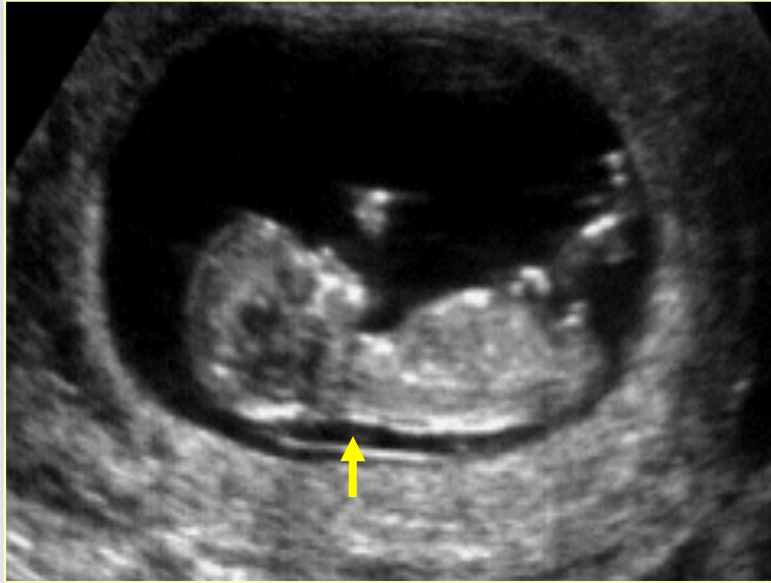


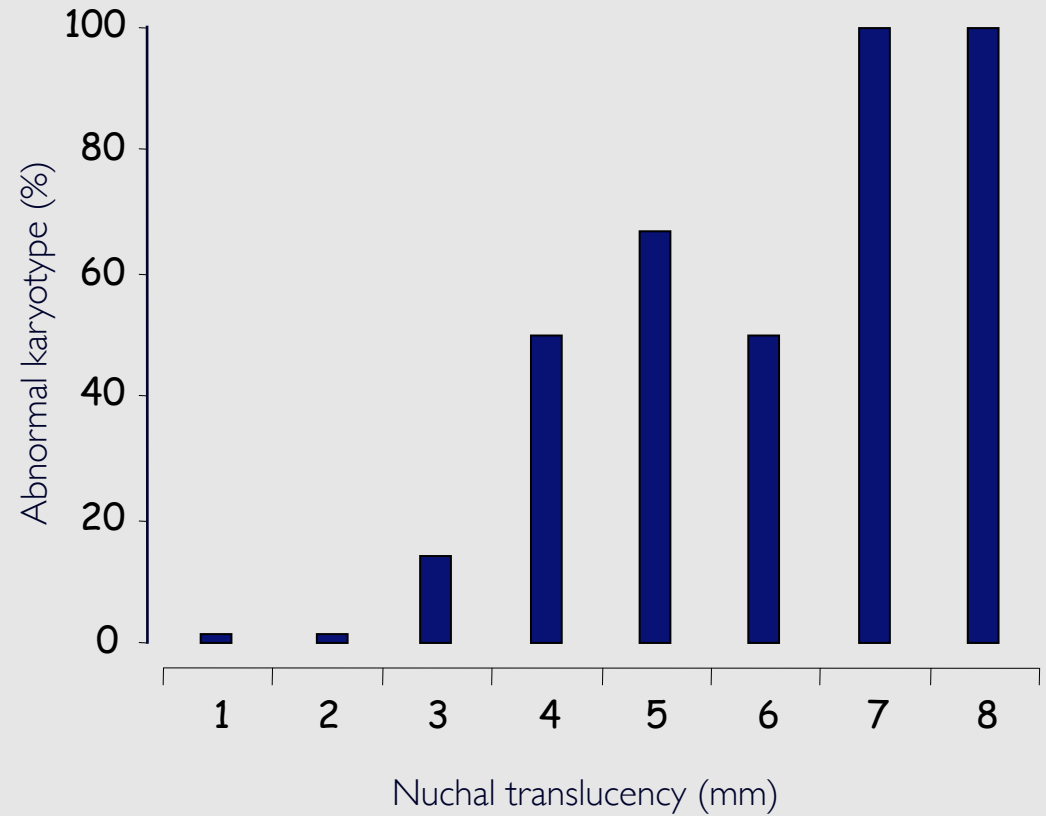
Pyramid of Care Importance of Ultrasound



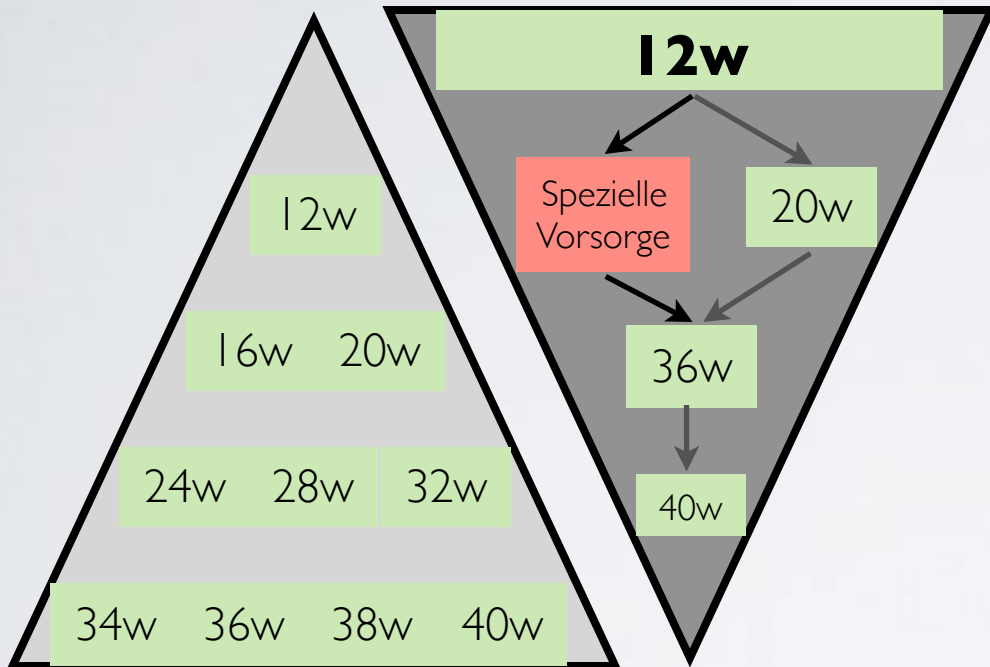
First Trimester Screening 1992



NT	Aneuploidy
<3mm	1% (10/776)
>3mm	35% (18/51)



