SOCIETY OF FETAL MEDICINE

Society of Fetal Medicine

SFM Bengal Chronicles

Artificial Intelligence in Fetal Medicine

Volume 01
Issue 03
November 2022

Inauguration Note

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"Rome has grown since its humble beginnings that it is now overwhelmed by its own greatness"
- Livy

When I was asked to write an inaugural note for the November 2022 issue of "SFM Bengal Chronicles", little did I realise what was in store for me. I am in awe! The Bengal chapter from its humble beginnings has truly shaped up for future under able stewardship of the present committee. I feel humbled to write this note about a subject, of which I know so little! Thank you, Mr President.

Life Is Like Riding A Bicycle. To Keep Your Balance, You Must Keep Moving"
- Albert Einstein

Till few years ago we only knew of natural instinct, natural intelligence and natural intellect. The word 'artificial' was not welcome. It now seems Darwin's theory of natural selection is selecting artificial over natural ! To keep learning one has to constantly learn, unlearn and relearn.

The volume and complexity of what we know has exceeded our individual ability to deliver its benefits correctly, safely, or reliably"
- Atul Gawande

The chapter "AI for the skinny" sets the ball rolling by taking us through 'deep learning' and the mathematical model of 'convolutional neural network'. "AI applications in FM" discusses how AI helps to carry out routine repetitive work through pattern recognition, thereby reducing errors and the time consumed. "Assessment of fetal lung maturity by AI" is an eye opener and would go a long way to decide to-be or not-to-be delivered. "Quantitative assessment of cervical texture by AI" in predicting preterm birth is a paradigm shift from the conventional assessment of cervical length and funnelling. Last but not the least "AI in genomic diagnosis" truly has a limitless potential of guiding the human brain through maze and alleys of various algorithms and databases used in perinatal genetics.

The Secret To Getting Ahead, Is Getting Started"
- Mark Twain

One of the great realisations of life is not to stop. We don't need to see the whole staircase to take the proverbial first step. Let us start where we are with what we have. The intention to move-on is important. Let us make some space to make daydreams a possibility. Who knows 'AI in Fetal Medicine' might become a reality sooner than we ever thought! Every moment is a fresh beginning.

"If you want something different you must do something different"
- Jack Canfield

From The President's Desk

Welcome back to SFM Bengal Chronicles.

Artificial Intelligence(AI) has been all pervasive, sneaking into our daily lives, ranging from autocompletion of typing to shopping suggestions based on our recent searches. The past few years have seen application of AI in medicine to improve decision making, to avoid misdiagnosis and even to recommend treatments. AI in advanced Fetal Medicine may still be in it's infancy or in the "Silicon Valley-dation" phase but it's not going to be long before clinical imaging gets revolutionised to this mode.

In the recent years we have witnessed a continuous rise in AI applications in the healthcare sector, mainly aiming at facilitating repetitive tasks and thereby enhancing workflow. Obstetric ultrasound is no exception. SonoNT, SonoBiometry, FINE fetal echo are all based on AI and getting more user-friendly by the day.

The concept of imaging is steadily getting transformed. The current practice of converting pixels/voxels into words is expected to change into more robust and quantitative approach using advanced mathematical analysis. Here comes the role of radiomics, another member in the 'omics' family. Various studies have been published highlighting the potential of radiomics. Different AI techniques would be needed to extract the desired information from the enormous amount of data available in the images.

Like radiology the other specialities such as pathology and dermatology, relying heavily on pattern recognition are also expected to be affected by AI in the near future. And it is not just the pattern-centric practices. The clinicians without patterns are also not going to be spared. For them AI presents a lot of adjunctive opportunities augmenting various functions. The protagonists are already carried away claiming organisms including their (e)motions are nothing but algorithms which can be represented in mathematical formulas. They see the authority being transferred from an image specialist to AI. But an eternal optimist would always say that Homo sapiens will never be an obsolete algorithm! They just have to keep pace with the recent developments.

It is high time to start getting used to the AI lexicon and upskill ourselves to be future-ready. The current issue of newsletter deals with some of the recent AI-based advances in the field of Fetal Medicine. Thanks to the enthusiastic authors who have taken the challenge of dealing with topics that are not so familiar in their day today practice.

Happy reading.

Dr. Kanchan Mukherjee
President, Bengal Chapter
Society of Fetal Medicine

"AI For The Skinny"

Dr. Kanchan Mukherjee, FRCOG

Artificial intelligence (AI) is bound to bring tremendous changes in the way we make a diagnosis and predict their course of progress particularly in the specialities relying on pattern recognition. The practice of radiology is going to witness a seismic shift in the coming years with increasing application of natural language processing, deep learning and so on. It is high time to embrace changes and remain up to date with recent developments as the virtual medical assistants powered by AI can give doctors the much needed gift of time while improving the precision in diagnosis and management.

Practitioners often use the applications in the most appropriate manners but without having much insights into the background science or necessary knowledge behind these technological evolutions.

Short History

As the term "Artificial Intelligence" was coined by John McCarthy in 1955, the US Navy in 1958 revealed the "embryo of an electronic computer" expected to be "able to walk, talk, see, write and reproduce itself and be conscious of its existence" (1). Excessive amount of pessimism, lack of research outputs and paucity in fundings led to much known "AI winter" in the subsequent two decades. By the late 1980s, the concept of "deep learning" emerged and the interest revived not just within the AI community but across different industries as a whole. The public interest started to rise when the then world chess champion Gary Kasparov got defeated by IBM's supercomputer 'Deep Blue' in 1997. The interest was further rekindled when self driving cars became a reality in 2004. Three years later ImageNet project was launched with a massive database of 15 million labelled images. The idea has been to create a large visual database designed for use in visual object recognition software.

These huge resources came handy as the most useful tool for computer vision(2). Natural language processing for speech recognition based on Deep Neural Network was also moving in full swing at Microsoft and Google. Research team at University of Toronto made significant contributions in image recognition at scale, back in 2012 (3). Notable breakthrough in recognition of unlabelled images also happened in the same year when Google Brain's team developed a system based on one hundred computers and 10 million images that could recognise cats in YouTube videos. Much of AI's wonders are underpinned to the success of deep neural network (DNN). The deeper the network by the number of layers, the more complex work it can perform. These networks have successfully been applied in games, images, voice & speech and driverless cars before being used in medicine. While recognition of human face became the point of interest for biometric password to unlock various gadgets, facial features were used to help diagnose rare congenital diseases through Face2Gene app(4). Thus the past two decades have been particularly eventful in the field of AI and it's increasingly successful applications in medicine.

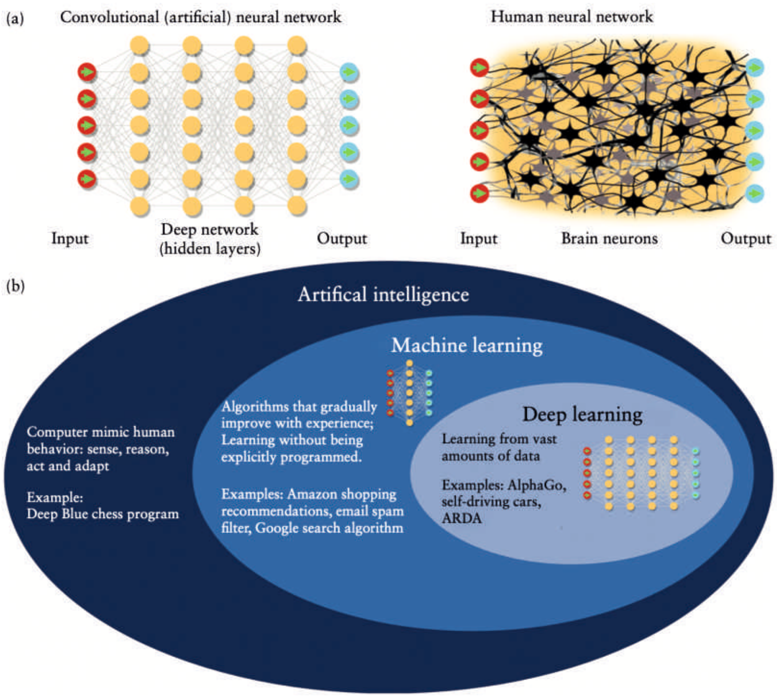
Basics in Brief

Automation is often confused with AI. The former helps streamlining the repetitive, onerous tasks but AI can mimic and even supersede human intelligence and behaviour. Automation runs on the pre-programmed instructions while AI has the ability to evolve itself by learning from previous experiences. The cognitive part of AI has historically tried to simulate the framework of biological neural networks. This Artificial Neural Network (ANN) also known as Convolutional Neural Network (CNN) is believed to function like adaptive human neurons without depending on masterly inputs from other sources. Such abilities of the computers to learn without being explicitly programmed is called machine learning(ML). A more advanced subset of ML is called Deep Learning, composed of complex algorithms inspired by the structure and functionality of human brains. Natural language processing (NLP) is another application of computational techniques to understand spoken or written language like humans. An ANN having multiple hidden layers between the input and output layers is called a deep neural network (DNN).

Glossary of commonly used terms in AI (5)

Artificial Intelligence	The science and engineering of creating intelligent machines that have the ability to achieve goals like humans via a constellation of technologies
Neural Network	Software constructions modelled after the way adaptable neurons in the brain were understood to work instead of human guided rigid instructions
Deep Learning	A type of neural network , the subset of machine learning composed of algorithms that permit software to train itself to perform tasks by processing multi layered networks of data
Machine Learning	Computers' ability to learn without being explicitly programmed
Natural Language Processing	A machine's attempt to "understand" speech or written language like humans
Convolutional Neural Network	Using the principles of convolution, a mathematical operation that basically takes two functions to produce a third one; instead of feeding in the entire dataset, it is broken into overlapping tiles with small neural networks and mix -pooling, used especially for images

Graphic representation of artificial intelligence (6)



Pictures legends (a) Human neural network architecture and its resemblance to a deep artificial neural network. (b) Relationship between artificial intelligence, machine learning and deep learning. ARDA, automated retinal disease assessment

The concept of images are changing. They are a lot more than pixels. All images can be converted to data which can be read more efficiently and consistently by the computers. A new field, called 'radiomics' has emerged to extract a large number of quantitative features from medical images using data characterisation algorithms(7). The improved data assessment has the potential to interpret disease characteristics well beyond the capacity of human vision. The only way forward is to embrace the new technologies and add holistic value to patient care instead of performing repetitive rote tasks.

