SHOULD THE USE OF NIPT AFFECT FIRST TRIMESTER ULTRASOUND PROTOCOLS

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WHAT ARE THE GOALS OF NIPT?

Reduce exposure of fetus to risk
Reduce false positives
Enable a high detection rate

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Reduce false positives
Enable a high detection rate

NIPT TECHNOLOGY OVERVIEW

Data adapted from Wellesley, D, et al., Rare chromosome abnormalities, prevalence and prenatal diagnostic rates from population-based congenital anomaly registers in Europe. 
Eur J of Hum Gen, 1 January 2012.

Prenatal Prevalence of Chromosomal Abnormalities

Percent of Reported Chromosome Abnormalities

Major fetal aneuploidies

Down Syndrome Testing with 5% Screen Positive Rate.

CURRENT DIAGNOSTIC OPTIONS - KARYOTYPE

Trimester - Test | Sensitivity | Specificity
--- | --- | ---
1st - CVS | 99.25% | 98.65%
2nd - Amniocentesis | 99.4% | 99.5%

Definitive answers, but are invasive and come with risk to the patient Most are unnecessary due to the high rate of false positives in screening1,2


FETAL CELL-FREE DNA IN MATERNAL BLOOD

• Released through apoptosis
• Fetal cfDNA likely arises from cytotrophoblastic cells of placenta
• Released into bloodstream as small DNA fragments (150-200bp)
• Reliably detected after 7+ weeks gestation
• Undetectable within hours postpartum

A Reliable Analyte During Pregnancy
Fetal DNA fragments in maternal blood. Cell free DNA fragments are then sequenced. Compare the individual sequenced chromosomes against a reference for analysis.

DNA SEQUENCING USING CELL FREE DNA

TEST PERFORMANCE

<table>
<thead>
<tr>
<th>Aneuploidy</th>
<th>Sensitivity</th>
<th>95% CI</th>
<th>Specificity</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21</td>
<td>99.9%</td>
<td>98.7 – 100.0</td>
<td>99.3%</td>
<td>98.5 – 100.0</td>
</tr>
<tr>
<td>Trisomy 18</td>
<td>97.4%</td>
<td>96.2 – 99.9</td>
<td>99.6%</td>
<td>98.5 – 100.0</td>
</tr>
<tr>
<td>Trisomy 13</td>
<td>87.5%</td>
<td>81.7 – 95.5</td>
<td>99.9%</td>
<td>99.2 – 100.0</td>
</tr>
<tr>
<td>Monosomy X</td>
<td>95.0%</td>
<td>75.1 – 99.9</td>
<td>99.0%</td>
<td>97.6 – 99.7</td>
</tr>
<tr>
<td>XX</td>
<td>97.6%</td>
<td>94.8 – 99.1</td>
<td>99.2%</td>
<td>97.2 – 99.9</td>
</tr>
<tr>
<td>XY</td>
<td>99.1%</td>
<td>96.9 – 99.9</td>
<td>98.9%</td>
<td>96.9 – 99.8</td>
</tr>
<tr>
<td>XXX, XXY, XYY</td>
<td>99.8%</td>
<td>99.2 – 100.0</td>
<td>99.2 – 100.0</td>
<td></td>
</tr>
</tbody>
</table>


NIPT TEST COMPARISON AND WHY FIRST TRI U/S IS IMPORTANT

<table>
<thead>
<tr>
<th>Result Types</th>
<th>Harmony Failure Rate</th>
<th>MaterniT21 Failure Rate</th>
<th>NIPT Failure Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aneuploidy Detected</td>
<td>&lt;0.7%</td>
<td>4.6 – 4.9%</td>
<td>1%</td>
</tr>
<tr>
<td>Aneuploidy Suspected</td>
<td>5.9 – 12.6%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Risk score incorporating maternal, gestational age</td>
<td>Positive</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>Sample</td>
<td>T21, T18, T13</td>
<td>Optional sex chromosome aneuploidies</td>
<td>T21, T18, T13</td>
</tr>
<tr>
<td>Test Menu</td>
<td>Yes (with data)</td>
<td>No</td>
<td>Yes (with data)</td>
</tr>
<tr>
<td>Published Clinical Validation</td>
<td>Large-scale, blinded clinical validation</td>
<td>Large-scale, blinded clinical validation</td>
<td>Large-scale, blinded clinical validation</td>
</tr>
</tbody>
</table>

