



Prof. Kypros Nicolaides, Kings College Hospital, London, UK.

*VISIONS spoke with
Prof. Kypros Nicolaides
about using Canon's
Aplio i-series systems
in fetal medicine.*

Revolutionizing Fetal Medicine for Decades

The Fetal Medicine Foundation, based in London, United Kingdom has made a significant contribution to advancing fetal medicine globally for more than 20 years. Established by Prof. Kyprianos 'Kypros' Nicolaides, it aims to improve the health of pregnant women and their babies through research and training in fetal medicine. Ultrasound scanning is, of course, absolutely fundamental in its work, and for many years, the Foundation has leveraged Canon Medical's latest technology to advance science in this field.

Prof. Nicolaides is one of the world's most well-known pioneers in fetal medicine. He has a real passion for fetal ultrasound.

How it all started

"As a medical student in 1978 at Kings College Hospital in London, I got to watch the moving image of a fetus within the uterus for the first time, and it just fascinated me. I fell in love with this. A thousand questions were raised in my mind; What does the fetus feel?

How does the fetus think? How does it interact with the mother? How does it grow? How does it respond? And importantly, what happens if there are any problems with the pregnancy?" he explained. "So, I found my mission! After I qualified in medicine, my whole life was completely preoccupied with fetal medicine. I studied Obstetrics and Gynecology, because there was no other route into this area of medicine at the time, but my obsession, my love, was for fetal medicine."

“When I started in clinical practice, everything we were seeing was completely new,” he remarked. “Now, we have moved on from an era, in which you could see hardly anything, to being able to see fetal anatomy in

very great detail. This then expanded from an era of trying to diagnose fetal abnormalities, to assessing pregnancy and predicting and preventing many of the main pregnancy complications.”

1980s Shift to visual diagnosis

The 1980s, developments in ultrasound enabled a whole new era in fetal medicine to unfold.

“We were describing how the fetus grows, producing normal ranges of various parameters, and we studied fetal physiology,” remarked Prof. Nicolaides. “It was a very exciting time when we were assessing and investigating fetal physiology. The equipment we were using was becoming better and better, and our way of thinking was advancing too. We were diagnosing fetal growth problems, and then increasingly, diagnosing fetal abnormalities. We also discovered how babies with Spina Bifida presented with changes in the shape of the head and cerebellum. Allowing us to challenge the traditional method of screening for this condition, with a better alternative – by looking at the shape of the head of the fetus.”

In the early 1980s there was still a lot of Rhesus disease, in which the mother’s blood proves negative, the babies blood group can be positive and the babies become anemic.

“Blood sampling was done by fetoscopy, but by the mid- 1980s we were able to do ultrasound-guided puncture of the umbilical artery to directly sample fetal blood and determine fetal hemoglobin,” he continued. “With the newly introduced Doppler ultrasound, we were able to discern a direct correlation between Doppler indices and fetal blood hemoglobin and I wrote important papers on this hot topic by then.”

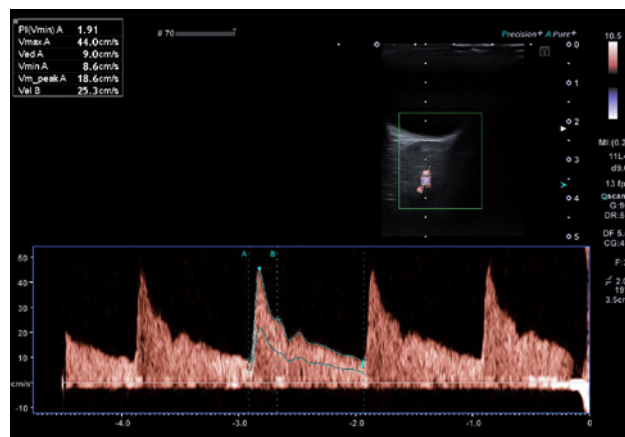
“There was a gradual shift away from indirect measures of fetal anomalies into direct visualization of fetal anomalies,” he added. “We also began with fetal therapy techniques. For example, We developed a method in which you could safely put a tube into the fetal chest, to drain the fluid from the



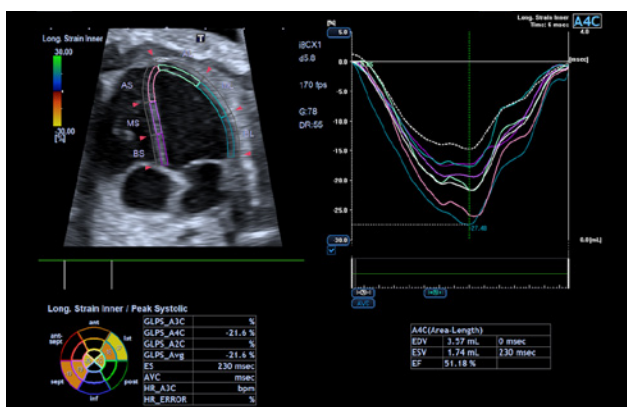
Prof. Kypros Nicolaides, Kings College Hospital, London, UK.