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Artificial Intelligence-based Applications in Fetal Ultrasound

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The application of artificial intelligence (AI) technology to medical imaging specially in prenatal ultrasound (US) screening has great impact in improving work efficiency, providing quantitative assessments, standardizing measurements, improving diagnostic accuracy, and automating image quality control.

Artificial intelligence (AI) is the ability to interpret data and learning for specific purposes through flexible adaptation like human brain. AI involves Machine learning (ML), a powerful set of computational tools that trains models on descriptive patterns obtained from human inference rules and deep learning, a branch of ML. Deep learning (DL) uses the convolutional (Artificial) neural networks (CNN or ANN), involves learning from vast amounts of data and performs especially well in pattern recognition within data. Consequently, it is often used for image pattern recognition and classification. DL is the most powerful tool in AI applications of medical imaging where automated image recognition is necessary.

There are too many AI applications are put into action in the premium ultrasound machines of different makes providing intense support in high quality crisp imaging, semi-automated and automated acquisition, measurement, annotation and even interpretation. Few of them will be discussed here with some example illustrations.

APPLICATION OF AI IN FIRST TRIMESTER

Gestational Sac

GS is the first important structure observed by US in pregnancy providing the gestational age by mean sac diameter. Zhang et al. designed an automatic solution to select the standardized biometric plane of the GS and perform measurements during routine US examinations. The quantitative and qualitative analysis results showed the robustness, efficiency, and accuracy of the proposed method. This is not available in many current machines.

Fetal Biometry Assessment

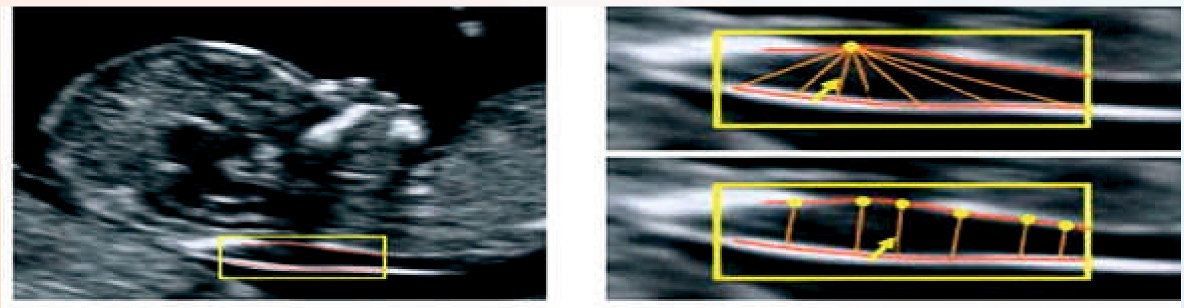
The automation of image-based assessments of fetal anatomies in the initial trimester remains a rarely studied and arduous challenge. Ryou et al. developed an intelligent image analysis method to visualize the key fetal anatomy and automate biometry in the first trimester. But results are not satisfactory till date.

Nuchal Translucency

Initially, the thickness of NT could be measured by manual selection of the region of interest , and semi-automatic approaches were proven to produce reliable measurements compared to traditional manual methods. Later, experts made attempts to automatically identify and measure NT in midsagittal section images and the NT detection results were accurate in most cases. Following studies of the automatic detection of the fetal midsagittal plane in US researchers developed sufficiently accurate methods for the automatic recognition of the standard NT plane as well measurement.

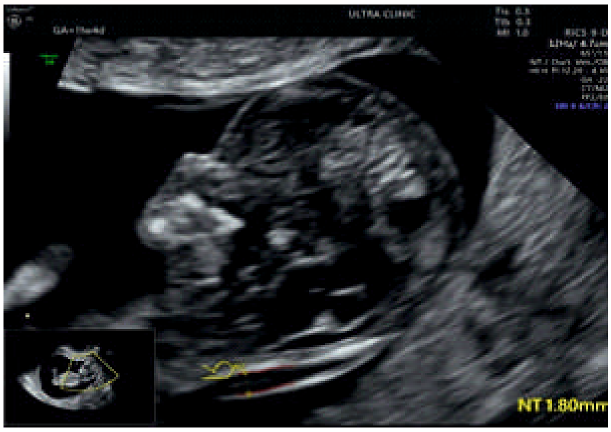
SonoNT by GE (GE Healthcare, Chicago, IL, USA)

Following acquisition of the magnified mid-sagittal view of the fetus in neutral position, SonoNT Region of Interest (ROI) over the Nuchal space is placed. In the event that magnification of the image is inappropriate, a magnification notice signal is displayed. The software will propose an NT measurement, to be accepted or rejected. SonoNT Report will display the accepted NT measurement.



Automatic segmentation of the nuchal membrane and the edge of the soft tissue overlying the cervical spine

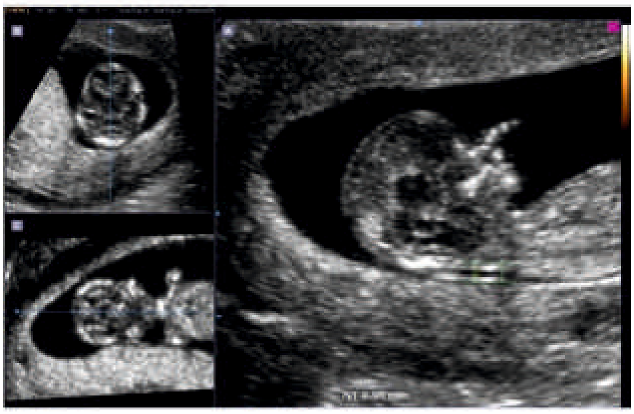
Calculates the minimum vertical distance between the two lines and computes the largest as the NT measurement

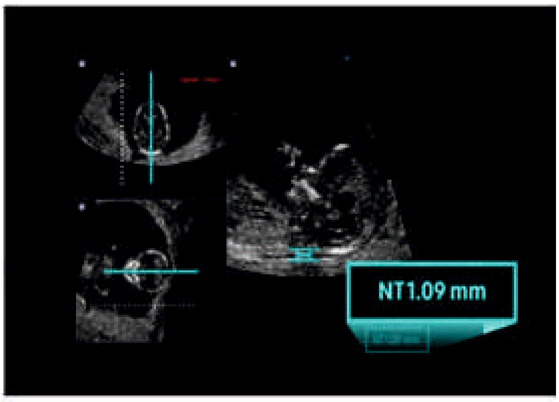


Volume NT by Samsung / 5D NT (SAMSUNG MEDISON Co., Ltd, Seoul, Korea).

Offers nuchal translucency measurement through an approximated mid-sagittal section determined by conventional B-mode ultrasound applying this Volume NT technique that automatically archives mid-sagittal plane views and measures the maximum NT distance. This is specifically useful when obtaining proper midsagittal view is difficult or imaging by less experienced sonologist.

Fetus - nuchal translucency, Volume NT





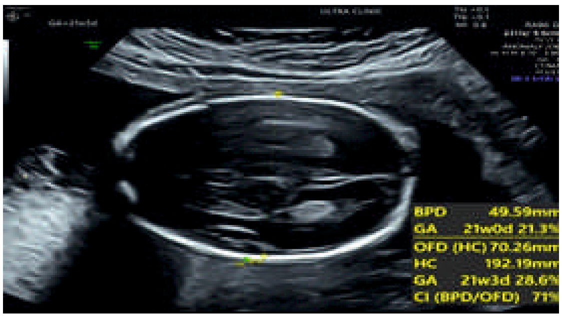
Fetal NT thickness measured with Volume NT & IT

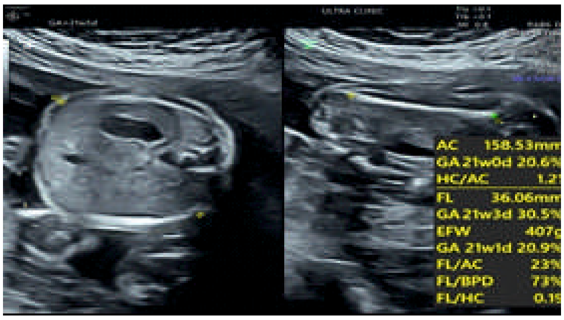
APPLICATION OF AI-AIDED ULTRASOUND IN SECOND- AND THIRD TRIMESTER

Sono Biometry software by GE or Samsung's View Assist and Biometry Assist

These AI software's act as a Fetal biometric plane finder-- Standard fetal biometric planes are automatically acquired, measured and stored. It reduces repetitive calliper adjustment clicks, reduces operator bias and makes instant quality control. They Efficiently eliminate keystrokes and support semi-automated measurement of BPD, HC, AC, FL, HL, CM, VP, and Cerebellum.

Recently, machine-learning techniques have brought significant advancements in US image classification, localization and automated measurement in the field of obstetrics is very promising in reducing redundant manual steps and improving accuracy of structure localization, caliper placement and measurement and includes annotations also.





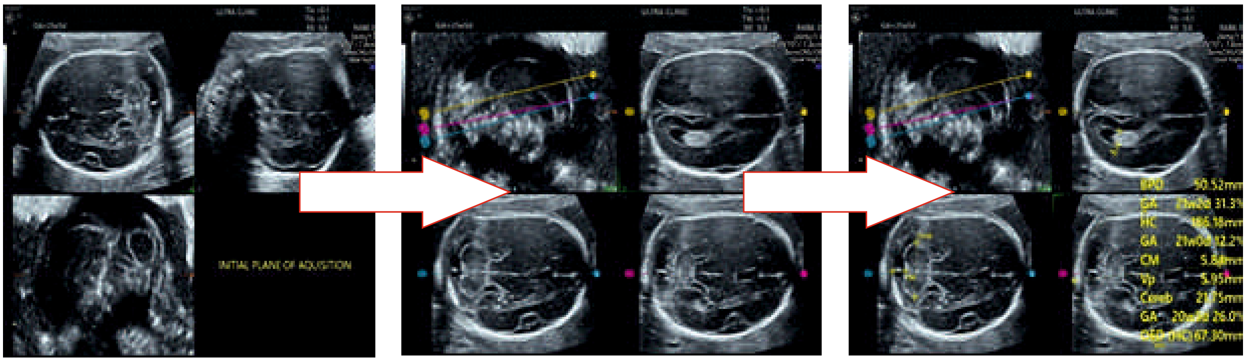
View Assist TM and Biometry Assist TM are built-in, commercially available automated ultrasound imaging software installed on the high-resolution ultrasound system. Recently, upgraded to include standard measurements on axial fetal head planes based on machine learning.