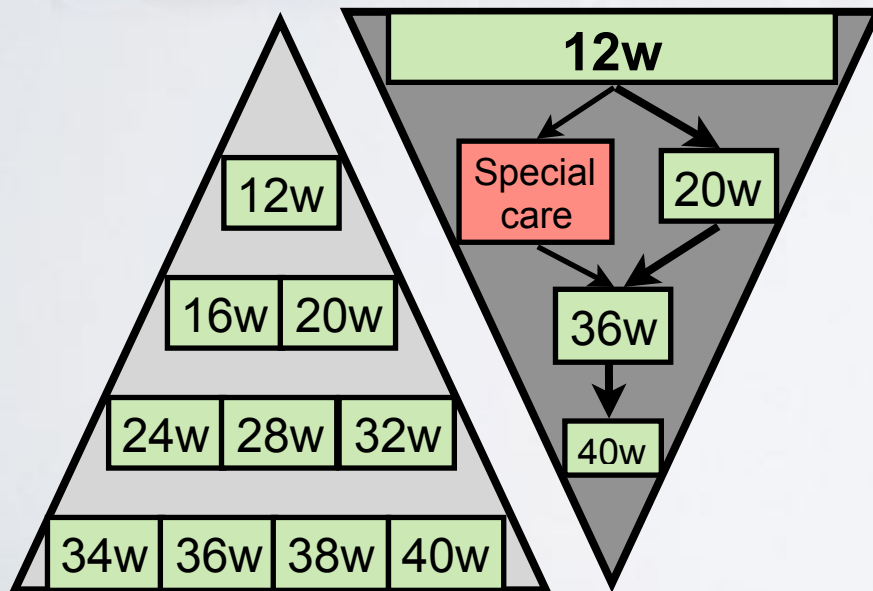
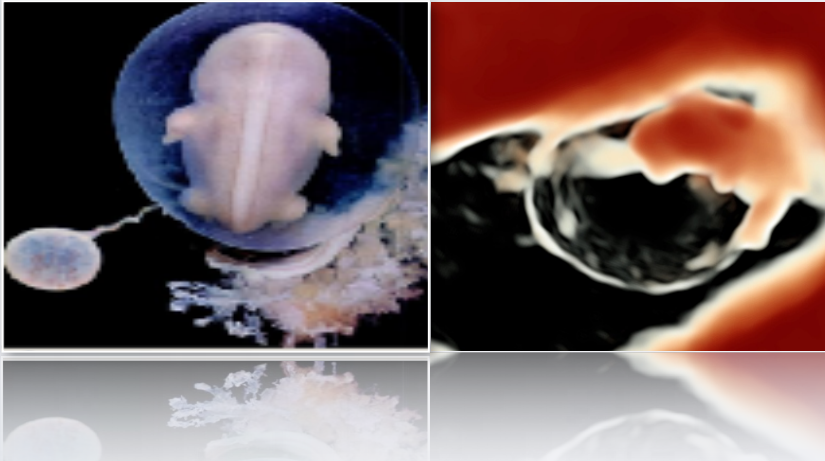
First Trimester Screening



Pyramid of care

- Aneuploidy
- Fetal defects
- Preeclampsia and IUGR
- Preterm birth
- Macrosomia and gestational diabetes
-

Contemporary First Trimester Screening



	DR	FPR
• ANEUPLOIDY	90 - 99%	1 - 5%
• FETAL DEFECTS	50%	?
• PREECLAMPSIA	>90%	10 %
• IUGR / SGA	50%	10 %
• PRETERM DELIVERY	60%	10 %
• GESTATIONAL DIABETES	85%	40 %

cfDNA Screening Performance



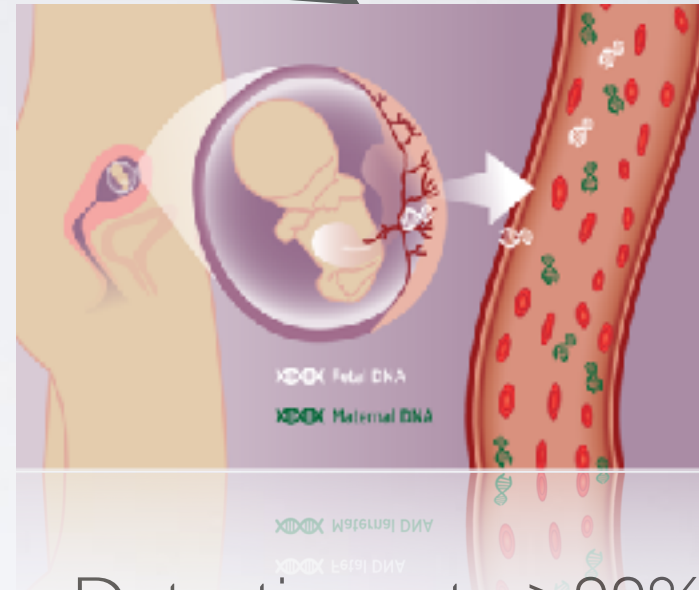
	DR	FPR
Trisomy 21	99.7 %	0.04 %
Trisomy 18	98.2 %	0.05 %
Trisomy 13	99.0 %	0.04 %
Turner	95.8 %	0,14 %

