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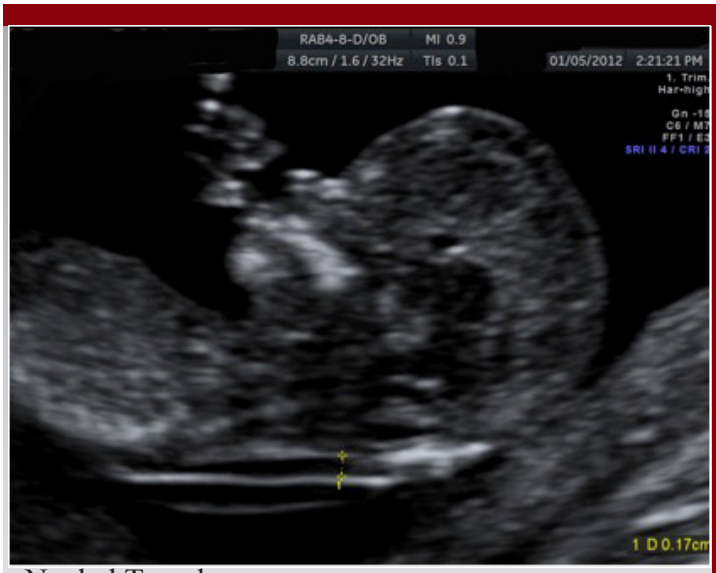
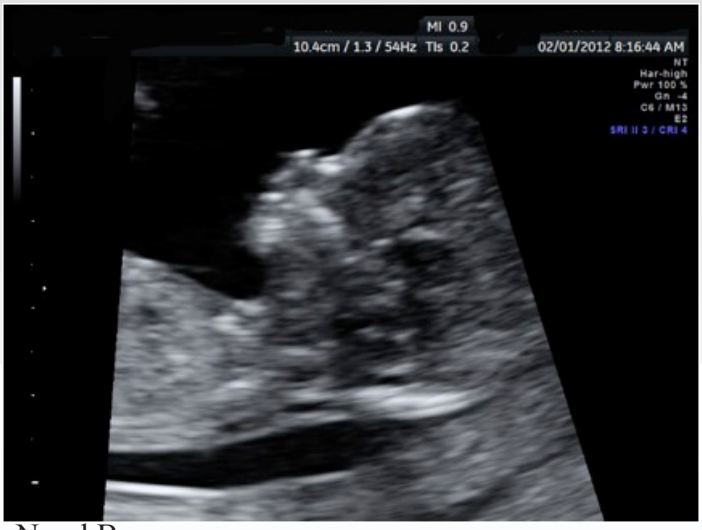


Nuchal Translucency



Nasal Bone

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WHAT's WRONG WITH THESE IMAGES

by Bryann Bromley, MD,
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The images themselves are good examples of the required components for measuring the nuchal translucency (NT) and evaluating the nasal bone (NB). The problem with these images is that the practitioner has overlooked their responsibility of adhering to the ALARA principle.

ALARA is an acronym that stands for *As Low As Reasonably Achievable* and is the fundamental principle of using diagnostic ultrasound to obtain good quality images at an acoustic output level that is as low as possible. While there is no evidence that appropriately used diagnostic ultrasound produces harm in the developing fetus, there is the potential for an unrecognized risk.

Most studies on fetal bioeffects were conducted on equipment manufactured prior to 1992, when the FDA limited output for obstetrical exams to 94mW/cm^2. In 1992, in the interest of improving the diagnostic capabilities of imaging systems, the FDA increased this limit to 720 mW/cm^2. Concurrently, they required that manufacturers display an indication of the potential for ultrasound-induced bioeffects. This is referred to as the Output Display Standard (ODS) and consists of an on-screen display of the Thermal Index (TI) and Mechanical Index (MI). While manufacturers will provide "default settings" for specific obstetrical indications, the output is under the control of the imager. It is therefore the responsibility of the imager to consider the safety of the fetus and obtain a diagnostic image while adhering to the ALARA principle.