GE's SonoLyst AI software, which can auto recognize 20 standard fetal views in the second trimester protocol by ISUOG, ensures Anomaly scan completeness.The goal is to speed exam times and make the exams more accurate, even for less experienced sonographers. The AI can tell users what any image is when they freeze the frame. This can be used to help cue up measurements and appropriate annotations. The AI also can tell the user if all the required anatomical structures are in an image needed for the exam protocols.

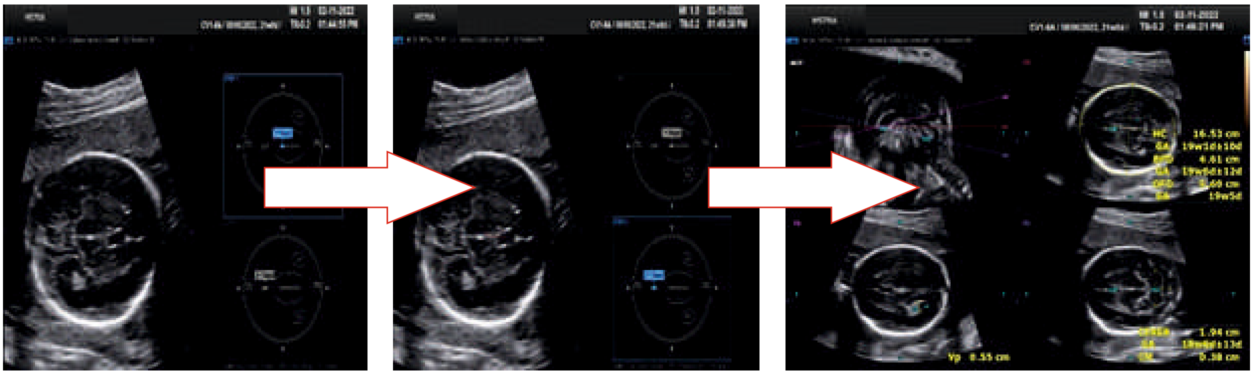
The AI helps reduced exam time with up to 80 percent fewer clicks, 99 percent accuracy as the AI automatically recognizes the anatomy on standard 2-D scan planes so there is less inter-operator variability. This anatomical identification also helps automate measurements and make them more reproducible. Anomaly scan checklist of mandatory planes is populated automatically Ensure completeness of imaging and that all parts of anatomy are checked.

SonoCNS and 5D CNS+ softwares

Using deep learning technology—it helps properly align and display recommended views and measurements of the fetal brain. This provides nine planes (axial, coronal, sagittal planes) of the fetal brain with anatomical landmarks and biometric measurements. 5D CNS+ combines clinical knowledge-based cues with pattern classification algorithms to determine the best standardized planes that are clinically significant. It complies with the International Society of Ultrasound in Obstetrics and Gynecology (ISUOG) guideline for the fetal brain. A success rate of over 90% was obtained under clinical evaluation. The number of operations is significantly reduced to about 85% (from 13 to 2). The examination time is shortened from 5 minutes to 20 seconds.



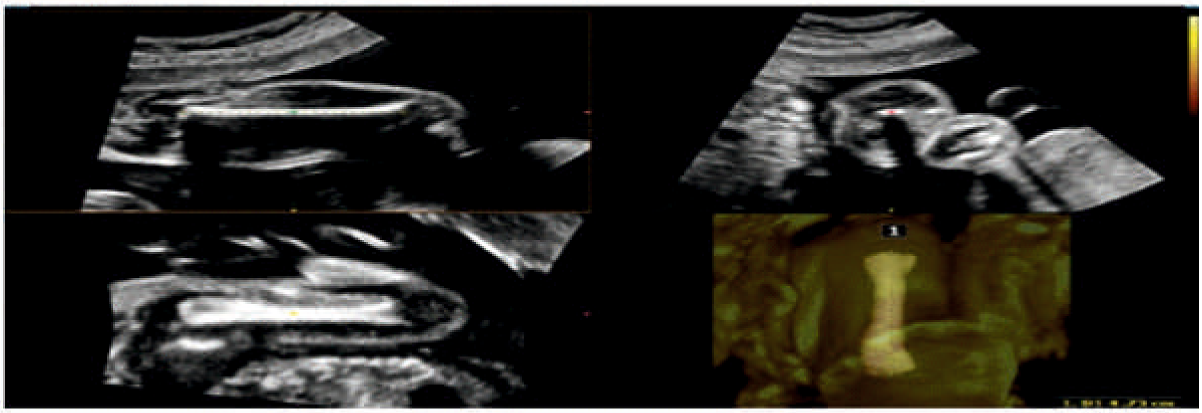
SonoCNS, automatically providing 3 orthogonal planes and measurements with annotations



5DCNS, semi automatically providing 3 orthogonal planes and measurements

5D LB

5D LB efficiently locates, displays and measures fetal long bones (Radius, Ulna, Humerus, Femur, Tibia and Fibula) from within the 3D dataset, streamlining workflow while enhancing measurement reproducibility. Evaluation of fetal condition becomes more efficient as 5D LB improves measurement accuracy while reducing exam time.



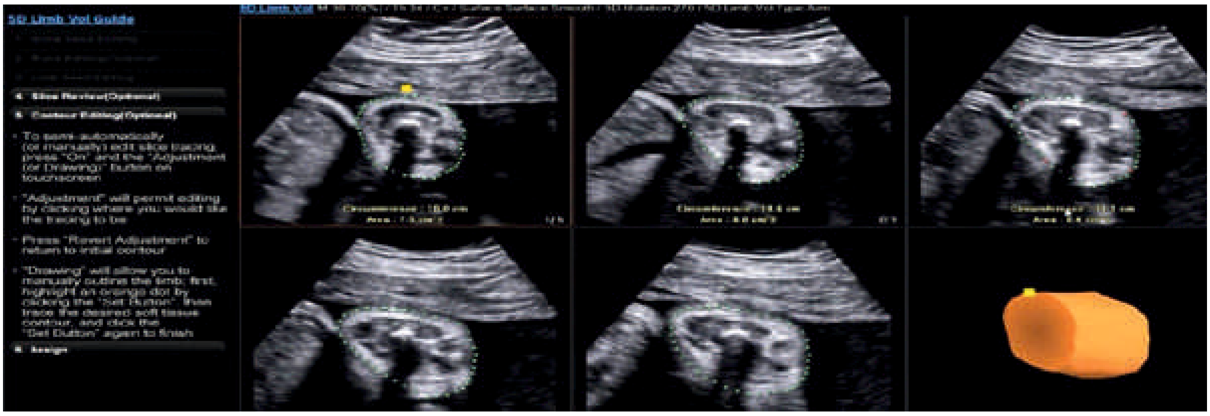
Fetal long bone measurement with 5D LB

5D Limb Vol

A new soft tissue parameter known as Fractional limb volume is measured from 3D ultrasound of the fetal limbs. This parameter helps to examine limb fat, muscle, and bone. Fractional arm volume (AVol) and fractional thigh volume (TVol) are used and based on 50% of the long bone diaphysis length.

Current fetal weight prediction models do not include soft tissue parameters because they are difficult to standardize, measurement with 3D ultrasound is time consuming and soft tissue borders are poorly delineated at the ends of fetal long bones.

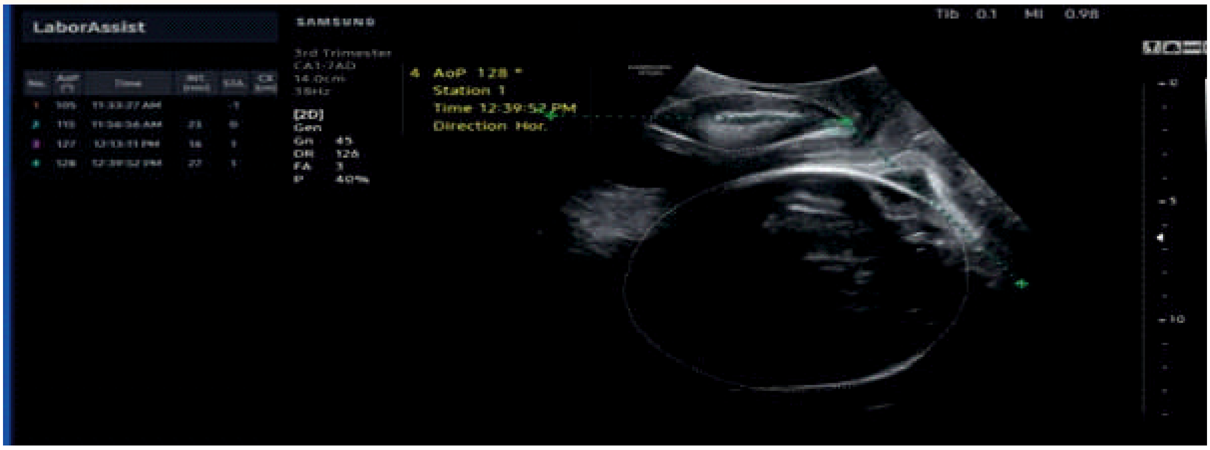
These challenges overcome by the 5D Limb Vol technology by providing working model to rapidly measure fractional limb volume. Added to conventional 2D ultrasound measurements of the fetal head (BPD) and abdomen (AC), this improves the precision of estimated fetal weight (EFW). This computer-assisted technology has great potential to diagnose and monitor malnourished fetuses with growth abnormalities.



LaborAssist by Samsung/ SonoVCAD™ labor

This AI software automatically analyses and estimates the fetal angle of progression (AoP) during labor for a better understanding of a patient's birthing progress, without the need for repeated and uncomfortable digital vaginal exams .