Screening for common trisomies



Detection rate 90%
False positive rate 3-5%

+



Detection rate >99%
False positive rate <0.1%

Other defects than common trisomies, cost, infrastructure, ~2% failure rate

Contingent Screening



High
risk

Invasive
testing

cfDNA:
other aneuploidies
time

Borderline
risk

Additional
tests

cfDNA

Low
risk

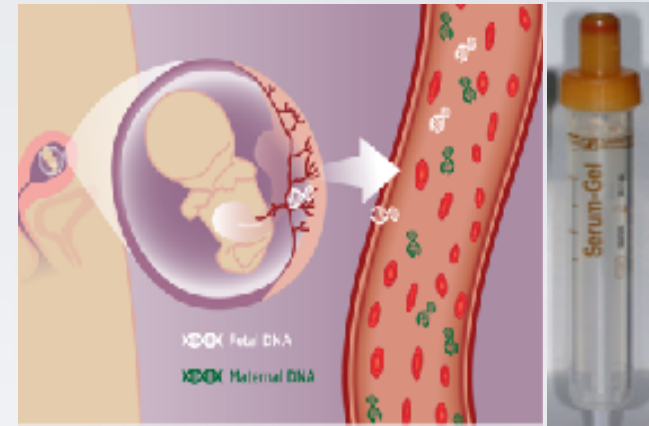
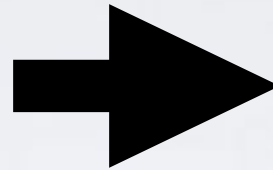
No further
tests

cfDNA:
not cost effective

Future „Combined“ FTS?



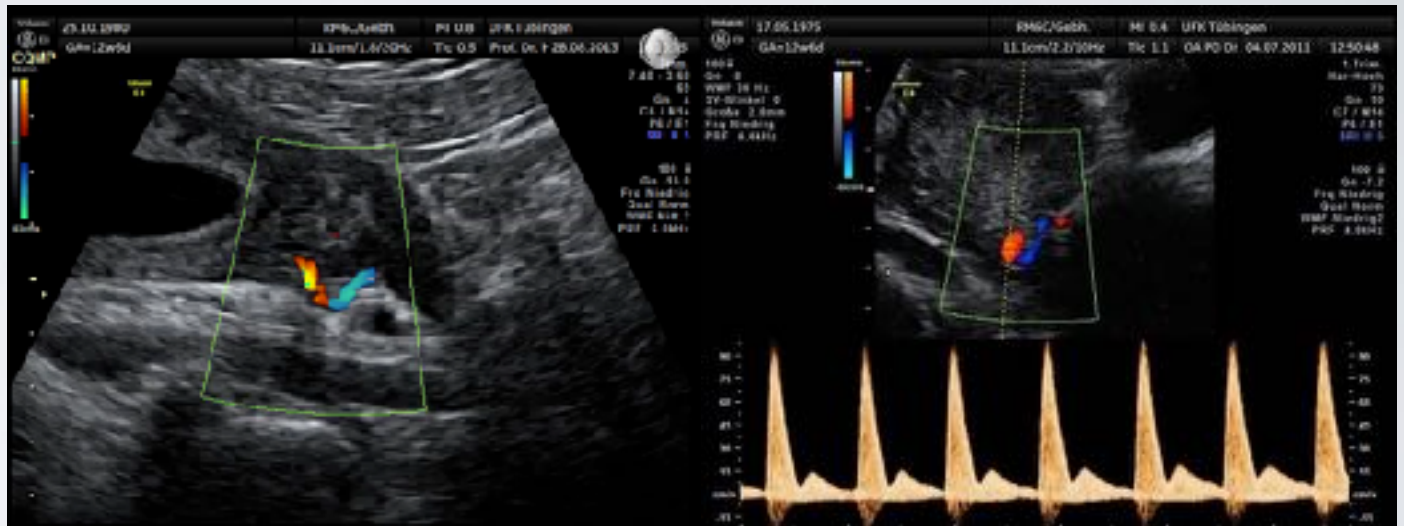
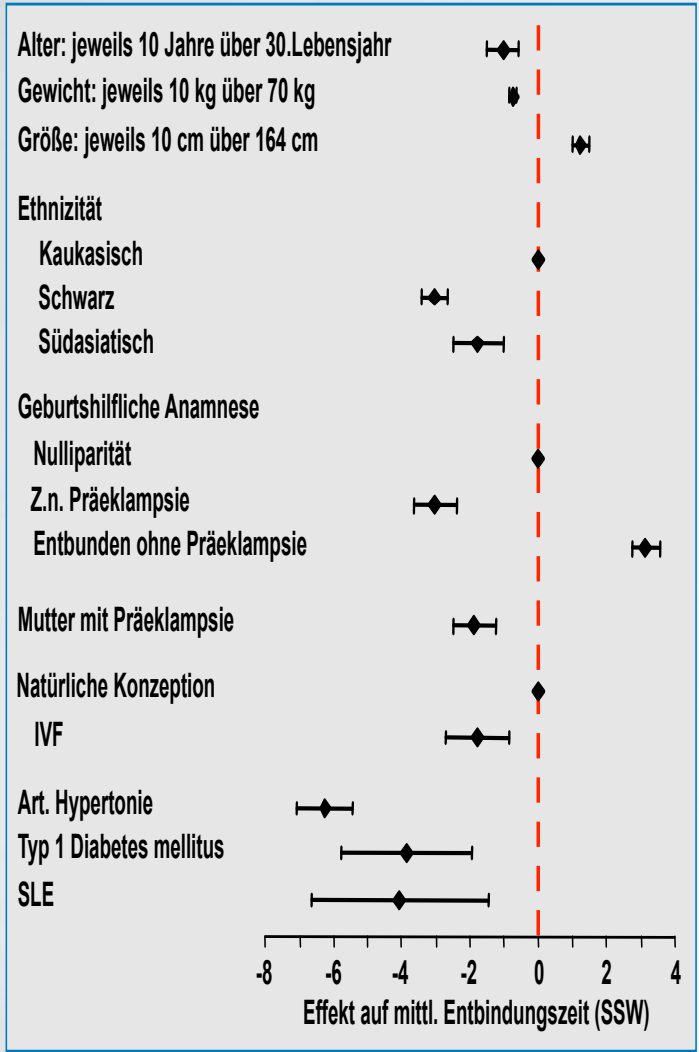
Fetal defect, NT > 3,5mm



