in Taipei. And from that, we were able to show differences in the thresholds of upper limits of normal, et cetera, in Chinese versus Caucasians. For example, Chinese actually have slightly higher ST thresholds than white Caucasians do. The next development there was that I had a cardiologist from Nigeria wishing to come to Glasgow to study for a higher degree. So provided his work and he obtained over a thousand ECGs from blacks in Nigeria. And again, we showed differences between the black population and the white population. I've also been very lucky to visit India many times, arising from a specific conference. And we set up a study there in three centers. But we didn't show any difference between these South Asian ECGs and the white Caucasians. So, it's different reasons, different ways, that we've been looking at age, race and sex and the ECG. And I maybe missed out, one thing was that we actually recorded 1,750 ECGs on neonates, infants and children. You're welcome to fall asleep, anybody, if you're still

Dr. Kashou: No. You know, I think this is amazing. Because you don't like to, at least from our conversation, take credit for a lot of the criteria, but it's clear that your work has had significant influence and maybe you weren't the one riding it but it's influence, you know, our colleagues that have helped to devise some of the criteria we use today. The age sex and race are important because that's how we're able to generalize the criteria across all patients. And I think that was such an important kind of leap forward for the ECG not thinking in Glasgow and our surrounding area, but how do we make this in India, Asia and all across, blacks, whites, and it's incredible. Now, before we end, from someone that's taken this work from the very beginning and seen it through, what does the future of the Glasgow technique look like? And even the field of computerized electrocardiology, where are we going?

Dr. Macfarlane: Well, I think I should speak in general terms in case anybody thinks what I see is a specific plan with commercial implications for what might happen in Glassgow. So, I'm speaking as an individual, shall we say, and not on behalf of any company or anything like. We have no fantastic immediate plans if I'm honest. Two ways of looking at it. One side of this got to be the software development and the other side's got to be the hardware development. On the software's side, and it's an area, of course, that you're very interested in, is the artificial intelligence in ECG interpretation. I think, and this is just a guess, I think that maybe over the next few years, we'll see an integration of the more conventional approach with the use of AI in certain aspects of ECG interpretation. I think there'll be a reluctance to put ECGs into black box, out comes the report, and the clinicians has to accept what it says without any idea why the diagnosis has been, maybe not even any intervals presented, et cetera, et cetera. I see a certain reluctance there. And that's why think there would be a marraige of conventional approach with the AI machine learning type basis of interpretation. On the other side, look at the phenomenal developments where we've come from hugely sized equipment to record an ECG in a computer that was half our soccer pitch or American football pitch, to interpret an ECG. Now we can do it now on a wristwatch. I think the question here is whether ECG interpretation is centralized on a large computer. And it's just every ECG is transmitted to this large computer, instantaneously analyzed by whatever super duper method you wish to have, including convolution, neural networks, if that's the better way to go, I don't know. And then the result is quickly passed back

to the device. That's possible just now, of course. But to make it more widely possible, I think maybe would be a few years down the line and a commercial vendor is willing to take it on. The alternative way is to say, well, looking at the way computers have evolved, as I said, half a football pitch into a watch, maybe all this phenomenal power could go into a small ECG machine. And so we'll continue to have media interpretation on the device. The advantage of the centralized approach is if you want to update the software, you can update the software immediately or for whatever it takes. And all these hundreds of ECG machines that are feeding in there automatically benefit from that single change to a program. Otherwise, if you've got hundreds of thousands of ECG machines out there and you want to upgrade them, that's a big problem unless you've got equal similar methods to download software into the machines. All of these things are possible. I can't say which way it's going to go. But these are my thoughts.

Dr. Kashou: Yeah. And I agree with you. You know, as someone that does a lot of work in the AI space and the deep learning models, it seems like AI is going to be inevitably a part of the ECG interpretation analysis. Now, I probably would agree with you that the rule-based and the current system that we have, it's probably gonna be a mesh of the two for us to have the best interpretation, because we could base that on what we can see with the underlying physiology. And so I would agree with you, but it's interesting, you know, there's that software side of how far we've come to now using deep learning convolutional neural networks. And then the hardware side from the football field, as you mentioned, to a watch. Small devices that are even now recording even 12-lead ECGs from home. It's clear that the whole field is evolving before our eyes and it's amazing what's going on. The number of lives saved by computerized ECG interpretation programs like that from the University of Glasgow is immeasurable. The clinical value the interpretive tool adds to medical practice can sometimes be overlooked. Nevertheless, it is clear that the ability to detect, capture, and interpret cardiac biosignals in clinical practice has no end in sight and that the only way forward is to further refine such programs for our colleagues and the patients we serve. Professor Macfarlane, what an incredible work you and your team have done. You have been a pioneer in this field and represent an inspiration to so many, including myself. On behalf of our team, thank you for taking the time out of your day to join us. It's been a true pleasure.

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