Ultrasonographic markers currently utilized to measure the fetal station during labor include head-perineum distance (HPD), fetal head direction and angle of progression (AoP). AoP can be defined as the angle between a line drawn from the midline of the pubic symphysis and a line drawn from the inferior apex tangentially to the fetal skull. Fetal head station 0 corresponds to an AoP of 116°. Head direction, an indirect marker of head station, is defined as the angle between the longest recognizable axis of the fetal head and the long axis of the pubic symphysis, measured in a midsagittal transperineal view. It is classified categorically as 'head down' (angle < 0°), 'horizontal' (angle 0°–30°) and 'head up' (angle > 30°). As the baby descends toward the pelvic floor, the head direction changes from downward, to horizontal, to upward. AI automatically depicts the pubic symphysis outline, fetal head outline and provides AoP which is calculated by the two outlines. AoP is a key measurement parameter for labor progression, for information on fetal head direction and for estimated head station based on the value of AoP. Therefore, it provides clinicians unfamiliar with intrapartum ultrasound tools to automatically calculate AoP data and easily integrate it into clinical scenario.



APPLICATION OF AI IN FETAL ECHOCARDIOGRAPHY

One of the earliest interests was 3D computer-aided analysis(CAD) of the fetal heart. One study showed that satisfactory views of the four-chamber heart, outflow tracts, and stomach were only obtained in 43% to 65% of cases, and less in settings of obesity or fetal spine up. More recently, spatiotemporal image correlation (**STIC**) volume data sets have been used to identity nine standard fetal echocardiographic views with up to 98% sensitivity for screening congenital heart disease. Some other examples include the fetal thymus, for which CAD has assisted with border identification and accurate volume measurement of this complex pyramidal structure in 77% of cases.

The intelligent fetal heart imaging system based on **STIC**, identifies the fetal arterial duct arch and then gradually realizes the imaging of the fetal heart screening sections. For the diagnosis of congenital cardiac defects, researchers have developed an AI diagnosis system .The system uses big data sets of confirmed normal and abnormal fetal heart images in combination with cloud computing to detect congenital fetal heart malformations.

A software named **Fetal Intelligent Navigation Echocardiography (FINE)**, which utilizes intelligent navigation technology on STIC data sets. Once the tags were completed, nine standard fetal echocardiography views are automatically generated. These views included a four-chamber view, a five-chamber view, a section of the left ventricular outflow tract, a short axis of the aorta/section of the right ventricular outflow tract, a section of the three-vessel view, an abdomen/stomach bubble section, an arterial ductal arch section, an aortic arch section, and a superior and inferior vena cava section.

Several studies have used FINE technology to arrive at a diagnosis of fetal tetralogy of Fallot combined with pulmonary atresia. Based on the big database of characteristics of fetal heart structures, it adopted deep learning to construct an intelligent fetal heart structure recognition system that could distinguish different anatomical structures, combine the information with the user' input to determine the search range of the fetal heart structures, identify the positions of the main anatomical structures in the volume measurement data, and generate a standard section of the fetal heart according to the positions of the main anatomical structures. Nevertheless, the current fetal heart intelligent imaging system was still susceptible to interference from the fetus, whose movement cannot be controlled. Therefore, suitable algorithms, matrix probe, and real-time 3D ultrasonography are still required.

SonoVCAD (Sonography based Volume Computer Aided Diagnosis) Heart /5D Heart Color

Following manually set four-chamber view, identifies all standard planes, extracts them automatically from an echo volume, arranging them together with the four-chamber view on the monitor. This automatically displays nine standard fetal echocardiography views with blood flow dynamics simultaneously in a single template. The intuitive workflow can simplify examination of the fetal heart and reduce operator dependency in high end Samsung machines

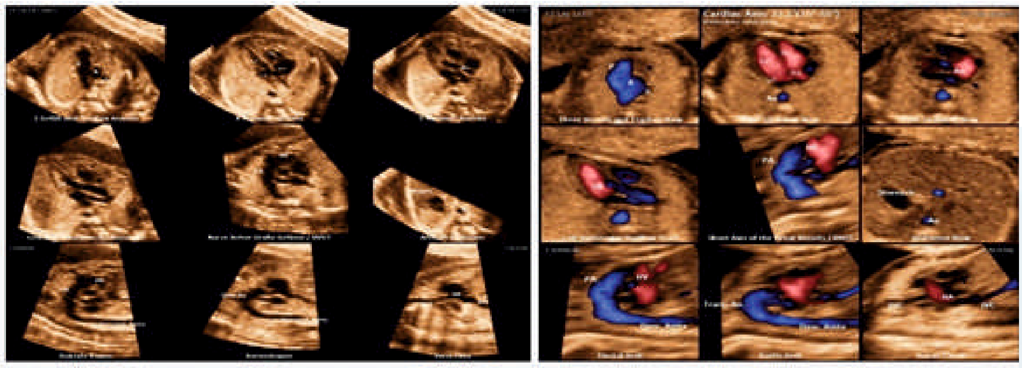
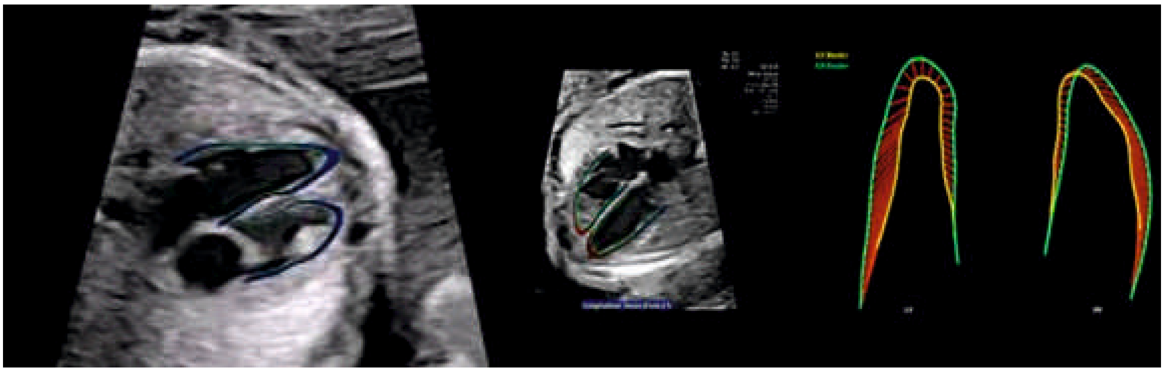


Fig. 1 Reconstruction of all diagnostic cardiac planes derived from a single STIC volume followed by application of 5D Heart Color™ (left panel), additional color Doppler information in 5D Heart Color™ (right panel).

Fetal HQ

This application developed by GE helps to conduct an easy and comprehensive evaluation of the size, shape, and contractility of the fetal heart from the 4-chamber view with the help of measurements on 2D imaging and speckle tracking techniques. FetalHQ also have an detailed report page that includes Z-scores and percentiles for each of the cardiac measurements. Research is going on for its potential applications in areas of fetal health and disease conditions.



CONCLUSIONS:

The combination of AI and ultrasonography actually benefit patients by assisting clinicians in the diagnosis of a variety of conditions and diseases improving efficiency of imaging. Significant achievements have been made in the application of AI in the fields of obstetrics though it's just the beginning, but the universality and effectiveness of many models still require further studies for validation. With the constant optimization and modification of algorithms clinicians should have knowledge of AI so that they can eliminate or standardize subjective bias to achieve objective, fair, and unified generalization standards. Along with further development and optimisation of techniques and multidisciplinary integration, there will be a lot more that AI can offer in the field of obstetric ultrasound.

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Artificial Intelligence in Prenatal Ultrasound Diagnosis Fujiao He, Yaqin Wang, Yun Xiu, Yixin Zhang and Lizhu Chen* Department of Ultrasound, Shengjing Hospital of China Medical University, Shenyang, China

Artificial Intelligence in Obstetric Ultrasound: An Update and Future Applications

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FETAL PULMONARY MATURITY ASSESSMENT IN PERSPECTIVE TO AI

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Immature fetal lung invites many adverse outcomes including respiratory distress syndrome (RDS) and transient tachypnoea of the newborn (TTN). Although gestational age is the strongest predictor of lung maturity, RDS and TTN are not only limited to premature births (< 34 weeks) but also can be observed more in late pre term (34-36 weeks gestation) and early pre term (37-38 weeks gestation) neonates than in neonates delivered at or after 39 weeks[1] .

Thus fetal lung maturity is the key factor for the survival of the prematurely delivered baby. In preterm and early pre term infants, lung immaturity is still the leading cause of neonatal morbidity and mortality. Respiratory distress syndrome affects about 1% of premature infants and is their leading cause of death [2]. Reports show that about 12% of all babies born in the United States are born prematurely, and about 10% of these babies have RDS. Younger premature infants are more likely to have RDS. Babies born at 29 weeks have a 60% chance of being born with RDS. In 2003, the number of live births in the United States was 4,089,950, of which about 0.6% had RDS (about 24,000 or 6:1000 live births). In 2005, the number of live births in the United States was reported 4,138,000 and the rate of preterm births increased from 6.11% to 12.7% due to increasing birth rates (34 to 36 weeks of gestation) [3]. RDS mortality in early African American infant was 2.6 times higher than Caucasian infants, although Caucasian infants were at higher risk [2].

So knowledge of fetal lung maturity has pivotal role in making decision for continuation or termination of pregnancy. Several methods have been implemented since several decades to assess the maturity of fetal lungs.
Before analyzing into the methods to assess the fetal lung maturity, we should know the devepmental anatomy of lungs.