For *obstetrical* ultrasound, the primary concern for potential injury is the heating of tissue as a result of energy absorption. The TI provides a *relative* indication of the temperature rise in the tissue being examined. Mathematically, TI is a ratio of the

emitted power to the power that would be necessary to raise the temperature of the tissue by 1^0 C. The index is modeled to take into account that temperature rise depends on many factors including the scanning mode, duration of exposure and the type of tissue being evaluated. For example, bone absorbs significant energy and this increases the likelihood of a temperature rise, furthermore, the heat is conducted to the adjacent soft tissue. Clinically, this results in two different TI displays for *obstetrical* imaging. The TI for soft tissue (TIS) which assumes that the ultrasound beam only crosses through fluid and soft tissue and the TI for bone (TIB) which takes into consideration the presence of bone within the imaging field. For both of these settings, the maximum temperature is at the focal point of the ultrasound beam.

Prior to 10 weeks gestation (from LMP) the TI for soft tissue (TIS) is used. Thereafter, bone ossification is evident and the TI for bone (TIB) is used to monitor the potential thermal effect. There has been debate as to a specific value of TI that should be used to limit risk. In general, a TI of < 0.5-0.7 is considered safe for an "extended" period of scanning. Spectral and Power Doppler may increase the TI significantly, and should only be used in the first trimester if clinically indicated. Higher TI values should be approached cautiously with a clear understanding of the potential risks and the benefits of the information being sought.

The MI is the mechanical index and is an indicator for non-thermal effects such as cavitation. This is not a significant consideration in fetal imaging due to the absence of gas bodies and the contraindication of contrast agents. Nevertheless, MI values should be kept low as theoretical bioeffects are always possible.

Now, look back at the images and you will notice on the ODS on the top of each image demonstrates that the fetus was scanned using a TI for soft tissue, and therefore, the operator can't adequately assess the thermal risk that is occurring given the presence of bone. Similarly, the power need not be at 100%.

Ultrasound should be limited to clinically-indicated examinations and be performed by qualified personnel. The ODS must be observed, and the TI/MI correctly set by the practitioner based on the gestational age of the fetus. For the NT exam (11-14 weeks), the TI for bone should be used. The TI and MI values chosen should be as low as possible, while still achieving a diagnostic image. The extent of fetal exposure is another consideration, and the ultrasound beam should not be kept in one place for a prolonged period of time. The exam should be as expeditious as possible within the parameters of obtaining a diagnostic image.

To check your own settings, you must understand the "knobology" of your own system. Refer to your user manual or call your application specialist. In the event that the transducer and system is not capable of exceeding an MI or TI of 1, no display is required.

Below are references that are excellent for further education on the important principle of ALARA and biosafety.

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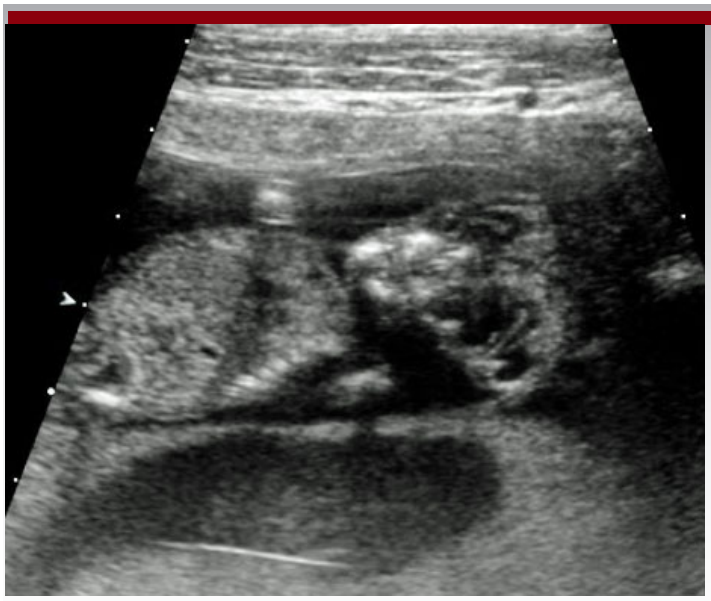