NIPT AND ULTRASOUND

How it affects

First trimester Ultrasound
Second Trimester Ultrasound
Invasive Procedures

NIPT IS A GAME CHANGER
• Observed an increased uptake of NIPT following abnormal 1st screening compared with abnormal 2nd screening (56% vs 37%)
• This study revealed that women with a positive aneuploidy screening result are influenced by NIPT for their follow-up testing
• When the procedure-associated risk is eliminated, women may be less likely to decline testing

**UPTAKE OF NIPT IN WOMEN FOLLOWING POSITIVE ANEUPLOIDY SCREENING**
CHETTY S, GARABEDIAN MJ, NORTON ME. PRENAT DIAGN 2013; 33: 542-546

**IMPACT OF NIPT IN REGIONALLY DISPERSED MEDICAL CENTERS**

• 6 different regionally based centers, results collected between Feb-Nov, 2012
• 2-proportion Z-test analyses performed
• NIPT performed on 1,477 pts
  - 693 (47%) were from centers in the West
  - 522 (35.3%) were from centers in the East
  - 262 (17.7%) from 1 center in the Midwest
• Statistically significant differences observed between West and non-West coast sites for GA (14.1 wks, p <.0001)
• AMA-only was the most frequent indication in 5/6 sites (range, 21.8-62.9%)

• More invasive procedures were performed following negative NIPT results (n=61) vs. abnormal NIPT (n=30)
• Overall rate of patients undergoing invasive procedure after an abnormal NIPT was 32.6% (30/91)
• All 6 centers reported a decrease of invasive procedures after NIPT indication

**NIPT DECREASED DIAGNOSTIC BUT NON-1ST TRIMESTER SCREENING**
LARION S, MLYNARCZYK M, ET AL. OBSTET GYNECOL 2014; 123 (SUPPL 1): 88S

• Study period April 2010 – March 2013
• 3,794 1st trimester screens + NIPT
• 607 diagnostic tests (CVS, amnio)
• Average # of monthly screening procedures per 100 targeted U/S - not different between any time period or after introduction of NIPT
• Suggesting rate of 1st trimester screening was unaffected by NIPT
• However, average # of monthly diagnostic procedures and procedures/100 targeted U/S significantly declined post-NIPT introduction
• Diagnostic testing and testing/100 targeted U/S also declined by 44.0% and 41.0%, respectively

**EFFECT OF NIPT ON INVASIVE TESTING: EVMS**

• Invasive procedure update by month (7/2010 through 3/2013)

**INVASIVE PROCEDURE UPDATE BY MONTH**
**Impact of Invasive Testing in Patients with a Positive First or Second Trimester Screen**

- Total patients seen 6/1/2010 – 3/31/2013: 808
- Total procedures performed 6/1/2010 – 3/31/2013: 539
- Total singleton, non-ONTD patients seen: 728
- Total singleton, non-ONTD procedures performed: 500

<table>
<thead>
<tr>
<th>Year</th>
<th>Total Patients Seen</th>
<th>Total Procedures Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/31/2010 – 3/31/2013</td>
<td>446</td>
<td>238</td>
</tr>
</tbody>
</table>

**NIPT Status and Declining Invasive Testing**

- NIPT Yes
- NIPT No

**Changing Trends in Prenatal Diagnosis The Platt Experience**

<table>
<thead>
<tr>
<th>Year</th>
<th>Amnio (%)</th>
<th>CVS (%)</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010</td>
<td>8.0</td>
<td>4.0</td>
<td>12.0</td>
</tr>
<tr>
<td>2011</td>
<td>6.0</td>
<td>3.9</td>
<td>9.9</td>
</tr>
<tr>
<td>2012</td>
<td>4.2</td>
<td>3.0</td>
<td>7.2</td>
</tr>
<tr>
<td>2013</td>
<td>3.0</td>
<td>3.3</td>
<td>6.3</td>
</tr>
<tr>
<td>2014</td>
<td>2.89</td>
<td>2.3</td>
<td>5.19</td>
</tr>
</tbody>
</table>

**NIPT -- Sex Chromosomal Aneuploidy**

- Beware of False Positive 45x, 47xxx

1. Maternal Chromosomes
   - A. Known Maternal Aneuploidy
   - B. Unknown Maternal Aneuploidy
2. Offer invasive testing (Amnio)

McNamara et al Ob Gyn Vol 125 no2 Feb 2015 390-392

**Consideration of NIPT for Cystic Hygroma**

- Highly associated with common aneuploidies including monosomy X (Turner syndrome) that are associated with pregnancy loss and are medically significant at birth.