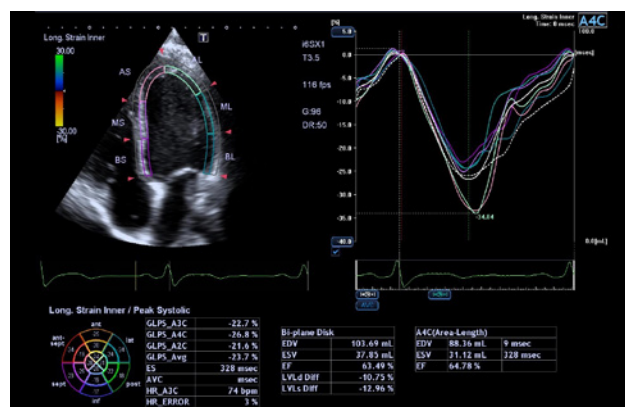
Nuchal Translucency Fetus 12 weeks.



Maternal ophthalmic artery Doppler.



Fetal speckle tracking showing inner longitudinal strain of left ventricle.



Maternal speckle tracking showing inner longitudinal strain of left ventricle.

thoracic cavity into the amniotic cavity, and the same in the cases of obstructive uropathy to decompress the bladder."

1990s

Significant discoveries

Prof. Nicolaides acknowledges several life-changing events from the 1990s that have also steered a new course for fetal medicine. In 1992, he discovered that fluid behind the neck in the twelfth week of the pregnancy could signal several defects, including Down Syndrome. This led to the introduction of the nuchal translucency scan. Also in 1992, together with Prof. Yves Ville, he discovered a therapy for Twin-to-Twin Transfusion Syndrome (TTTS) with an endoscopic laser.

Fetal medicine in the 1990s was then devoted towards a shift in ultrasound from the second to the first trimester.

improvement in imaging, improvement in training, and certification of competence.

“We established a method of training, certification and international audit in the new techniques that we were developing, because we recognized the benefit of them. However, things were moving so fast with diagnoses of fetal abnormalities, fetal pregnancy complications and then methods of improvement and interventions, that actually, it was almost beyond the scope of the regular funding bodies at that time,” said Prof. Nicolaides. “I felt that I had to find alternative sources of income. Therefore, in 1995, I created first a charity– The Fetal Medicine Foundation⁴ – and then a source of income for this charity through a private clinic – The Fetal Medicine Centre – both of which are in London.”

2000s

Expanding upon new techniques

“Over the years, we gradually started describing that increased nuchal translucency is associated not only with Down’s Syndrome, but also other genetic syndromes and many defects, such as cardiac defects,” he said. “Then, we combined nuchal translucency with biochemistry. That remained the dominant method of screening for chromosomal abnormalities up until the mid-2010s, when cell-free DNA testing advanced.”

In 2000-2002, Prof. Nicolaidis with Prof. Jan Deprest and Prof. Eduard Gratacos expanded the endoscopic technique used in TTTS to place a balloon in the fetal trachea to reduce the risk of pulmonary hypoplasia in diaphragmatic hernia.

2010s

Large scale studies and algorithms

For Prof. Nicolaides, the 2010s were about improving methodology and beginning long-term studies. From an era of trying to diagnose fetal abnormalities, there was an expansion into the assessment of pregnancy and prediction and prevention of the main pregnancy complications that could otherwise lead to death and handicaps.

“For example, measuring the cervical length as a method of predicting preterm birth, we showed that if we measure the cervical length and find the cervix to be short. If we give these women progesterone, we can substantially reduce the risk of preterm birth,” the Prof. explained. “Another example is measuring the uterine artery Doppler as a method of predicting fetal growth restriction, pre-eclampsia and still birth. Our results showed that we

could dramatically reduce the rate of severe early and preterm pre-eclampsia in the high-risk group by treatment with aspirin in first trimester.”