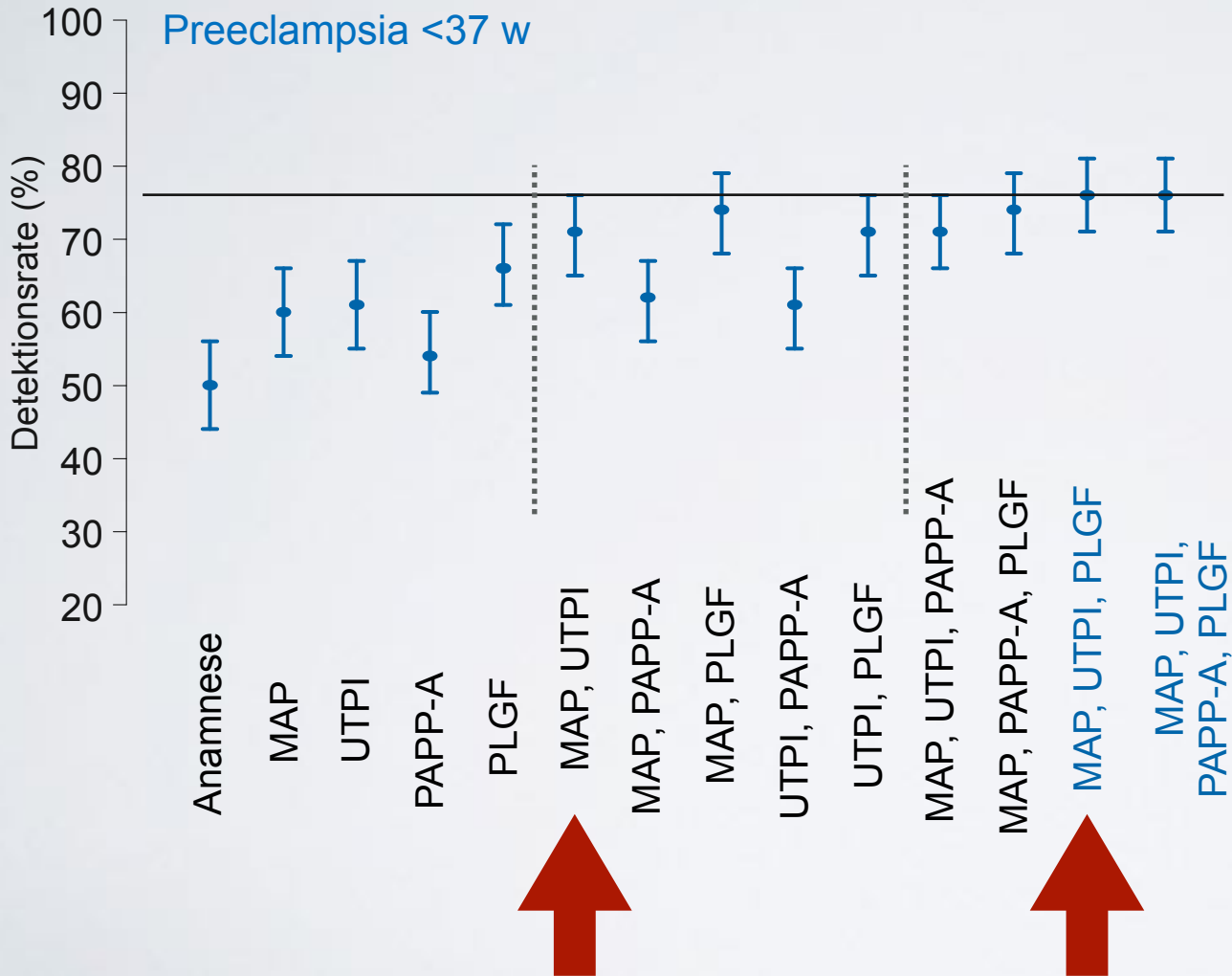
No results



Screening for Preeclampsia



Screening for Preeclampsia



Method of screening	DR for FPR 10%	
	PE <37w	TOTAL
Anamnese	50	41
MAP	60	48
UTPI	59	44
PAPP-A	55	44
PLGF	66	47
MAP, UTPI	70	52
MAP, PAPP-A	62	50
MAP, PLGF	74	54
UTPI, PAPP-A	60	45
UTPI, PLGF	70	49
PLGF, PAPP-A	67	48
MAP, UTPI, PAPP-A	68	52
MAP, UTPI, PLGF	77	54