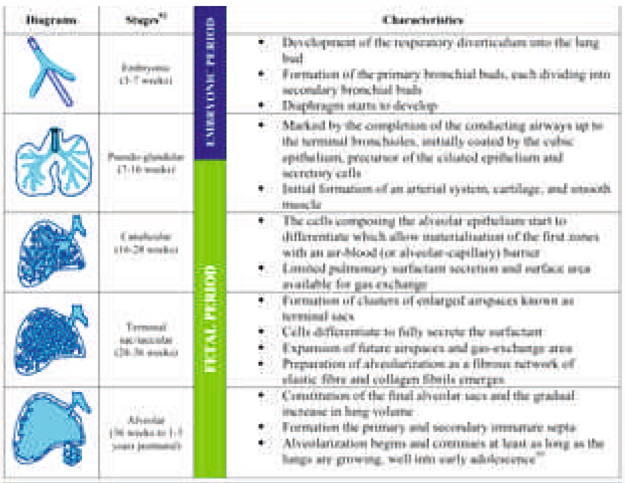


Diagram	Stages		Characteristics
	Embryonic (3-7 weeks)	EMBRYONIC PERIOD	• Development of the respiratory diverticulum into the lung bud • Formation of the primary bronchial buds, each dividing into secondary bronchial buds • Diaphragm starts to develop
	Pseudo-glandular (7-16 weeks)		• Marked by the completion of the conducting airways up to the terminal bronchioles, initially coated by the cubic epithelium, precursor of the ciliated epithelium and secretory cells • Initial formation of an arterial system, cartilage, and smooth muscle
	Canalicular (16-28 weeks)	FETAL PERIOD	• The cells composing the alveolar epithelium start to differentiate which allow materialisation of the first zones with an air-blood (or alveolar-capillary) barrier • Limited pulmonary surfactant secretion and surface area available for gas exchange
	Terminal sac/saccular (28-36 weeks)		• Formation of clusters of enlarged airspaces known as terminal sacs • Cells differentiate to fully secrete the surfactant • Expansion of future airspaces and gas-exchange area • Preparation of alveolarization as a fibrous network of elastic fibre and collagen fibrils emerges
	Alveolar (36 weeks to 1-3 years postnatal)		• Constitution of the final alveolar sacs and the gradual increase in lung volume • Formation the primary and secondary immature septa • Alveolarization begins and continues at least as long as the lungs are growing, well into early adolescence

Avena-Zampieri. Assessment of the fetal lungs in utero. Am J Obstet Gynecol MFM 2022 [4] .

The development of the fetal lung is divided into five stages the (i) Embryonic covering the period up to 7 weeks, (ii) Pseudoglandular covering the period 7–16 weeks, (iii) Canalicular covering the period 16–25 weeks, (iv) Saccular covering weeks 25–36 and (v) Alveolar covering weeks 36!38. It is usually at the end of the Canalicular stage that epithelia differentiation occurs, with type II pneumocytes differentiating to type I and lamellar bodies (in which surfactant synthesis begins by 20 weeks) forming in type II pneumocytes. By the end of this period, the preterm lung is potentially viable [5]. The presence of amniotic fluid is critical to the development of fetal lungs especially for the 2nd and 3rd stages. Anhydramnios before the 20nd week of gestation is associated with pulmonary hypoplasia that is unlikely to support extra-uterine survival, but when it occurs after the onset of surfactant production, the lungs may be able to support the neonate . It is important to remember other causes of pulmonary hypoplasia, examples of which are congenital diaphragmatic hernia, some forms of skeletal dysplasia associated with a narrow chest, congenital cardiac malformations and cysts in the lungs and pleural effusion. While lung development continues into the late third trimester (the Alveolar stage), a significant number of babies are delivered well before this period .

Methods of determination of lung maturity are [6] .

1. Clinical Methods :

    -Menstrual history & Last menstrual period (LMP)

    -Per abdomen examination

    -Date of quickening

2. Ancillary methods :

    -Amniocentesis

    -Radiography

    -Ultrasonography

Clinical methods have drawbacks. In many cases patients do not know the exact LMP or date of quickening. Per abdominal examinations can also give erroneous results in cases such as polyhydrominos or multiple gestation or IUGR. Amniocentesis is an invasive technique. Biochemical indicators like lecithin, sphingomyelin, phosphatidyl choline are measured in amniotic fluid to determine the fetal lung maturity.

Few amniotic fluid tests used to determine the fetal lung maturity are

- Lecithin to sphingomyelinratio(L/S ratio)
- Phosphatidyl glycerol levels in amniotic fluid
- DPPC (Dipalmitoylphosphatidyl choline)levels in amniotic fluid Fluorescence polarization of amniotic fluid.
- Optical density of amniotic fluid at 650 nm
- Shake test

Ultrasonography :

- Placentalgrading[7]

  Grade III maturation of placenta indicates the fetal lung maturity

- Bi-parietaldiameter (BPD)

  BPD >90 mm- 40 weeks also indicates fetal lung maturity[7].

- Lower limb epiphyseal centers .Distal femoral epiphysis (DFE) and proximal tibial epiphysis (PTE) appearance is an indicator of fetal lung maturity[7]
- Antenatal detection of DFE and PTE and their size is seen to correlate with amniotic fluid L/S ratio.
- Appearance of free floating particles in the amniotic fluid is also one of the indicators of fetal lung maturity on ultrasound[8]
- Measuring fetal pulmonary artery doppler indices [9].
- Objective study of grey scale histogram by ultrasonography [10].
- Assessment of fetal lung growth in utero with Echo planar MR imaging [11].
- Role of 3D for assessment of fetal lungs [12].
- Fetal lung maturity assessment by automatic quantitative ultrasound lung texture analysis (Quantus FLM) [5, 13].

We will be discussing the few non invasive methods of assessment of lung maturity which are practical USG based and can be initiated during daily routine care .

Quantus FLM(fetal lung texture ananlysis) :

For several decades, ultrasound has been proposed as a possible tool for the assessment of fetal lung maturity. This has been applied to gray measurement [14], fetal lung tissue motion assessment [15], and assessment of fetal lung images relative to fetal liver and fetal placental images [16]. The diagnostic accuracy of this was unfortunately poor and therefore was not found to be of clinical value.

Quantitative ultrasound fetal lung maturity is a new technique aimed at assessing fetal lung texture using ultrasound (quantusFLM).

The objective is to predict fetal lung maturity and subsequently fetal respiratory morbidity. This has become possible because of developments in two areas, (i) image resolution and (ii) computer capacity [17]. Fetal lung images are obtained by ultrasound at the level of 4- chamber heart view (fig 1). Subsequently, these images are analyzed using a computed method which can detect textural changes of lung images that are invisible to the human eye [18]. Using gray scale US, the fetal lung is visualized at the level of the four chambers heart view (Fig. 1). The region of interest (ROI) - is defined in the fetal lung and delineated by the operator. The information on the fetal lung is obtained in pixels. These images are then uploaded via a web- based application. These US images of the fetal lung are analyzed at a remote center and reliable results are obtained within minutes.

Ultrasound image reconstruction depends on detection of changes occurring at the histological level which include collagen, fat, water and other substances. These various structures affect the ultrasound signal of the fetal lung. As earlier mentioned, these computerized quantitative ultrasound analyses detect extremely subtle changes not seen with the naked eye. These lung images display certain features that correlate well with the fetal gestational age or the result of FLM determined by examination of the amniotic fluid [19,20].

Potential clinical use of Quantus FLM :

1. QuantusFLM has the potential of determining fetal lung maturity before elective delivery in conditions such as severe hypertensive disorders of pregnancy, poorly controlled diabetes in pregnancy and severe intrauterine fetal growth restriction where there is no urgency in delivering either for fetal or maternal indication).
2. QuantusFLM makes it possible to avoid using an invasive technique to predict neonatal respiratory morbidity in clinical practice. This new software, QuantusFLM, uses a cutting-edge image analysis technology that can effectively predict with accuracy the degree of fetal lung maturity (see Fig. 2).
3. This technique was evaluated in a large prospective multicenter study. Palacio et al. studied over 800 images of fetal lung at different centers in different countries [20]. These images were taken between 25–39 weeks of gestation. All the images were analyzed with QuantusFLM. The perinatal outcome in terms of transient tachypnea of the newborn or respiratory distress syndrome were recorded. They concluded that QuantusFLM was accurate in predicting neonatal respiratory morbidity and that the accuracy of this new technique is as good as a previously prescribed invasive method of determining fetal lung maturity.
4. This non – invasive technique has a major advantage over other techniques used for assessing fetal lung maturity. It has the potential to reduce the use of antenatal corticosteroids for fetal lung maturity. Antenatal corticosteroids are over used in most units – in ours for example, we have shown that 60 % of patients who received antenatal corticosteroids went on to deliver at term [21]. Antenatal corticosteroids can cause maternal and fetal side- effects. The use of antenatal steroids can cause intrauterine fetal growth restriction and early onset neonatal sepsis [22].

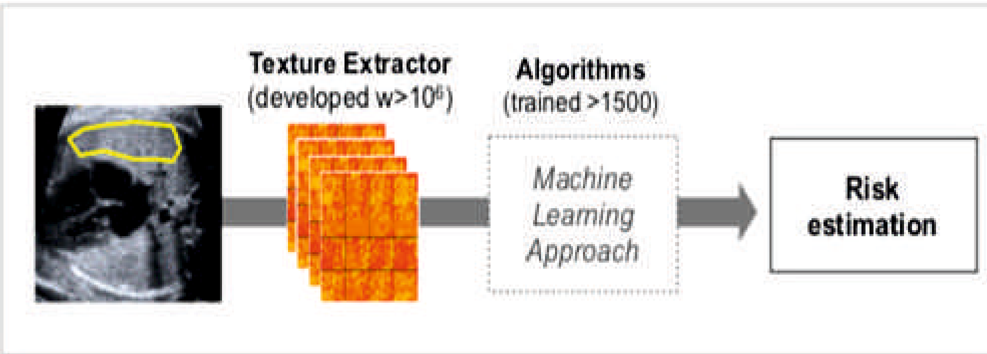


Figure 1

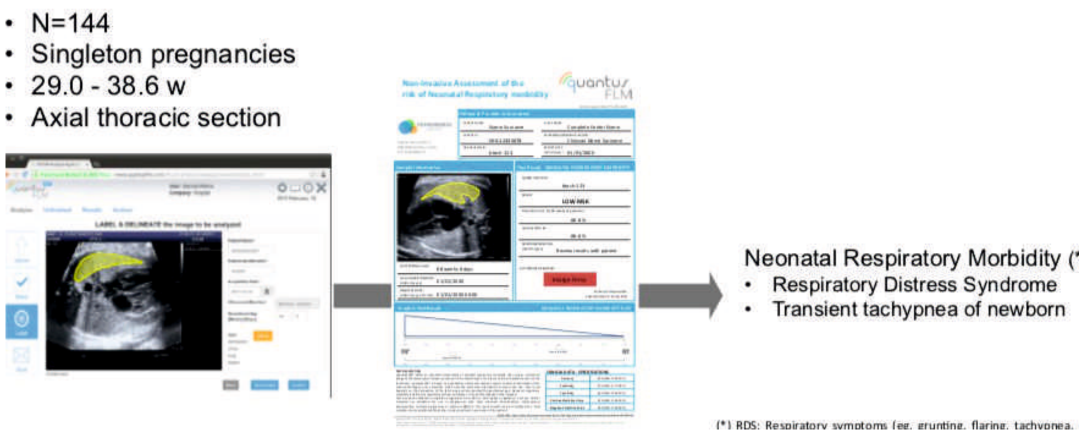
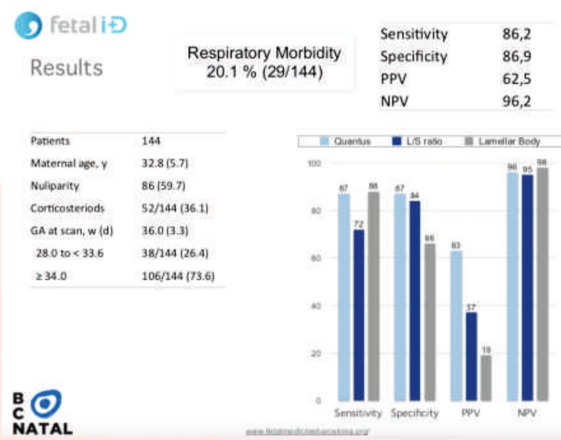


Figure 2 : Lung maturity prediction by quantitative ultrasound analysis :E Bonet, M Palacio, T Cobo, A Perez, M Lopez, E Gratacoswww.fetalmedicinebarcelona.org [23].



