INTRODUCTION

Congenital abnormalities account for 20-25% of perinatal deaths. Now, many genetic and other disorders can be diagnosed early in pregnancy. Prenatal diagnosis uses various noninvasive and invasive techniques to determine the health of, the condition of, or any abnormality in an unborn fetus. Techniques of fetal visualization are:

- **Noninvasive techniques**; Ultrasound, Fetal echocardiography, Magnetic resonance imaging (MRI).
- **Invasive techniques**; Embryoscopy, Fetoscopy ***(Glenn, 2010).***

The central nervous system is a common site for congenital anomalies. Neural tube defects (NTDs) such as anencephaly and spina bifida, which result from failure of closure of the neural tube during embryonic Development. Central nervous system (CNS) malformations are the second most frequent category of congenital anomaly, after congenital heart disease ***(Stevenson et al., 2008).***

Ultrasound (US) detection of prenatal central nervous system (CNS) anatomic anomalies is very important in making decision about therapeutic termination. It is a non-invasive technique, which is more acceptable by patients. Several studies have shown an accuracy of 92% to 99.7% for US detection of CNS anatomic anomalies ***(Tahmasebi et al., 2007).***

The neural tube formation starts during the fourth week (22 - 23 days) after fertilization and fuses approximately between the days 25th and 27th.

Diagnostic sonography can show a detailed visualization of the fetal intracranial anatomy such as cerebral hemispheres, midbrain, thalami, and lateral ventricles. They also can measure the ratio between lateral ventricular and cerebral hemispheric width.

It gives an excellent window for viewing and evaluating the fetal central nervous system during the second trimester through the lateral ventricles and transthalamic view, thus effectively contributing in the diagnosis and treatment of its congenital anomalies ***(Alsharif et al., 2015).***

In many countries, the 11 – 13 weeks ultrasound scan has been introduced in routine screening programs as it allows to determine gestational age, confirm number and location of pregnancies and is used as a screening for aneuploidies. Due to advances in ultrasound technology and increasing sonographer familiarity with scanning in early gestation, many fetal malformations can now be detected in the first trimester ***(Van Mieghem et al., 2015).***

First trimester evaluation of the fetal central nervous system is difficult, as this organ system evolves considerably over gestation. Although the transabdominal approach is most

frequently used in routine screening, complementing it with a transvaginal scan is often useful in early pregnancy. Indeed, even though transvaginal probes cannot be manipulated with as many freedom as transabdominal probes, they are closer to the fetus and have better resolution ***(Lim et al., 2013).***

3D/4D ultrasonography has been used as an adjunctive imaging modality to 2D ultrasonography. Thus, the current paradigm consists of performing 3D/4D ultrasonography as part of a target scan, after an initial diagnostic impression has been established by 2D ultrasonography ***(Bornstein et al., 2008).***

Three-dimensional (3D) ultrasonography has been increasingly used for examination of the human fetus. This technology allows examiners to move from a 3D mental reconstruction of two-dimensional (2D) images to actual 3D/4D visualization of anatomical structures ***(Tahmasebi et al., 2007).***

AIM OF THE WORK

To determine the extended Imaging of 3D, 4D ultrasonography in prenatal assessment of anatomical structure of central nervous system and early diagnosis of the CNS congenital anomalies.

EMBRYOLOGICAL DEVELOPMENT OF THE CENTRAL NERVOUS SYSTEM

EMBRYOLOGY REVIEW

During weeks 2 to 6 of gestation the neural tube development occurs and proceeds through a complex, multi-step process. There is still a great deal unknown about the formation of the neural tube and the mechanism of associated defects. The defects in this process that lead to impaired formation of paraxial mesodermal, ectodermal, or neuroectodermal structures lead to Craniospinal dysraphism. A general knowledge of this process allows for a better understanding of these anomalies. A brief review of the relevant steps and prevailing theories is presented here ***(Matthew et al., 2015).***

GASTRULATION

The process by which the bilaminar embryonic disc becomes trilaminar known as Gastrulation, which consisting of endoderm (future gut lining), mesoderm (future muscle, bone, cartilage, vasculature, and dermis), and ectoderm (future epidermis, skin adnexea, and nervous system)., a neurenteric canal also forms During gastrulation, which is a temporary connection between the dorsal and ventral surface of the trilaminar disc. Split cord malformations and neurenteric cysts

are thought to arise from a persistent accessory neurenteric canal ***(Matthew et al., 2015).***

Primary Neurulation and Disjunction

The formation of the brain and spinal cord to the midsacral region known as Primary neurulation (Fig. 1). A special collection of mesodermal cells in the midline forms the notochord, which induces the overlying ectoderm to differentiate into neuroectoderm. The neuroectoderm begins as a neural plate that invaginates centrally and folds upward to fuse in the midline and form the neural tube. Current data suggest that this is a discontinuous process that is initiated at multiple closure sites and then proceeds in a zipper-like fashion bi-directionally ***(Matthew et al., 2015).*** Defects in primary neurulation lead to Open NTD ***(Copp, 2013)***.