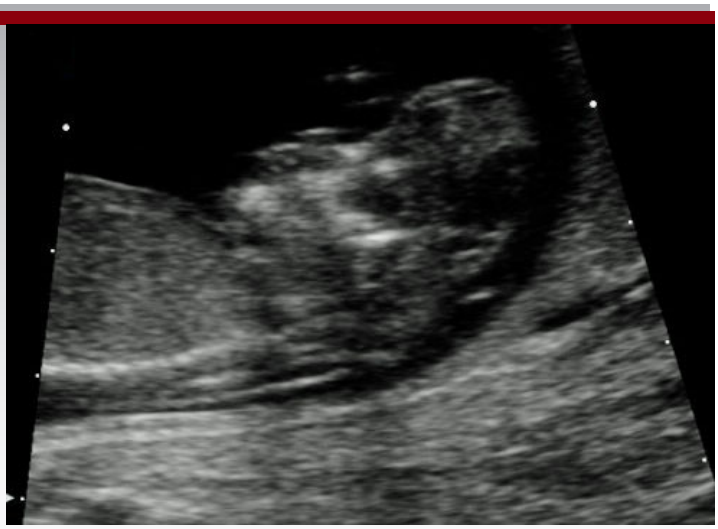

Anencephaly imaged during the first trimester.

BEYOND ANEUPLOIDY SCREENING:
ADDITIONAL BENEFITS OF 1ST TRIMESTER COMBINED SCREENING

Karin Fuchs MD and Mary D'Alton MD

Over the last decade, first trimester combined screening using the nuchal translucency measurement and serum analyte concentrations has become the mainstay of aneuploidy screening for women presenting for prenatal care early in gestation. The emergence of non-invasive prenatal testing for fetal aneuploidy using cell free fetal DNA, however, has led many to question the role of first trimester combined screening for aneuploidy in the future. Although their role in aneuploidy screening may eventually be usurped by other methods, the individual components of the first trimester combined screen, the 11-14 week ultrasound, the nuchal translucency measurement itself, and serum screening, each offers valuable information that justifies their continued performance.

One of the most valuable benefits of the 11-14 week ultrasound is confirmation of pregnancy dating. Gestational age is defined as the time that has elapsed since the first day of a patient's last menstrual period, and includes a period of time that precedes both ovulation and conception. Because of the variation in the length of menstrual cycles between women and because of the recall bias inherent in a patient's memory of the first date of her last cycle, menstrual dating is prone to error. Ultrasound, however, can provide a more accurate estimate of gestational age and pregnancy dating, especially when performed in late first trimester. Although ultrasound measurements are also associated with an underlying margin of error, ultrasound dating is most accurate in the mid- to late- first trimester with margins of error of $\pm$ 3 days from 7-10 weeks of gestation and $\pm$ 5 days from 10-14 weeks'.[1] Accurate dating is vital to countless aspects of pregnancy management including determination of the timing of diagnostic procedures (i.e. CVS and amniocentesis), interpretation of biochemical assays used in serum screening, administration of antenatal steroids and other interventions to prevent preterm birth, and determination of delivery timing. Use of early ultrasound to determine pregnancy dating has been associated with increased rates of preterm delivery and decreased rates of induction of labor for postterm pregnancy.[2,3]

First trimester ultrasound also plays a vital role in the early detection of multiple gestations and in the accurate determination of chorionicity. Several studies have demonstrated that when routine ultrasound is not performed early in pregnancy, a significant number of twin pregnancies are not recognized until the third trimester which prevents the opportunity for increased surveillance early in gestation and which may delay appropriate intervention when complications develop. Because monochorionic multiples, whether diamniotic or monoamniotic - are at increased risk of several adverse outcomes, prenatal determination of chorionicity

and amnionicity is essential to guide the clinical management of multiple gestations. Although sonographic determination of chorionicity in dichorionic gestations becomes less reliable later in pregnancy due to the fusion of placental discs and thinning of the intertwin membrane, sonographic determination of chorionicity has its highest sensitivity and specificity prior to 14 weeks' gestation. Specifically, from 6 to 10 weeks', chorionicity can be determined by the number of gestational sacs whereas the number of yolk sacs can be used to predict amnionicity. Later in the first trimester, systematic evaluation of placental number, fetal gender, and the insertion of the intertwin membrane into the placenta allows accurate prenatal diagnosis of chorionicity. The "twin peak" or lamba sign, defined as visualization of a triangular projection of placenta between the layers of a thick dividing membrane at their attachment to the placenta > 97% sensitivity and 100% specificity 100 percent in predicting dichorionicity.[4] In contrast, the finding of a "T-sign" with a characteristic thin intertwin membrane inserting directly into the placenta at a 90 degree angle has 100% sensitivity and >98% specificity for detecting monochorionic diamniotic gestations.[4]