Comparison of Sensitivities, specificities, negative and positive predictive values of some of the historical and/or currently used tests for fetal lung maturation.

Test	Sensitivity	Specificity	Negative Predictive value (NPV)	Positive Predictive value (PPV)	Reference
Gestational age only	88.8 %	73.5 %	97.7 %	34.45	
Amniocentesis (L/S ratio)	74.6 %	82.5 %	96.4 %	34.1 %	Palacio et al. [50]
Amniocentesis (phosphatidyl – glycerol)	82.7 %	54.4 %	96.3 %	18.0 %	Palacio et al. [50]
Amniocentesis (Surfactant/Albumin ratio)	88.5 %	77.7 %	98.5 %	28.5 %	Palacio et al. [50]
Amniocentesis (Rapid visual test)	90.8 %	70.3 %	N/A	N/A	Sbarra et al.
Foam stability test	87 %	54 %	92 %	42 %	Taborda et al.
Lung profile	100 %	76 %	100 %	61 %	Taborda et al.
Lamillar body count	84.2 %	74.4 %	97.6 %	27.9 %	Palacio et al. [50]
Lung-liver signal intensity	100 %	73 %	N/A	N/A	Oka et al.
(Pulmonary artery Doppler wave acceleration/ ejection time ratio	73 %%	93 %	87 %	85 %	Schenone et al.
	90.9 %	77.1 %	95.4 %	52.7 %	Büke et al.
Fetal Tibia epiphysis	95.5 %	91.7 %	73.3 %	98.8 %	Abdulla et al.
Fetal femur epiphysis	97.7 %	50.0 %	75.0 %	93.5 %	Abdulla et al.
Thalamic echogenicity	77.3 %	75.0 %	31.0 %	85.8 %	Abdulla et al.
Amniotic fluid vernix	63.6 %	66.7 %	20.0 %	93.3 %	Abdulla et al.
Biparietal diameter	56.8 %	83.3 %	20.8 %	96.2 %	Abdulla et al.
Placental grading	60.2 %	75.0 %	20.5 %	94.6 %	Abdulla et al.
QuantusTLM	74.3 %	88.6 %	95.5 %	51 %	Palacio et al. [50]

Table 1: Ahmed B et al . Fetal lung maturity assessment : a historic perspective and non-invasive assessment using an automatic quantitative ultrasound analysis . European J of Obst & Gynae Reprod Biol 2021[5]

Recently Gratacos & Palacio group have again depicted the prediction of neonatal raspiratory morbidity in twins by a non invasive lung texture analysis with over all good specificity , NPV and accuracy . QuantusFLM® may be useful in planning indicated delivery of twin pregnancies because of medical conditions and may help to avoid repeated doses of corticosteroids when the fetuses have already been exposed and the risk of preterm delivery is still present. Therefore, in adequate facilities, this technology can be incorporated into protocols according to gestational age and may be helpful in the decision-making process when delivery is planned [13].

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Role of Artificial Intelligence aided Obstetric Ultrasound in Preterm birth

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Overview

Preterm birth (premature birth) is a significant public health problem across the world because of associated neonatal (first 28 days of life) mortality and short- and long-term morbidity and disability in later life. Preterm is defined by World Health Organization (WHO) as babies born alive before 37 completed weeks of gestation or fewer than 259 days of gestation since the first day of a woman's last menstrual period (LMP). According to WHO, every year about 15 million babies are born prematurely around the world and that is more than one in 10 of all babies born globally. In India, out of 27 million babies born every year (2010 data), 3.5 million babies born are premature.

Risk Factors of Predicting Preterm Birth

Previous preterm labour or premature birth, pregnancy with twins, triplets or other multiples, shortened cervix, maternal health problems, problems with the uterus or placenta are some risk factors of preterm labour. Risk of preterm birth is inversely associated with cervical length, and mid-trimester cervical length is currently the strongest clinical risk factor for predicting preterm birth

This chapter addresses various ultrasound techniques and role of artificial intelligence (AI) for cervical assessment and measurement. In this review, we outlined the benefits of AI technology in obstetric ultrasound by optimizing image acquisition, quantification, segmentation, and location identification, which can be helpful for obstetric ultrasound diagnosis in different periods of pregnancy.

Discussion

Cervical incompetence

Cervical incompetence refers to a painless spontaneous dilatation of the cervix and is a common cause of second trimester pregnancy failure. Patients at high risk for preterm delivery include those with: uterine anomalies , exposure to diethylstilbesterol (DES), previous cervical trauma or surgery, previous premature delivery, multifetal pregnancy etc.

Altered consistency of the cervix can lead to early labour and preterm birth, which is universally evaluated with Bishop's scoring and USG measurement of the cervical length. The assessment of the uterine cervical length is unreliable and variable. The correlation of the previous obstetrics, clinical history, fetal fibronectin, Bishop's score and USG measurement of the cervical morphology (funnelling & shortening) can lead to better prediction of the preterm birth.

Recently, the role of sonographer in the cervical assessment has been enhanced by virtue of the arrival of the elastography and other variable Artificial intelligence techniques.

Sonography of cervix

Evaluation of maternal cervix is an integral part of routine obstetrical USG. There are three approaches for cervical scanning which are transabdominal, transvaginal and translabial.

Conventional Transvaginal method.

"Short cervix" is called when cervical length is less than 25mm. The earlier in gestation, the shorter the cervix, the greater is the risk of pre-term birth. Rate of cervical change or progressive shortening of the cervix is more important than a single measurement, hence a term 'short and shortening' or 'short but stable' cervix is described. The presence of cervical funnelling is also an important finding. Greater than 50% funnelling before 25 weeks is associated with an 80% risk of preterm delivery. The risk of preterm delivery is inversely proportional to cervical length i.e., 18% for <25 mm, 25% for <20 mm, 50% for <15 mm.

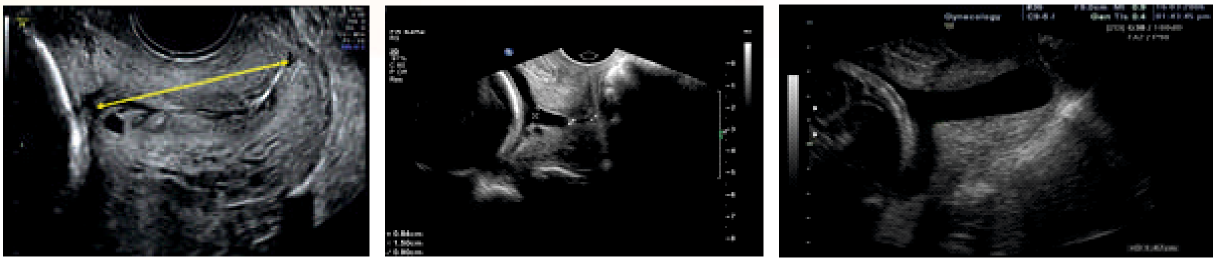

Figure 1: A. TVS image of a normal cervix. B. Short cervix with funnelling. C. Severe shortening of cervix with funnelling.

Cervical elastography

Elastography is an USG based imaging technique for assessment of the consistency of the cervical tissue/internal os. The gradient of the strain produced is displayed on color coded and a grey scale map. Red colour indicating soft, yellow (medium soft), green (medium hard) and blue or purple (hard). The grading was done on proportion of the colours on the color map. However, the cervical softening and prediction of the preterm is primarily based on red to yellow color. Cervical elastography is done in the second trimester of gestation on patients presenting with clinical signs and symptoms of preterm labour and preterm premature rupture of membranes for the morphological assessment of the cervix. However, this Real Time Elastography (RTE) method is subjected to inter as well as intra observer variation; hence lacks standardization. Bishop's scoring, cervical length and RTE of the cervix can be correlated for the assessment of the risk of preterm birth

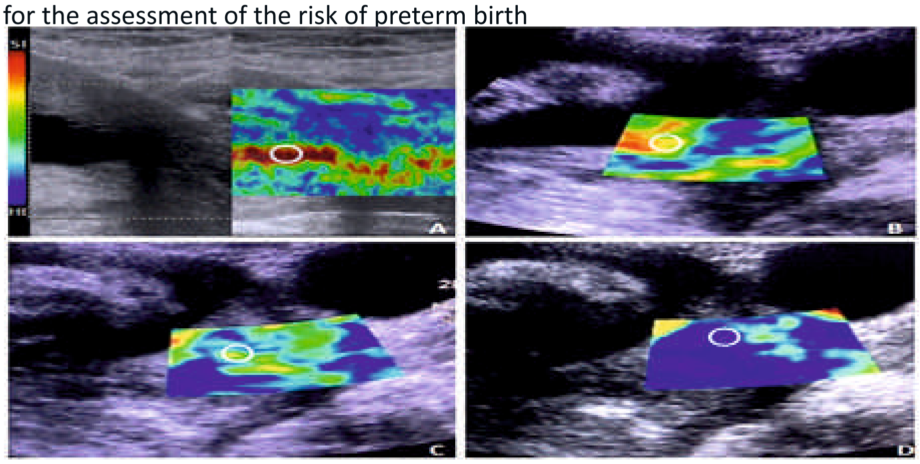

Figure 2 Elastography Images of the cervix at internal os (circles), (A) showing red -soft; (B) red and yellow-medium soft; (C) yellow and green-medium hard and (D) green and blue-hard. The color coding map is shown from the soft (SF) level to Hard level (HD) attached to the image A.