- Prevalence ~1:285

To study, we examined performance of NIPT for patients with cystic hygroma in the MEUSSA study

MPS and Fetal Nuchal Cystic Hygroma

Table 3. Prevalence of Chromosomal Abnormalities in Cystic Hygroma

<table>
<thead>
<tr>
<th>Abnormality</th>
<th>Fetal echography</th>
<th>AMIUSA—High-Risk Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic hygroma</td>
<td>18.0 (3.5)</td>
<td>24.2 (2.4)</td>
</tr>
<tr>
<td>Trisomy 21</td>
<td>46.2 (5.1)</td>
<td>46.1 (3.8)</td>
</tr>
<tr>
<td>Other</td>
<td>1.8 (0.6)</td>
<td>0.5 (0.4)</td>
</tr>
</tbody>
</table>

2ND TRIMESTER “SOFT MARKERS”: WHAT BENEFIT DO THEY HAVE AFTER AN 11-14 WEEK SCAN?

- Retrospective, cohort study
- Fetuses referred for NT/NB screening
- Anatomic survey (screen risk was not known)*
- 9692 fetuses (42 with T21)
  - 28/42 (67%) by 1st trimester US
  - 14/42 (33%) by 2nd trimester US


2ND TRIMESTER “SOFT MARKERS”: WHAT BENEFIT DO THEY HAVE AFTER AN 11-14 WEEK SCAN?

- 14/42 (33%) by 2nd trimester US
- 9 had normal anatomic surveys
  - All had at least one marker
  - 5/9 had thick nuchal fold (but NT < 3 mm)
  - 5 with newly diagnosed anomalies


A-V CANAL DEFECT

Trisomy 21
WHAT ROLE DOES ULTRASOUND HAVE AFTER A CFDNA?

- 35 yo, G2P1 – opted for cfDNA
- First Draw: Non-informative
- Repeat Draw: Positive Trisomy 18
- CRL 56 mm, NT 1MM

WHAT IS THE PROBABILITY THE FETUS HAS T18?

1. ~ 90%
2. ~ 50-75%
3. ~ 25 – 50%
4. Who cares? Just do karyotype!

TRISOMY 18

- Revised Risk = A priori x Positive LR
- 35 y/o – Risk of T18 ... 1:600
- Positive LR = Sensitivity/1-Specificity
- NIPT + T18:
  - Sensitivity = 100%
  - Specificity = 99.6%

\[
\frac{1}{600} \times 100/4 = \frac{250}{600} \\
\text{Probability T18} = 30\%
\]

NORMAL STRUCTURAL SURVEY

- Sensitivity = 90%
- Specificity = 90%

CELL FREE DNA > 10 WKS GA

<table>
<thead>
<tr>
<th>Abnormal</th>
<th>Sensitivity</th>
<th>FPR</th>
</tr>
</thead>
<tbody>
<tr>
<td>T21</td>
<td>99%</td>
<td>0.08%</td>
</tr>
<tr>
<td>T18</td>
<td>96.8%</td>
<td>0.15%</td>
</tr>
<tr>
<td>T13</td>
<td>92.1%</td>
<td>0.20%</td>
</tr>
<tr>
<td>45X</td>
<td>88.6%</td>
<td>0.12%</td>
</tr>
<tr>
<td>Sex chromosome</td>
<td>93.8%</td>
<td>0.12%</td>
</tr>
<tr>
<td>Microdeletion</td>
<td>92 – 97%</td>
<td>&lt; 0.4%</td>
</tr>
</tbody>
</table>

Gil MM et al. Fetal Diagn Ther 2014; 35 (3): 156-73
TRISOMY 18

- Revised Risk = A priori x Negative LR
- Negative LR = 1 - Sensitivity/Specificity
- FISH – normal (disomy for 13, 18, 21; monosomy for X, Y)
- Karyotype: 46XX

\[ \frac{250}{600} \times \frac{10}{90} = \frac{2500}{54,000} \]