F u n d e d b y E U F P 7

ASPRE

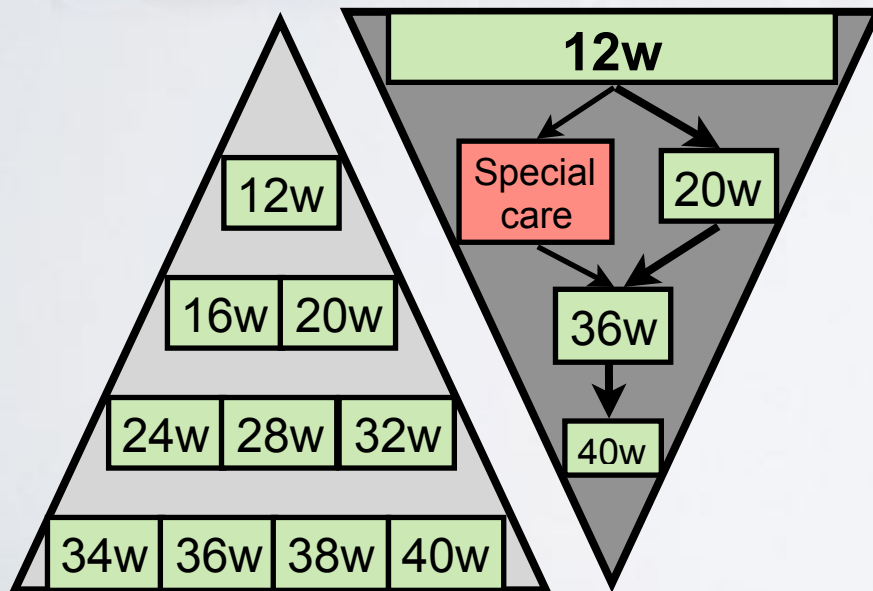
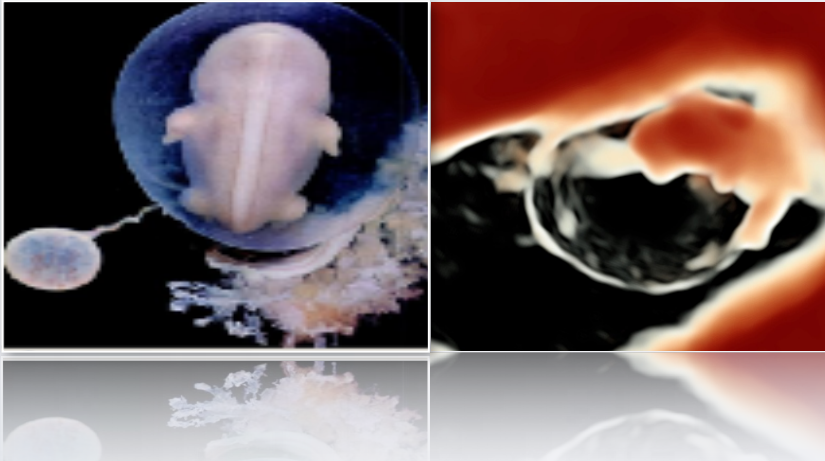
project



SEVENTH FRAMEWORK
PROGRAMME

Aspirin works!

Contemporary First Trimester Screening



	DR	FPR
• ANEUPLOIDY	90 - 99%	1 - 5%
• FETAL DEFECTS	50%	?
• PREECLAMPSIA	>90%	10 %
• IUGR / SGA	50%	10 %
• PRETERM DELIVERY	60%	10 %
• GESTATIONAL DIABETES	85%	40 %

Challenges in the diagnosis of fetal non-chromosomal abnormalities at 11–13 weeks

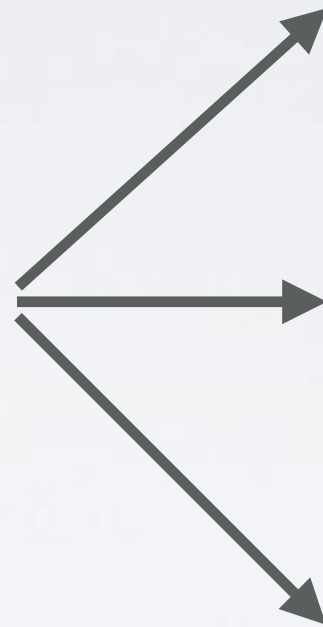
Argyro Syngelaki^{1,2,3}, Teodora Chelemen^{1,2}, Themistoklis Dagklis¹, Lindsey Allan¹
and Kypros H. Nicolaides^{1,2,3*}

Fetal defects

1.1% (488 / 45.000)

Aneuploid pregnancies

0.7% (332 / 45,000)



First trimester

43.7% (213 / 488)

Second trimester

53.6% (262 / 488)

Postnatal

2.7% (13 / 488)

First Trimester Anomaly Scan



GUIDELINES

ISUOG Practice Guidelines: performance of first-trimester fetal ultrasound scan

Quality Requirements for the early Fetal Ultrasound Assessment at 11–13⁺⁶ Weeks of Gestation (DEGUM Levels II and III)

Qualitätsanforderungen an die weiterführende differenzierte Ultraschalluntersuchung in der pränatalen Diagnostik (DEGUM-Stufen II und III) im Zeitraum 11–13⁺⁶ Schwangerschaftswochen



First Trimester Anomaly Scan

Ultrasound Obstet Gynecol 2013; 41: 100–113
 Published online in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/ug.12342