The neural tube separates from the surface ectoderm in a process known as disjunction this occur at the end of primary neurulation. Premature disjunction may allow mesodermal infiltration, leading to closed defects such as lipomyelomeningocele ***(Matthew et al., 2015).*** Incomplete disjunction may be the cause of a dermal sinus ***(Martınez-Lage et al., 2010).*** As disjunction occurs, the mesoderm migrates between the neural tube and surface ectoderm to form the meninges, vertebrae, skull, and paraspinal muscles. Neural crest cells are also involved in the formation of some craniofacial bones and portions of the meninges. Cephaloceles may represent a

postneural tube closure defect resulting from impaired interposition of mesoderm between the ectoderm and neural tube ***(Copp et al., 2013)***.

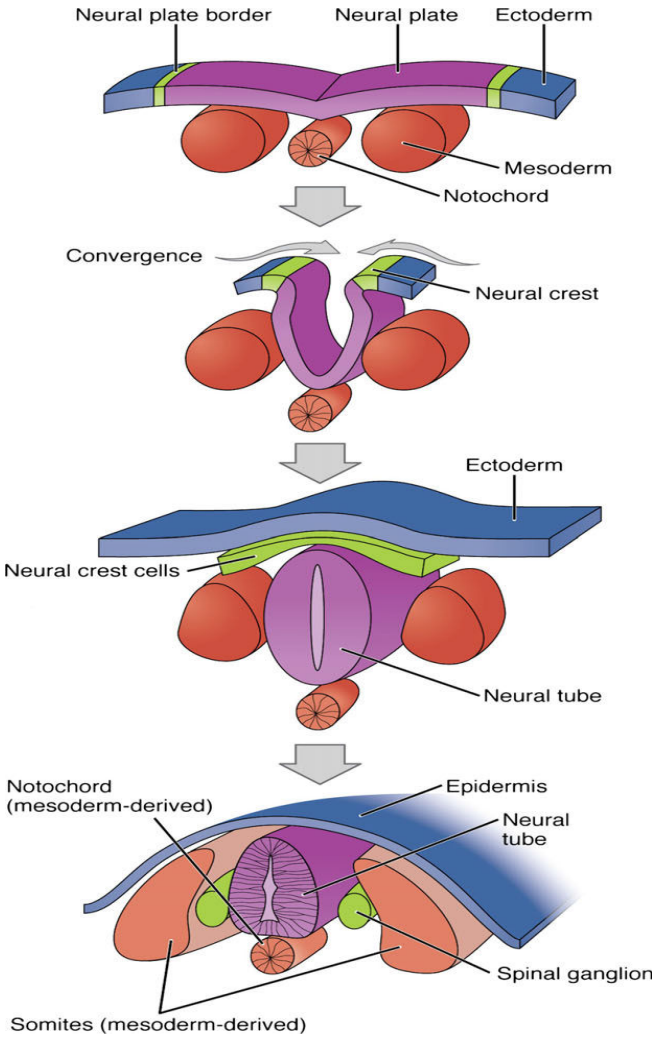

Figure (1): Primary neurulation ***(Matthew et al., 2015).***

Secondary Neurulation and retrogressive differentiation

The formation of the spinal cord caudal to the midsacral region is the Secondary neurulation (Fig. 2). There is a condensation of multipotent cells that coalesce in this region to form the tail bud. The secondary neural tube formed when this solid mass of cells undergoes canalization, which connects with the primary neural tube. The caudal portion of the tail bud undergoes regression and differentiation, known as retrogressive differentiation to form the conus medullaris (lower spinal cord) and filum terminale. The multipotent cells are also the source of all other nonepidermal tissues in this region, which may explain the presence of several tissue types in anomalies of the lower sacral and coccygeal area.