\text{Probability T18} = 4.4%

38 YO, G3P0

10 weeks GA

Neg. NIPT

12 WEEK SCAN

TOP: 47XY, POSITIVE T18

REASONS FOR ABNORMAL CFDNA

PLACENTAL (FETAL) AND MATERNAL

- False Positive
  - Confined placental mosaicism
  - Vanishing twin
  - Maternal chromosomal abnormalities

- False Negative
  - Confined placental mosaicism
  - Low fetal fraction of cfDNA ↑ aneuploidy
  - Mosaicism

G1P0 REFERRED FOR COMBINED 1ST TRIMESTER RISK ASSESSMENT AND NB

- Borderline megacystis → Opted for cfDNA

NEGATIVE

46,XY,ROB(13;21)(Q10;Q10)+DIC(13;?13 OR 21)(Q22;Q?)
MINOR MARKERS: NIPT

Fetal imaging: Executive Summary of a Joint Envisio Kennedy Sherber National Institute of Child Health and Human Development, Society for Maternal-Fetal Medicine, American Institute of Ultrasound in Medicine, American College of Obstetricians and Gynecologists, American College of Radiology, Society for Pediatric Radiology, and Society of Radiologists in Ultrasound Fetal Imaging Workshop

“In women who have undergone ... cell free DNA testing, ... the association of isolated soft markers and aneuploidy is generally no longer relevant.”

A PRIORI 1:500

Revised Risk = 1/500 x 2
1/250

Revised Risk = 1/250 x 0.01
1/25,000

Neg. NIPT

MARKERS ASSOCIATED WITH OTHER GENETIC ABNORMALITIES

Absent NB

Nuchal fold

Hyperechoic Bowel

Refer for Genetic Sonogram

NIPT: SCREENING

- False Positives: T18, T21, T13, T22, 45X, sex chromosome
- False Negatives: T18, "45X"
- Patient misperceptions
- Providers misperceptions

1) Negative cfDNA: Decrease risk of DS 100-fold. Difficult to quote residual risk for T13/T18.
2) Positive cfDNA screening: Increases risk of DS 1000-fold
NEW CHALLENGES: 36 AT EDC; G5P2SAB2

- NIPT
- “Non-reportable” x 2
- “Global Genomic Changes”
- Normal Detailed Survey
- Normal Karyotype and Microarray

No sig PMH

PRENATAL WORK-UP FOR MALIGNANCY: EXAM/BLOOD

- Whole body MRI
  - A 3.0 cm enlarged lymph node in right internal mammary region is suspicious for malignancy, including lymphoma and metastatic disease
  - Biopsy: Hodgkin’s Lymphoma

NIPT TEST COMPARISON AND WHY FIRST TRI US IS IMPORTANT

<table>
<thead>
<tr>
<th>Result Types</th>
<th>verifi®</th>
<th>Harmony</th>
<th>Ariosa</th>
<th>MaterniT21</th>
<th>Natera</th>
</tr>
</thead>
<tbody>
<tr>
<td>Risk-score incorporating maternal, gestational age</td>
<td>-Positive</td>
<td>-Negative</td>
<td>-Positive</td>
<td>-Negative</td>
<td>-Positive</td>
</tr>
<tr>
<td>Aneuploidy Detected</td>
<td>4.6 - 4.9%</td>
<td>1%</td>
<td>5.9 - 12.6%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aneuploidy Suspected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Aneuploidy Detected</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk score incorporating maternal, gestational age</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Egg Donors</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Sample</td>
<td>1 tube maternal blood</td>
<td>2 tubes maternal blood</td>
<td>2 tubes maternal blood</td>
<td>2-4 tubes maternal blood (best with paternal sample)</td>
<td></td>
</tr>
<tr>
<td>Risk Score</td>
<td>Yes (with data)</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Test Menu</td>
<td>T21, T18, T13</td>
<td>T21, T18, T13</td>
<td>T21, T18, T13</td>
<td>T21, T18, T13</td>
<td></td>
</tr>
<tr>
<td>Published Clinical Validation</td>
<td>Large-scale, blinded clinical validation</td>
<td>Large-scale, blinded clinical validation</td>
<td>Large-scale, blinded clinical validation</td>
<td>Small, blinded clinical validation</td>
<td></td>
</tr>
</tbody>
</table>

**Noninvasive prenatal testing for fetal trisomies in a routinely screened first-trimester population**

Kypreos H. Niskakis, MD; Anggoro Syngalas, RIA; Ghala Adnour, MD; Cohl Brudie, MD; Guido Toren, MD

The performance of screening for trisomy 21 and trisomy 18 by NIPT using chromosome-selective sequencing in a routine population is as effective as previously reported in high-risk groups with DR 99% and FPR 1%.