2020s

Leading fetal medicine

Today, the Fetal Medicine Centre is a major global institute in fetal medicine with around 20,000 patients per year.

“We have invested around £45 million in this to date and awarded around 700 scholarships to people. They come from all over the world to train for a two-year program, and many of them become leading Professors in their own countries. We have also invested hundreds of thousands of pounds in major screening studies and prevention studies for preeclampsia and preterm birth, as well as a building, which is now part of the UK National Health System (NHS). Women can

have their pregnancy care there free,” said the Prof. “The Fetal Medicine Foundation³ provides the highest standards of clinical care to pregnant women through the NHS.”

Despite the COVID-19 pandemic, the work of the Fetal Medicine Foundation³ continues to expand.

“At the beginning of the pandemic, I decided to host Zoom meetings with people from our field presenting their research, their findings, their knowledge in one hour webinars, which are held on Sunday afternoons. It started with 1,000 participants, and then very quickly there were 15,000+ people registering every time. It has created a new era on education beyond the traditional concept of having a congress,” explained Prof. Nicolaides. “The attendance shows a great interest in our field and a great deal of respect for the Fetal Medicine Foundation.⁴”



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Biography

Prof. Kypros Nicolaides is one of the world's most well-known pioneers in fetal medicine. He studied Biochemistry, Physiology, and Medicine at King's College London in the UK. He is specialized in Obstetrics & Gynecology since 1984 and is the Director of the Harris Birthright Research Centre for Fetal Medicine at King's College Hospital, London. Since 1992 he became Professor of Fetal Medicine at the King's College in London, UK and three years later Founder and Chair of the Fetal Medicine Foundation³. Prof. Nicolaides organizes the annual World Congress in Fetal Medicine and has been recognized through 15 honorary doctorates and is the recipient of many highly prestigious awards.

Future perspectives

Prof. Nicolaides finds the future difficult to predict. "Things are moving so extremely quickly really," he said. "Everybody is talking about Artificial Intelligence (AI), and how this could potentially replace the need for sonographers. It is inevitable that this will happen to a certain extent. Of course, we will not do away with the humans. They will still be there to be interpreting the findings, but I think that AI will revolutionize many things. Imaging modalities will continue to improve with AI. That has already happened."

Equipped for advanced research

Prof. Nicolaides and Canon Medical relationship started back in the early 90s with the Canon ultrasound system SSA-250A and is re-established with the Aplio i-series on a new high level research cooperation.

"We originally approached Canon, because we knew that they had the best system," remarked the Prof. "We had been interested in undertaking maternal cardiac assessment in pregnancy for more than 10 years prior to this. Originally, this was being researched by indirect methods of assessing cardiac output and peripheral resistance, but we wanted to undertake major studies on maternal and fetal cardiac function and adaptation in different pregnancy complications through more direct methods. I heard that Canon had excellent equipment to achieve both those objectives. We developed a collaboration and have now a well-established relationship."



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"We have been supported by Canon in our research for many years, and have carried out many thousands of investigations using the Aplio i-series," he added.

"More recently we have been studying the maternal ophthalmic artery Doppler. We obtained wonderful results to have an additional marker in the prediction of pre-eclampsia both in the second- and third trimester. This article was published in the January 2021 issue of the White Journal¹. We also carry out studies on this topic in the first trimester now."

High quality research

Advanced ultrasound capabilities, such as Canon Medical's Superb Microvascular

Imaging (SMI), Myocardial Performance Index² (MPI) and Speckle Tracking Echocardiography² (STE) have enabled research that has led to a better understanding of fetal and maternal physiology, pathophysiology of many conditions and has provided focus for further studies.

"I am very proud that we have extremely high quality systems from Canon Medical that allow us to carry out our research," concluded Prof. Nicolaides. "All our team are very happy with the excellent images, ease of use. With the data and information acquired, we can study measurable parameters that can be correlated to find new links in fetal medicine." //

References:

1



'Ophthalmic artery Doppler in combination with other biomarkers in prediction of pre-eclampsia at 19–23 weeks' gestation.

2



'Influence of birth weight on fetal cardiac indices at 35–37 weeks' gestation'.



'Fetal cardiac function at 35–37 weeks' gestation in pregnancies that subsequently develop pre-eclampsia.

3

'For more information on the Fetal Medicine Foundation visit: <https://fetalmedicine.org>.