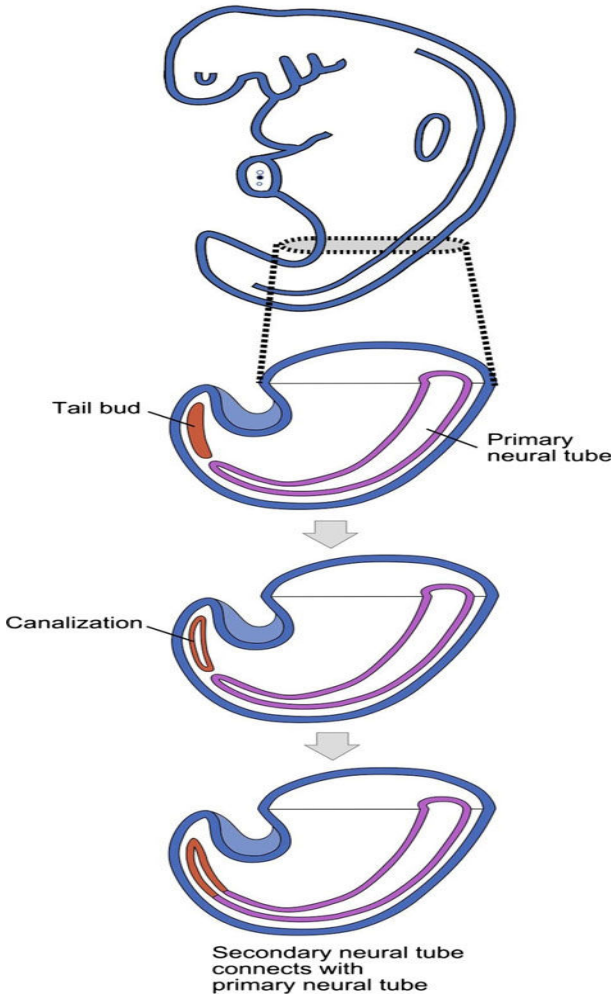

Figure (2): Secondary neurulation ***(Matthew et al., 2015).***

Defects in secondary neurulation give rise to closed defects such as tight filum terminale ***(Copp et al., 2013).***

Neuronal proliferation and migration:

Cell proliferation within the tube leads to thickening of the wall and many different cell types move to their correct locations ***(Verity et al., 2003).***

Up to 6 weeks of development, the neuroepithelium from which the brain and spinal cord arise appears as a homogeneous tissue comprising of neuroepithelial cells. During the following weeks, some zones become recognizable histologically: (i) the ventricular zone, which is composed of ventricular cells and dividing neural precursor cells; (ii) the subventricular zone; (iii) the intermediate zone, through which neurous migrate radially along radial processes; (iv) the subplate; (v) the cortical plate, where postmitotic neurous condense and will become layers **II-VI** of the mature cortex; and (vi) the marginal zone, the superficial layer important for establishing the laminar organization of the cortex.

Cortical neurous are generated in the ventricular zone, migrate radially and reach their destination. The radial migration is the mechanism by which developing neurous move along associated radial glial cells ***(Shiota, 2008).***

Myelination

For proper function of the axons of the fiber tracts it needs to be mylinated. Myelination in the CNS is occurring by oligodendrocytes, whereas that in the peripheral nervous

system (PNS) depends on neurilemmal cells derived from the neural crest. myelination is a rather slow process, and the earliest myelination is noted at the motor roots of the spinal cord around the 5th weeks of development and it proceed caudorostrally. In the brain stem, myelination starts at 8th weeks of development. The vestibulospinal tracts become meylinated at the end the second trimester, whereas the pyramidal tract begin at the end of the third trimester. myelination in these tracts is not complete until after birth and the rate of myelin deposition is greatest during the first two postnatal years ***(Shiota et al., 2015).***

PHYSICAL PRINCIPLES OF 3D/4D ULTRASOUND

Various 3D images are obtained through the following processes:

- ***Acquisition of 3D data***
- ***Construction of a 3D data set***
- ***Volume visualization***

Acquisition of 3D data:

The output from the video capture card is a real-time video stream and each frame is a full screen view of the ultrasound scanner.

Due to the undesirable boundary (i.e. description information like patient's name and exam date) in the full screen image, it is necessary to crop the undesirable boundary using the rectangle cropping tools provided in our data acquisition software system before performing the procedure of data acquisition. The selected area defines a ROI region for our following data acquisition.