**False-Positive Rates Significantly Lowered by NIPT**

Analysis for cfDNA blood across 1st and 2nd trimesters

<table>
<thead>
<tr>
<th></th>
<th>NIPT</th>
<th>Standard Screen</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21 (n = 5)</td>
<td>0.7% (4/1360)</td>
<td>5.7% (51/1360)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Trisomy 18 (n = 2)</td>
<td>0.1% (2/1361)</td>
<td>0.8% (11/1361)</td>
<td>0.01</td>
</tr>
</tbody>
</table>


**Specificity and PPV Higher by NIPT**

<table>
<thead>
<tr>
<th></th>
<th>NIPT % (95% CI)</th>
<th>Standard Screen % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 21 (n = 5)</td>
<td>Sensitivity &gt;99.9 (47.8–100.0)</td>
<td>&gt;99.9 (29.2–100.0)</td>
</tr>
<tr>
<td></td>
<td>Specificity 99.7 (99.3–99.9)</td>
<td>96.4 (95.4–97.3)</td>
</tr>
<tr>
<td></td>
<td>PPV 45.4 (16.7–76.6)</td>
<td>4.2 (0.3–11.7)</td>
</tr>
<tr>
<td>Trisomy 18 (n = 2)</td>
<td>Sensitivity &gt;99.9 (15.8–100.0)</td>
<td>&gt;99.9 (2.5–100.0)</td>
</tr>
<tr>
<td></td>
<td>Specificity 99.8 (99.6–100.0)</td>
<td>99.4 (99.0–99.7)</td>
</tr>
<tr>
<td></td>
<td>PPV 40.0 (5.3–85.3)</td>
<td>8.3 (0.2–38.5)</td>
</tr>
</tbody>
</table>


**Reduction in FPR in Detection of Trisomy 13 by NIPT**

Show Trend Toward Significance

Analysis for cfDNA blood drawn across all trimesters

<table>
<thead>
<tr>
<th></th>
<th>NIPT % (95% CI)</th>
<th>Standard Screen % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trisomy 13 (n = 2)</td>
<td>Sensitivity 0.1% (0.0%–1.7%)</td>
<td>0.7% (0.0%–1.7%)</td>
</tr>
<tr>
<td></td>
<td>Specificity 99.9 (99.9–100.0)</td>
<td>99.4 (99.0–99.7)</td>
</tr>
<tr>
<td></td>
<td>PPV 40.0 (5.3–85.3)</td>
<td>8.3 (0.2–38.5)</td>
</tr>
</tbody>
</table>


**NIPT MAKING PRENATAL DIAGNOSIS SAFER**

**Preventing Test Failures**

- With paternal sample
- Minimize Test Failures
- Natera1,2 Sequenom5,6
- Ariosa3,4 7,8
- Whole Genome Sequencing
- Targeted Sequencing

**Minimize Test Failures**

- NIPT Test Failure Rates
- Failure rates in table
- Requires retake of sample
- Clinical experience

<table>
<thead>
<tr>
<th></th>
<th>Natera1,2</th>
<th>Ariosa3,4</th>
<th>Sequenom5,6</th>
<th>Illumina</th>
</tr>
</thead>
<tbody>
<tr>
<td>Failure rate</td>
<td>8.3%</td>
<td>7.0%</td>
<td>9.8%</td>
<td>13.2%</td>
</tr>
<tr>
<td>Natera1,2</td>
<td>4.6%</td>
<td>4.0%</td>
<td>5.5%</td>
<td>20.0%</td>
</tr>
<tr>
<td>Clinical experience</td>
<td>5.1%</td>
<td>6.8%</td>
<td>1.8%</td>
<td>0.0%</td>
</tr>
</tbody>
</table>


**High Test Failure Could Lead to Missed Aneuploidies**

% of Aneuploidies Not Detected* in Published “Low Risk” Studies

- SNP Study - Low Risk Cohort (Natera)
- "NEXT" Study (Ariosa)
- "CARE" Study (Illumina)