Another recent advancement in the elastography technique is based on Acoustic Radiation Force Impulse (ARFI) which is a quantitative method for measuring the velocity of the shear waves from the tissue concerned. The technique is better known as Virtual Touch tissu [illegible] e (internal os in this scenario) and [illegible]

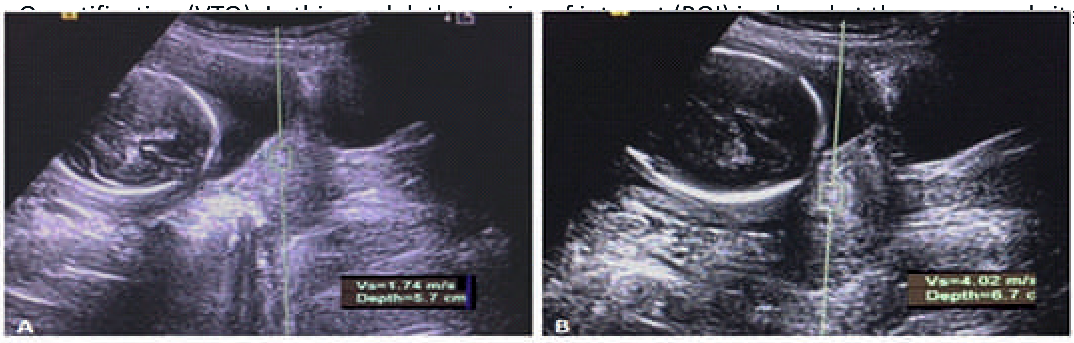

Figure 3 Shear wave elastography of the cervix.

(A) Shear wave velocity is reduced indicating soft cervix. (B) increased velocity indicating the hard cervix

Quantitative analysis of the cervical texture by Ultrasound.

Quantitative analysis of tissue texture in images was the main application point of AI in the evaluation of cervical insufficiency. Investigators from Spain applied the quantitative analysis of cervical texture in the evaluation of cervical tissue changes during pregnancy. A total of 18 features were extracted from each ultrasound image and area of interest, and a prediction model of GA based on features from the cervical image was established through data segmentation, feature transformation, and model calculation, which indicated that there was a strong correlation between cervical ultrasound images and GA. Based on the low specificity of cervical length for the assessment of cervical function, these investigators adopted the feature combination learning algorithm based on feature transformation and regression, selected the area of interest in the middle of the labium anterius, established the CTx score, and confirmed that the CTx score of pregnant women with a short cervix and term delivery was higher than that of pregnant women with a short cervix and premature delivery. This technique provided support for predicting the risk of premature birth in pregnant women with a short cervix.

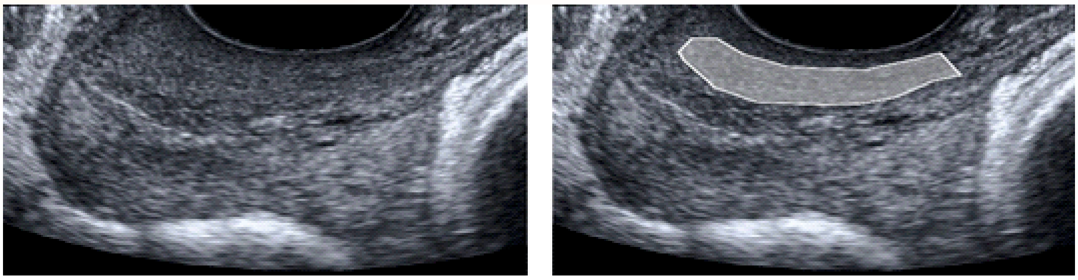

Figure 4 Sagittal view of cervix (a) and delineation of anterior cervical lip (b)

In addition to texture analysis, the application of proteomics to predict premature birth has also been useful. A previous study combined AI, proteomics, metabolomics, and ultrasonography, and used a variety of machine learning technologies, which included deep learning, to predict preterm birth, preterm latency, and neonatal treatment time in the NICU during the second trimester. Despite the small sample size, the study confirmed that deep learning had an advantage over other types of machine learning in the processing of complex data in the multifactorial prediction of cervical insufficiency.

The combination of AI and ultrasonography is assisting clinicians in the diagnosis of a variety of conditions and diseases, as it can improve efficiency, reduce the rates of misdiagnosis and missed diagnosis, effectively improve the quality of medical services, and ultimately benefit patients. Presently, significant achievements have been made in the application of AI in the fields of obstetrics and gynaecology, but the universality and effectiveness of many models still require further studies.

Artificial intelligence (AI) can support clinical decisions and provide quality assurance for images. Although ultrasonography is commonly used in the field of obstetrics and gynaecology, the use of AI is still in a stage of infancy. Nevertheless, in repetitive ultrasound examinations, such as those involving automatic positioning and identification of fetal structures, prediction of gestational age (GA), and real-time image quality assurance, AI has great potential. To realize its application, it is necessary to promote interdisciplinary communication between AI developers and sonographers.

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Genomic Diagnostics: The Limitless Potential of Artificial Intelligence

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The field of genomic diagnostics can greatly benefit from AI's capabilities. The application of AI to healthcare may be advantageous for genetic diagnoses.

Ironically, about half a billion people around the world suffer from a lesser known form of diseases, making rare diseases very common. Such disorders can be difficult to identify since common clinical diagnostics frequently miss important information about them. Additionally, genetic problems in people are the root cause of practically all rare disorders. Therefore, gene-based disease diagnoses that are quick and precise are essential in today's healthcare. However, a study found that it can take over five years on average for such a disorder to be adequately diagnosed, which means that roughly a third of children with one or more uncommon genetic disorders will lose away before they turn five.

Despite a few drawbacks, the application of AI in healthcare has largely benefited the industry and the technology. AI is ideally suited for a field as diverse and complex as healthcare because of its capacity to comb through enormous datasets and offer clarity for judgment through its unmatched pattern and anomaly recognition abilities.

The use of AI in the diagnosis of disorders caused by genetic anomalies is still developing. Recognizing these applications will help us predict how AI will progress in this area going forward. Here are some of the known applications of AI in genomic diagnostics:

Computer Vision-based diagnosis

A software called Face2Gene uses deep learning algorithms and computer vision to identify rare genetic disorders. The software is based on the idea that a number of congenital disorders can be easily identified in patients by looking at their facial features. In this application, rare genetic disorders are identified using AI's pattern recognition capabilities. The software applies a trial-and-error process to reduce the range of potential disorders in patients. The list of ailments is displayed on a screen once a face has been scanned, with the most obvious diagnosis typically appearing at the top.

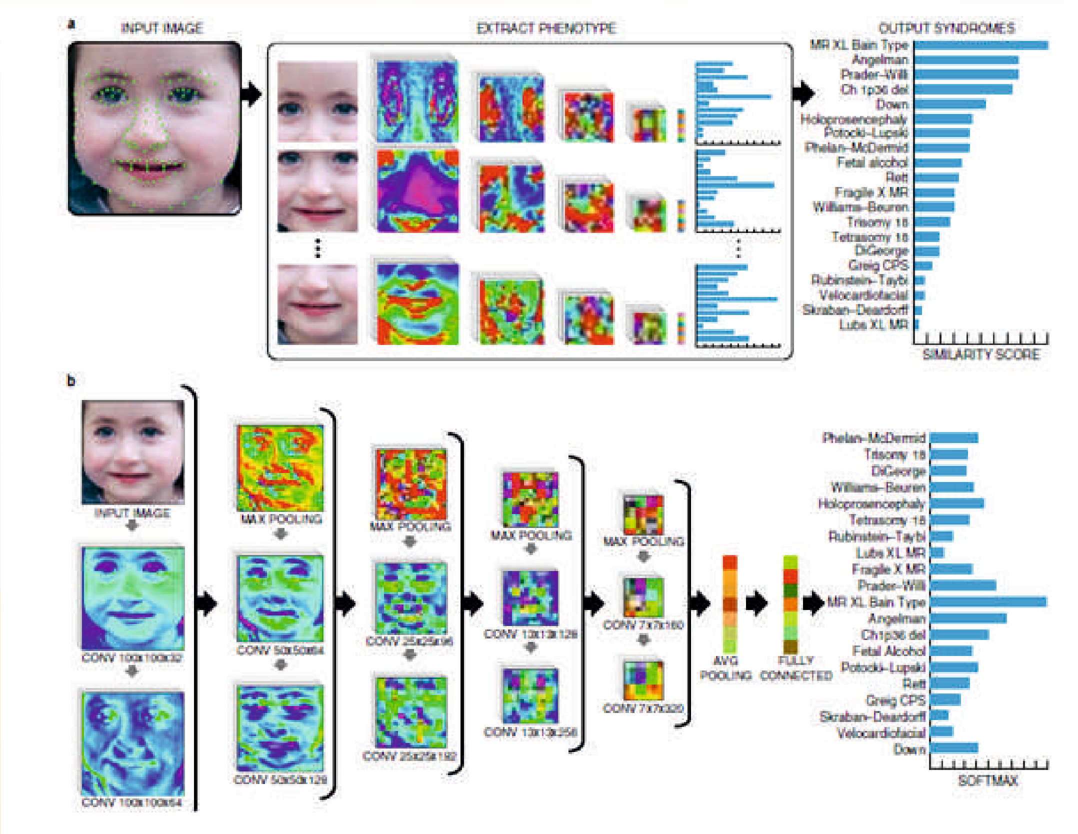

Figure 1: *DeepGestalt: high-level flow and network architecture.* ***a****, A new input image is first pre-processed to achieve face detection, landmarks detection and alignment. After preprocessing, the input image is cropped into facial regions. Each region is fed into a deep convolutional neural networks (DCNN) to obtain a softmax vector indicating its correspondence to each syndrome in the model. The output vectors of all regional DCNNs are then aggregated and sorted to obtain the final ranked list of genetic syndromes. The histogram on the right-hand side represents DeepGestalt's output syndromes, sorted by the aggregated similarity score.* ***b****, The DCNN architecture of DeepGestalt. A snapshot of an image passing through the network. The network consists of ten convolutional layers, and all but the last are followed by batch normalization and a rectified linear unit (ReLU). After each pair of convolutional (CONV) layers, a pooling layer is applied (maximum pooling after the first four pairs and average pooling after the fifth pair). This is then followed by a fully connected layer with dropout (0.5) and a softmax layer. A sample feature map is shown after each pooling layer. It is interesting to compare the low-level features of the first layers with respect to the high-level features of the final layers; the latter identify more complex features in the input image, and distinctive facial traits tend to emerge while identity-related features disappear.*

Source: *Identifying facial phenotypes of genetic disorders using deep learning, published in Nature Medicine*[2]

With the use of this information, individuals and healthcare professionals can corroborate the application's findings by seeking a second, possibly more qualified opinion and diagnosis. The application's inability to provide conclusive diagnoses for patients is one of its limitations, necessitating confirming diagnoses from medical specialists after receiving a report from the app.