The ROI represents a mask in our implementation and all other regions in the following video frames are masked out by the selected ROI. Fig.3 demonstrates the selection of ROI. From Fig. 3 we can see that the collected B-scans for following

volume reconstruction are the cropped images but not the full screen image frames ***(Tiexiang et al., 2013).***

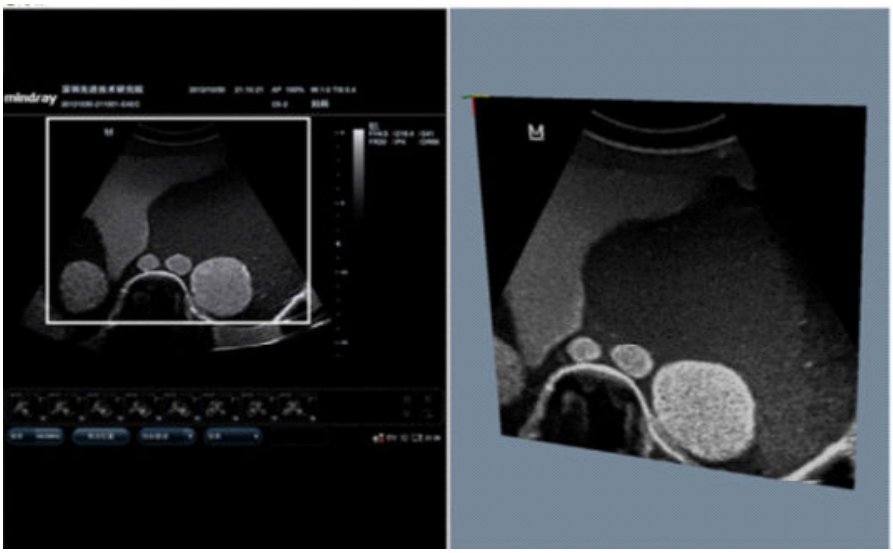

Figure (3): The selection of ROI in our custom-designed software system. On the left view pane, it demonstrates a rectangle selected ROI in B-scan video frame captured from ultrasound scanner. On the right view pane, it is the cropped ROI with its position and orientation adjusted in real-time according to the labeled spatial data during data acquisition ***(Tiexiang et al., 2013).***

Constructing 3D ultrasound images:

A number of approaches for constructing 3D ultrasound volume data have been reported and empirically evaluated in ***(Tiexiang et al., 2013).***

These approaches can be grouped into three categories:

- Dedicated 3D probes,
- Mechanical scanning approach,
- Freehand scanning approach.

Although the systems using 3D probes usually equip an oscillating mechanism to sweep a predefined region of interested (ROI) and can provide 3D volume data in real-time, they are expensive and have limitation on scanning large volume organs ***(Tiexiang et al., 2013).***

The mechanical scanning based systems usually use the conventional 2D transducer, which is translated or rotated by a stepping motor whose position and orientation data are recorded synchronously in the scanning heads ***(Toonkum et al., 2011).*** However, the mechanical scanning devices are usually limited by their scanning range ***(Huang et al., 2005).***

For freehand 3D ultrasound, conventional 2D probe is integrated with a positioning sensor for labeling position and orientation of each B-scan image Freehand 3D ultrasound has received increasing attention for its low-cost, inherent flexibility nature in comparisons with the dedicated 3D probes and mechanical scanning approaches ***(Tiexiang et al., 2013).***

Freehand scanning allows the user to manipulate the transducer and view the desired anatomical section freely. During freehand scanning, the 2D probe is manipulated by hand in an arbitrarily manner. A sequence of B-scan images are then captured along with its corresponding position and orientation. The collection of irregularly sampled B-scan images is then used to reconstruct 3D regular grids (i.e. volume data) by various interpolation or approximation algorithms ***(Tiexiang et al., 2013).***

Volume visualization:

The availability of three-dimensional images from CT and MRI systems has stimulated the development of many algorithms to help physicians and researchers visualize and manipulate three-dimensional medical images interactively.

Because US images suffer from shadowing, poor tissue–tissue contrast and image speckle, the display of a three-dimensional US image plays a dominant role in the ability of a physician to obtain the required information efficiently. Although many three-dimensional US display techniques have been developed and used, two of the most frequently used techniques are:

- Multi-planar reformatting (MPR).
- Volume rendering (VR).

(Fenster et al., 2011)

Multi-planar reformatting:

The MPR technique is the most commonly used three-dimensional US viewing approach. In this technique, two-dimensional US planes are extracted from the three-dimensional US images and displayed to the user with three-dimensional cues.

Users interact with a user interface utility by moving the planes to view the desired anatomy. Three MPR approaches are