<table>
<thead>
<tr>
<th></th>
<th>% of Aneuploidies Not Detected</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP Study - Low Risk Cohort (Natera)</td>
<td>44.4%</td>
</tr>
<tr>
<td>&quot;NEXT&quot; Study (Ariosa)</td>
<td>20.0%</td>
</tr>
<tr>
<td>&quot;CARE&quot; Study (Illumina)</td>
<td>0.0%</td>
</tr>
</tbody>
</table>

* Aneuploidies Not Detected includes false negative results as well as aneuploidies with test failure


**Clinical experience**

- Failure rate in twins
- ~5.0% 4.6%
- 13.2% 5.5%
- 1.9% 0.9% 0.1%
The discussion about test failures and missed aneuploidies continues...

Chromosomal abnormalities detected in patients with failure to obtain test results using non-invasive prenatal testing (Turocy et al. to be presented at SMFM Feb 2015)

2.3%
1.5%
13.8%
20%
66.2%

Karyotypes of test failures

<table>
<thead>
<tr>
<th>Aneuploidy</th>
<th>Normal Chromosomes</th>
<th>No Chromosomal Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>20%</td>
<td>66.2%</td>
<td>13.8%</td>
</tr>
<tr>
<td>1.5%</td>
<td>2.3%</td>
<td></td>
</tr>
</tbody>
</table>

NIPT Failure Rate

After second draw


PERFORMANCE OF 1ST TRIMESTER CONTINGENT SCREENING FOR T21, T18, T13 BY NT AND DV FLOW AND CFDNA TESTING

KAGAN KO, ET A. UOG 2015; 45: 42-47

- Compare screening performance for 1st trimester risk assessment (Mat Age + NT + DV PIV) followed by cfDNA among patients with an intermediate risk
- Meta-analysis of clinical validation studies (86,917 unaffected and 491 trisomic pregnancies)
- Screening for T21, T18, T13 per guideline, followed by invasive testing in the HR group (>1:10) and cfDNA for the intermediate-risk group (1:11-1:3000) can potentially detect 96% (T21), 95% (T18) and 91% (T13) [FPT 0.8%]

Conclusion:
Incorporating cfDNA testing to a contingent policy can detect a high proportion of affected cases with a low FPR

PERFORMANCE OF 1ST TRIMESTER CONTINGENT SCREENING FOR T21, T18, T13 BY NT AND DV FLOW AND CFDNA TESTING

KAGAN KO, ET A. UOG 2015; 45: 42-47

1ST TRIMESTER (10-11 WEEKS) CFDNA COMPARED TO COMBINED TESTING AT 11-13 WEEKS
QUEZADA MS, ET AL. ULTRASOUND OBSTET GYNECOLO 2015; 45: 36-41

- 2,905 singleton pregnancies, trisomy screening by cfDNA at 10-11 wks and by combined test at 11-13 wks gestation
- Median maternal age = 36.9 yrs (range 20.4-51.9)
- Results provided for 2,851/2,905 (98.1%) cases
- 2,848 (98%) available within 14 days
- 2,785 with a cfDNA result and known trisomic status - cfDNA correctly identified all 32 cases with T21, 9/10 with T18, and 2/5 with T13 (FPR 0.04%, 0.19% and 0.07%, respectively)
- In discordant cases (between cfDNA and karyotype) - median fetal fraction was lower than in those with concordant results (6% vs. 11%)
- T21 estimated risk was > 1/100 in all trisomic cases and 4.4% in non-trisomic pregnancies using the combined test

NIPT MAKING PRENATAL DIAGNOSIS SAFER

1. NIPT broadens the available prenatal testing options for women
2. NIPT offers an alternative to invasive diagnostic testing for women with screen positive fetuses
   - With high sensitivity and specificity for T18 and T21 (T13 performance somewhat poorer comparatively)
NIPT
MAKING PREGNATAL DIAGNOSIS SAFER

3. NIPT offers reassurance to those women for whom invasive diagnostic testing was not an acceptable option
4. NIPT removes the risk of procedure-related risks and women may be less likely to decline testing
5. NIPT makes comprehensive first trimester ultrasound essential

FUTURE HORIZONS

Exciting Time
• Advancement in ultrasound technology
  • Early & accurate diagnosis of fetal congenital abnormalities
• NIPT on cfDNA in maternal plasma
  • Early screening of fetal karyotypic abnormalities
  Expand access for fetal intervention