In addition to the value of the first trimester ultrasound in pregnancy dating and identification of multiple gestations, the nuchal translucency measurement obtained as part of the 11-14 weeks scan has particular benefit in screening for fetal anomalies. Among pregnancies with nuchal translucencies above 3.5 mm, the overall risk of a major structural malformation is ~ 7% - more than twice the baseline risk. Furthermore, among chromosomally normal fetuses, the risk of a structural anomaly is known to increase with increasing nuchal translucency with a 10% risk of structural malformations with nuchal translucencies from 3.5 - 4.4 mm, 19% for NTs from 4.5 - 5.4 mm, 24% for NTs of 5.5 - 6.4 mm, and 46% for NT > 6.5 mm.[5] Although nuchal translucency above the 99th percentile is associated with a 3% risk of fetal congenital heart disease [6], other malformations are also associated with an increased nuchal translucency including diaphragmatic hernia, renal anomalies, body stalk disruption, and abdominal wall defects. In addition, several malformations – including anencephaly, omphalocele, bladder outlet obstruction - can be detected at the time of the 11-14 week scan. Detection of an increased nuchal translucency should prompt a detailed anatomic survey and fetal echocardiogram in the second trimester; identification of increased risk in the first trimester will improve the likelihood of prenatal detection of fetal structural anomalies and help to ensure adequate time for referral to a tertiary care facility.

Low concentrations of PAPP-A and beta hCG have been associated with many adverse pregnancy outcomes and – beyond their role in screening for fetal aneuploidy – can be used to quantify the risks of fetal loss, preeclampsia, preterm birth, abruption, and poor fetal growth. Specifically, concentrations of either PAPP-A or beta hCG below the 1st percentile are both associated with an increased risk of pregnancy loss at < 20 weeks [OR 5.4 and 8.5], whereas IUGR occurs in 24% of pregnancies with a PAPP-A below the 1st percentile and 14% of pregnancies with a beta hCG below the 1st percentile.[7] Other studies have shown that PAPP-A levels below the 5th percentile are associated with statistically significant increases in the rate of low-birth weight, early and late fetal loss, preterm birth, abruption and hypertensive disorders of pregnancy.[8]

In conclusion, in addition to playing a vital role in aneuploidy screening over the last decade, the individual components of first trimester combined screening offer several additional benefits that affect patient counseling and pregnancy management. Specifically, first trimester combined screening leads to improved pregnancy dating, early detection of multiples and some structural malformations, more accurate determination of chorionicity, and identification of patients at increased risk for fetal anomalies and multiple other adverse pregnancy outcomes. Accordingly, even if the use of cell free fetal DNA becomes widespread, there will continue to be a role for the 11-14 week ultrasound, nuchal translucency measurement, and first trimester serum screening in the foreseeable future.

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IT IS OPEN!!!

CERVICAL LENGTH EDUCATION AND REVIEW (CLEAR)

http://www.perinatalquality.org

The Perinatal Quality Foundation convened a cervix education task force in November 2011. Representatives from multiple organizations including AIUM, ACR, ACOG, ACOOG, SDMS, and SMFM participated. The goal of the task force was to develop consensus education that presented, in a widely available format, the standard criteria for sonographic cervical measurements during pregnancy. The CERVICAL LENGTH EDUCATION and REVIEW (CLEAR) program is a product of task force discussion.

The Cervical Length Education and Review (CLEAR) program provides three lectures, an optional examination, and scored cervical image review. The lectures are available at no charge. Continuing medical education will be available to those who complete the examination. Documentation of completion of the CLEAR program as well as CME will be provided to those who complete the lectures, examination, and pass the image review.

The importance of measuring the cervix correctly has been stressed in multiple recent articles. The CLEAR process provides education regarding standard techniques and allows participants to apply these standard criteria to demonstrate their ability.

Be among the first to participate. Investigate CLEAR at http://www.perinatalquality.org

CLEAR

Cervical Length Education & Review

GENETICS COUNSELOR'S COLUMN
MULTIPLEX CARRIER SCREENING: A PRIMER

by Renee Chard, NSGC

What is multiplex carrier screening?
Advances in molecular genetic technologies have made it possible to screen patients for carrier status of many conditions with one test. Multiplex carrier screening may also be called expanded carrier screening, universal screening, multi-disease carrier screening or high through put carrier screening, and testing panels may include 10-15 conditions to as many as 100 or more. The majority of the conditions follow an autosomal recessive inheritance pattern and some are x-linked conditions.