GUIDELINES

ISUOG Practice Guidelines: performance of first-trimester fetal ultrasound scan



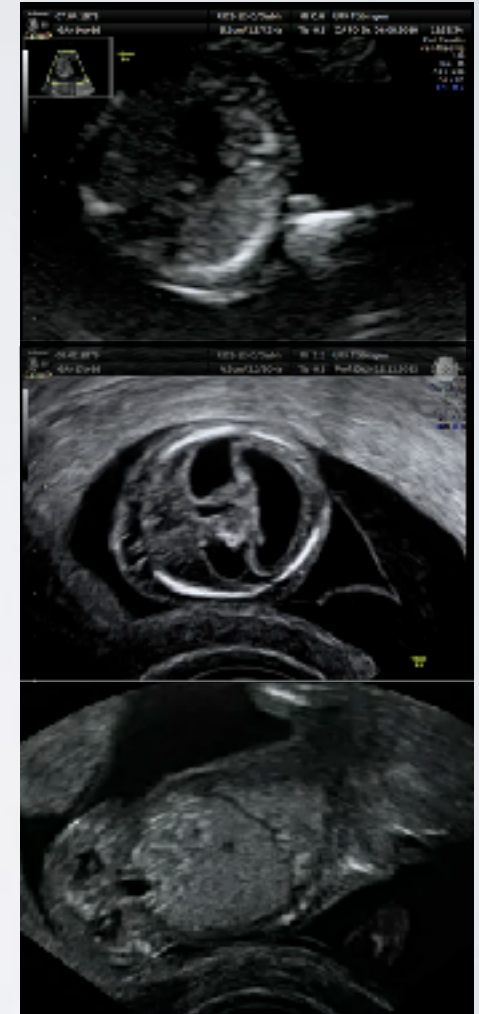
Table 2 Suggested anatomical assessment at time of 11 to 13+6-week scan:

Organ/anatomical area	Present and/or normal?
Head	Present Cranial bones Midline falx Choroid-plexus-filled ventricles
Neck	Normal appearance Nuchal translucency thickness (if accepted after informed consent and trained/certified operator available)*
Face	Eyes with lens* Nasal bone* Normal profile/mandible* Intact lips*
Spine	Vertebrae (longitudinal and axial)* Intact overlying skin*
Chest	Symmetrical lung fields No effusions or masses
Heart	Cardiac regular activity Four symmetrical chambers*
Abdomen	Stomach present in left upper quadrant Bladder* Kidneys*
Abdominal wall	Normal cord insertion No umbilical defects
Extremities	Four limbs each with three segments Hands and feet with normal orientation*
Placenta	Size and texture
Cord	Three-vessel cord*

*Optional structures. Modified from Foog *et al.*²⁴, McAuliffe *et al.*⁸⁷, Talpale *et al.*⁴⁰ and von Kalsenberg *et al.*⁸⁸.

Detection rate of the First Trimester Anomaly Scan

	Major defects	Detection rate
Hernandi et al 1997	35 / 3991	12 (34%)
Economides et al 1998	13 / 1632	7 (54%)
D'Ottavio et al 1998	88 / 4078	54 (61%)
Whitlow 1999	63 / 6443	37 (59%)
Carvalho et al 2002	66 / 2853	25 (38%)
Taipale et al 2004	33 / 4855	6 (18%)
Chen et al 2004	26 / 1609	14 (54%)
Souka et al 2006	14 / 1148	7 (50%)
Weiner et al 2007	22 / 1723	9 (41%)
Becker et al 2006	86 / 3094	72 (84%)
Syngelaki 2012	488 / 44859	213 (44%)
TOTAL	934 / 76285	456 (49%)



First Trimester Anomaly Scan

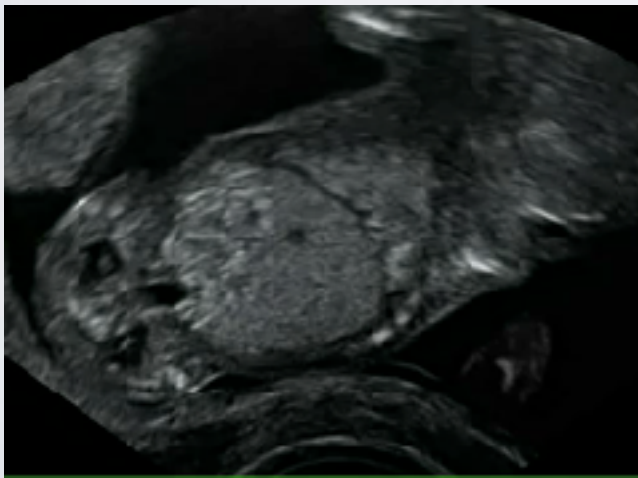


- Which defects should always be seen?
- Which defects could be seen?
- How could we improve the first trimester anomaly scan?

Which defects should always be detected?



Which defects could be detected?



Which defects could be detected?

Always detectable defects

Anencephaly, holoprosencephaly, exomphalos, gastroschisis, megacystis

Undetectable defects

Microcephaly and other CNS defects, fetal tumors, lung defects, some cardiac defects, most gastrointestinal and renal defects

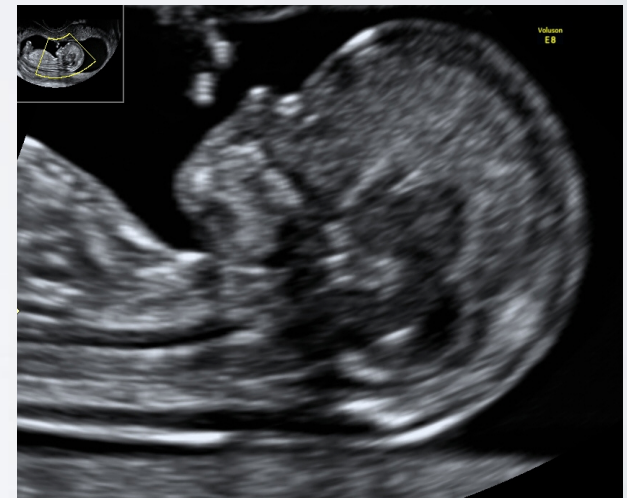
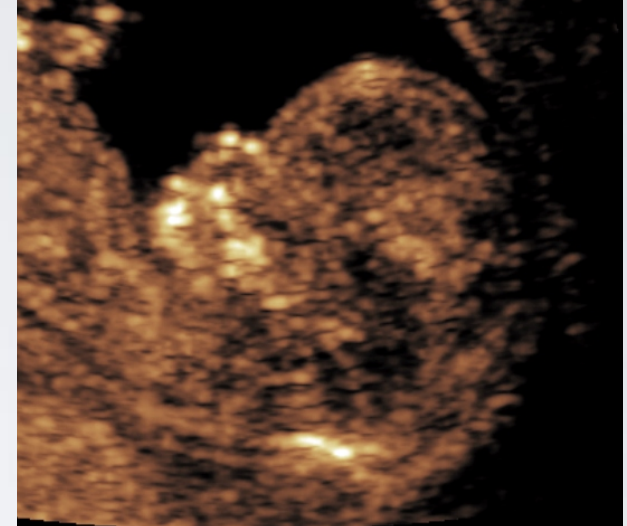
Potentially detectable defects