Augmented Intelligence

The other form of AI is used that can rapidly and precisely can diagnose rare disorders in critically ill infants. Annually, approximately 7 million infants are born with serious genetic disorders around the world. Life generally starts in intensive care for these children. Genetic Laboratories and scientists are now searching for genetic causes of disease by reading, or sequencing, the human genome's 3 billion DNA letters. While it takes hours to sequence the entire genome, diagnosing the disorder can take days or weeks of computational and manual analysis.

Machine learning is a very innovative method for identifying anomalies in an individual's genetic makeup. In order to obtain the most accurate data, several applications for gene-based diagnostics incorporate the AI component. To rapidly and accurately identify genetic diseases, researchers have created a machine learning-based method that also employs Natural Language Processing (NLP). The process, referred to as "augmented intelligence". The genomic sequencing of neonates is monitored using this procedure to determine whether recently born infants have any rare genetic disorders. The procedure, which was formerly known as rapid Whole Genome Sequencing (rWGS), is developed to shorten the time it takes to identify genetic defects using test subjects' blood samples.

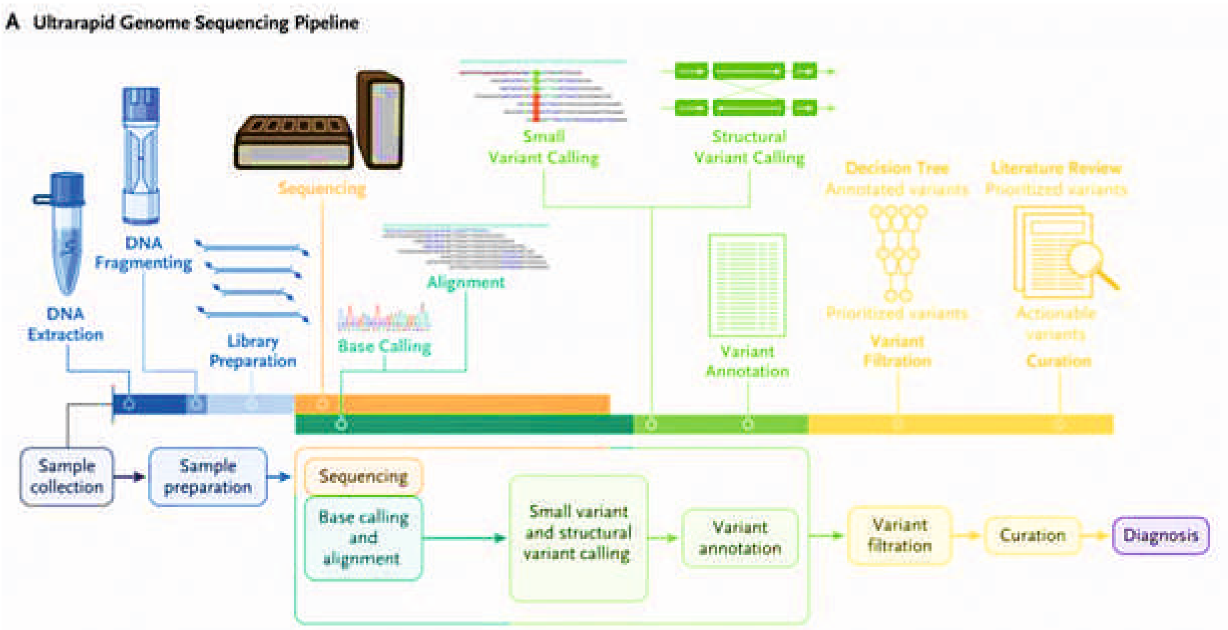

Figure 2: Panel A shows the ultrapid genome sequencing pipeline, indicating all processes from sample collection to a diagnosis. Vertically stacked processes are run in parallel. Source: Ultrarapid Nanopore Genome Sequencing in a Critical Care Setting was published in the New England of Medicine[3.]

Challenges and limitations of AI in Genomic Diagnosis

AI-based algorithms' capacity to decipher complicated data can be on a par with human intelligence. However, when used to data on human health, their strength and complexity can also lead to erroneous or even immoral and discriminatory judgments. The utility of these systems in clinical diagnosis is constrained without careful evaluation of the techniques and biases ingrained in a trained AI system. We thus conclude with a review of the difficulties and restrictions faced by AI in clinical diagnosis.

AI interpretability

For low-risk operations with flexibility for trial and error, the lack of transparency might not pose a significant issue. Healthcare-related operations, as we are all too well, do not fall under that heading. In fact, failing to comprehend how certain medical decisions were made may cause the loss of life. The "why" is an integral component of all varieties of medical procedures; as a result, the inexplicability of crucial judgments made by AI in healthcare prevents its application in the field of genomics. Human genetics, as we all know, involves billions of data strands, making it the most challenging area in healthcare. Due to the complex structure of our genetics, healthcare professionals would be unable to understand how certain diseases were diagnosed if tests were not easily interpretable

Regulatory Issues

A crucial component of the use of AI in any industry is governance. From the prior argument, it follows that regulatory authorities like the FDA would find sufficient justifications to prevent the use of AI in genetic diagnostics due to the technology's lack of explainability, transparency, and examples of bias.

As a result, AI in the field of genetic diagnostics will be very limited until data scientists and other tech specialists find solutions to the other issues with AI in healthcare.

As commonly known, AI possesses a wide range of attributes that enable it to succeed in virtually every industry. Its involvement in the field of genomics is also quite interesting for the future, as can be seen from the two applications mentioned above. But for the time being, AI's typical limitations keep it from becoming the dominant force in the field of genomic diagnostics.

Conclusions and future directions

Modern approaches have been outperformed by AI systems, which have acquired FDA approval for a number of clinical diagnostics, particularly imaging-based diagnostics. This increase in productivity is being caused by the availability of big training datasets, such as libraries of annotated medical images or massive functional genomics datasets, as well as improvements in AI algorithms and the GPU systems required to train them. The AI extraction of deep phenotypic data from images, electronic health records, and other medical equipment to guide subsequent genetic analyses appears to be one of the most potential applications of AI in clinical genomics at the moment. Given that AI relies on extensive training datasets, it is probable that scaling up the gathering of phenotypic data rather than genetic data will provide the bigger challenge to achieving this goal. Modern DNA sequencing technology enables the consistent and large-scale generation of genomic data, however the gathering of phenotype data necessitates a variety of data collecting methods and is frequently time-consuming, costly, and highly variable among collection sites. Finally, for AI technology to be widely accepted in any clinical diagnostic modality, the interpretability and detection of machine bias are crucial.

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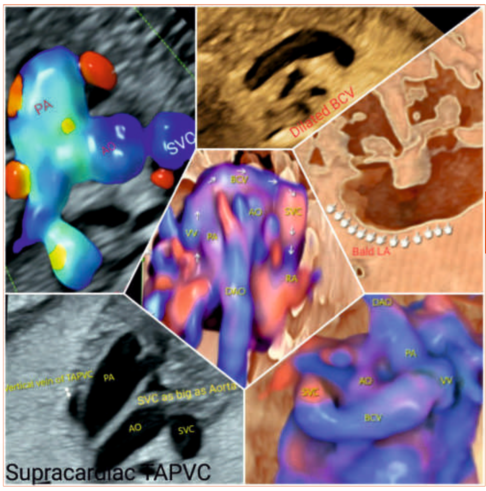
National Image Contest
Episode 3: SFM Bengal's Flagship Initiative

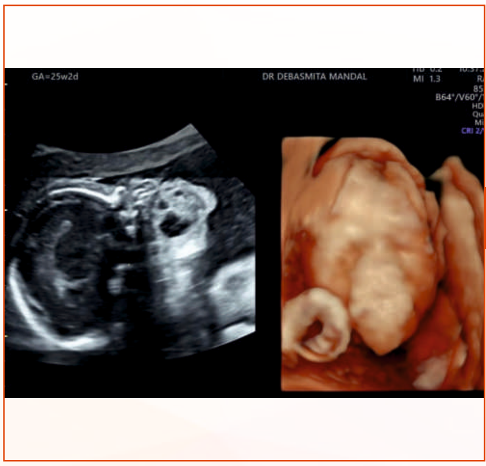
Image Contest run by SFM Bengal Chapter is being a big hit among the Fetal Medicine practitioners. This time we had **16 entries from various parts of the country**. The submitted images were anonymised before being presented to the respected judge. This time we had **Prof. Kamal Oswal, HoD, Radiology** at the Ramkrishna Mission Seva Pratisthan Kolkata to choose the best two.

The top two submissions came from:



Dr. Manoj Jadhav
MD Consultant Radiologist
Practicing at Taluka Place in rural Maharashtra

Supracardiac TAPVC at 30 weeks



Prof. Dr. Debasmita Mandal
Director Krishnaya Institute of Cardiac & Fetal sciences, Kolkata

Epignathus at 25 weeks

Many congratulations to the winners. The Bengal Team remains grateful to all those who have been kind enough in participating for this contest. It has been a daunting task for the judge to pick only two as the standards were very high. We look forward to having your images in the future episodes too.

Happy Imaging.

We thank our esteemed authors who despite their busy schedules spent valuable time to write for our newsletter.

We are grateful to our media partner
Conferences International,
without whose support we couldn't have published this newsletter.