Who is it for?
Each person carries an estimated 3-5 recessive, disease-causing gene mutations. Traditionally, carrier tests offered to a couple depends on ethnicity and family health history, and some screening panels target a specific population, for example expanded screening panels for individuals of Ashkinazi Jewish ancestry. Others are very broad and designed to be offered to any couple.

Expanded carrier screening may be particularly helpful when one or both members of the couple are adopted and information about family medical history is limited. Finally, consanguineous couples might want to consider expanded carrier screening, due to the fact that there is an increased chance for them to carry deleterious mutations for the same condition.

Multiplex carrier screening might NOT be the appropriate choice for someone with a family history of a specific genetic disorder, even if the condition is on the testing panel. Many genetic disorders can result from many mutations in the same gene, for example over 120 mutations in the HEXA gene are known to cause Tay-Sachs disease, and more than 1500 mutations have been reported in the CFTR gene. In these situations multiplex carrier screening will include common mutations, but not all mutations. So, it is important to confirm that the mutations identified in the affected family member will be on the testing panel.

What should be considered when choosing a panel?
There are several things to consider when choosing a screening test, for example, what is the cost of the test? What are the specificities and sensitivities of the tests? How severe is the condition for which screening is being performed? Is onset in infancy, childhood or adulthood? Is it relevant to family planning? What can be done if a screening result is positive? Does the panel include conditions relevant to my patient's ethnic background?

What are the options if a couple is found to be at 25% risk for a condition?
Options available to couples in which both are found to be carriers of the same condition depends on when this information is discovered. If a pregnancy is already underway, the couple could have chorionic villi sampling or amniocentesis for prenatal diagnosis. When performed preconceptionally, the couple may decide to avoid pregnancy either by remaining without children or by adopting a child, to utilize donor gametes, or turn to assisted reproductive technologies for preimplantation genetic diagnosis. Couples may decide to conceive naturally and have prenatal diagnosis or not have testing at all.

Advances in genetic technologies are opening many doors for patients, but sometimes the information can be confusing. Genetic counselors are uniquely trained to help providers and patients evaluate the options and select the testing that will be best for their situation.

If you would like more information or if you want to make a referral, you can locate a genetic counselor in your area at the National Society for Genetic Counselors' website, nsgc.org, under the find a counselor tab.

RISK CALCULATORS

The Nuchal Translucency Quality Review Program (NTQR) provides an NT-only calculator within participants accounts on the individual's summary page. This page is seen upon log-in or may be found under MY-ACCOUNT/summary on the upper menu after log-in. The calculator uses a model, based on the combination of crown-rump length, maternal age, and NT thickness to estimate Down syndrome risk. This combination is also known as "NT alone" because serum analytes are not utilized. The calculator is a screening tool, it does not provide diagnostic information. American College of Obstetricians and Gynecologists (ACOG) Practice Bulletin Number 77, January 2007 states as a Level A recommendation: "Measurement of nuchal translucency alone is less effective for first trimester screening than is the combined test (nuchal translucency measurement and biochemical markers)." NT alone is inferior to the combination of NT and serum screening tests in estimation of risk in singletons, and may be most useful in high-order multiple pregnancies (i.e. three or more fetuses). The NTQR calculator is versatile and has been used by clinicians for multiples, twins, and in some cases singletons. The results of the calculation are not a substitute for clinical judgment.

Recently a new calculator specifically for twins has been reviewed. This calculator may be accessed at https://screeninfo.co.uk/twins/default.aspx. This calculator takes into consideration the nuchal translucency of the co-twin. The NTQR encourages participants to try this calculator for twins and to send your comments.

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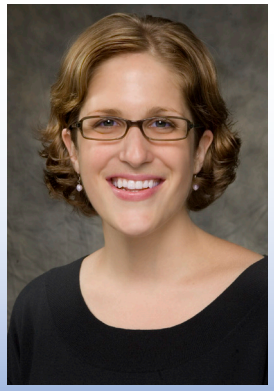

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