Facial defects, spina bifida, cardiac defects, renal agenesis, diaphragmatic hernia, skeletal dysplasia

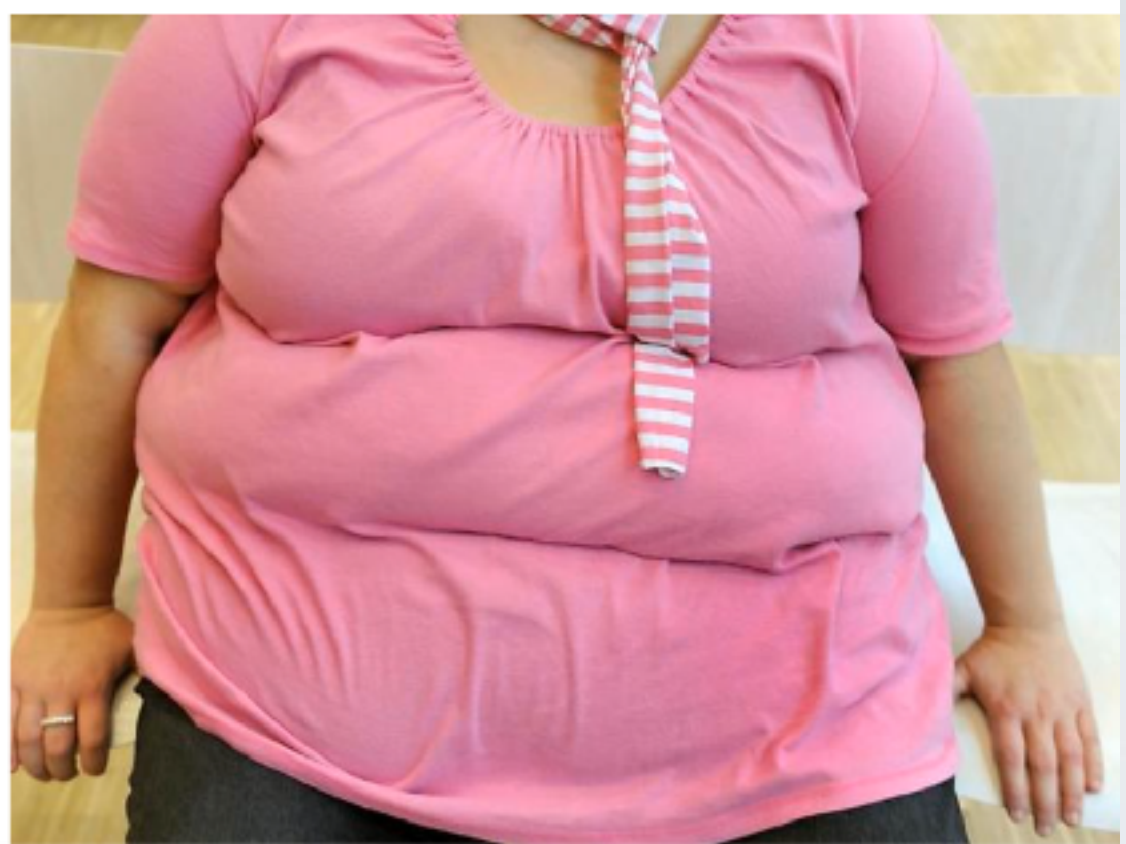
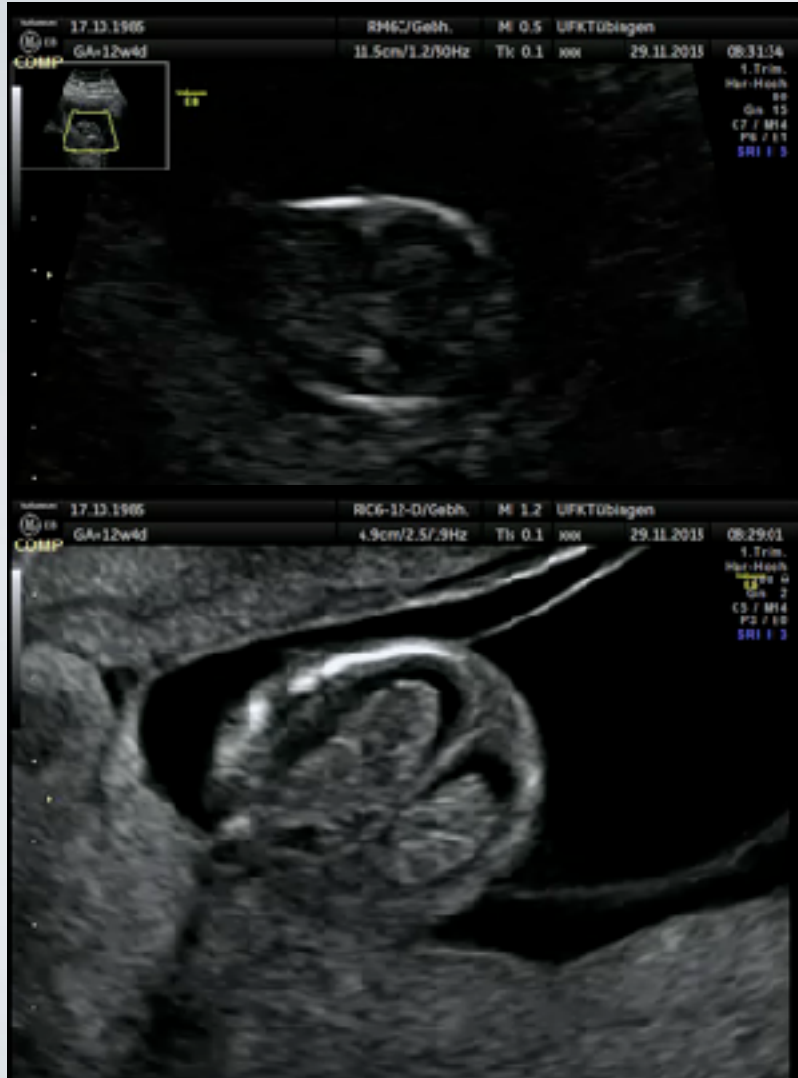
Accuracy of Ultrasonography at 11–14 Weeks of Gestation for Detection of Fetal Structural Anomalies

A Systematic Review

A. Cristina Rossi, MD, and Federico Prefumo, MD, PhD



TRANSVAGINAL ULTRASOUND



Detailed screening for fetal anomalies and cardiac defects at the 11–13-week scan

R. BECKER and R.-D. WEGNER

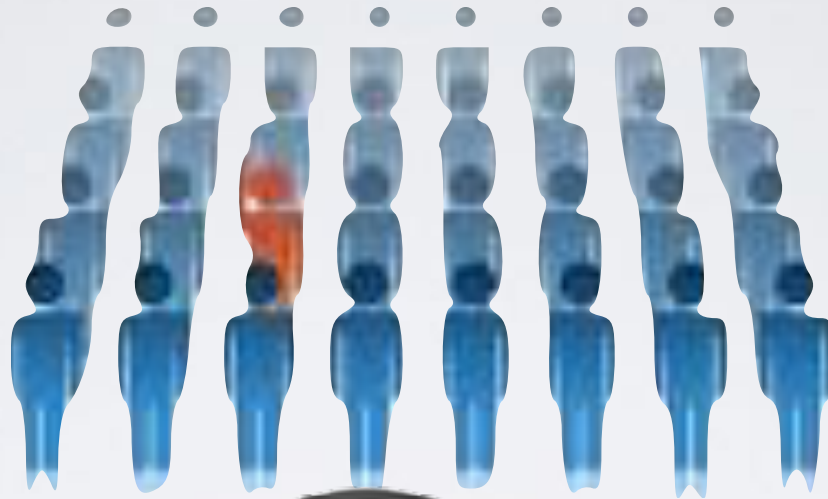
Center for Prenatal Diagnosis, Berlin, Germany



86 major defects
11 - 13 weeks

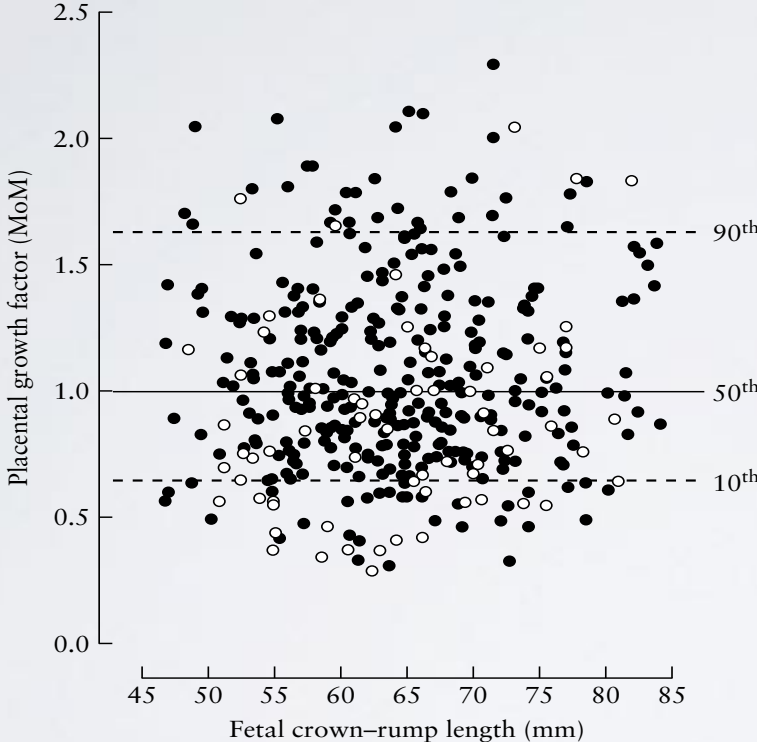
Detection rate: 72/86 (83,7%)

Screening parameters for major defects

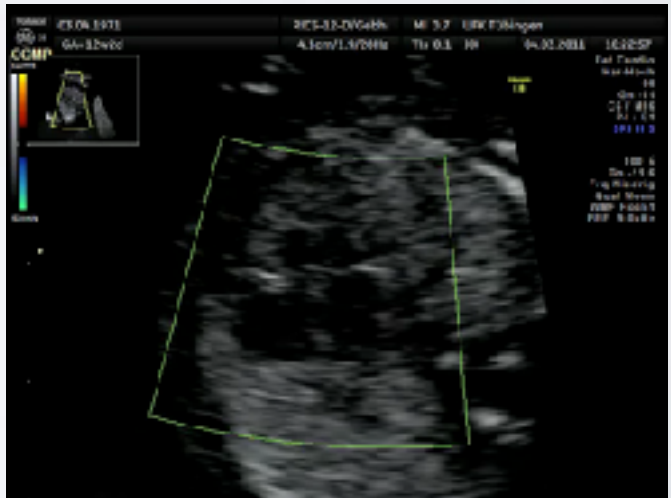
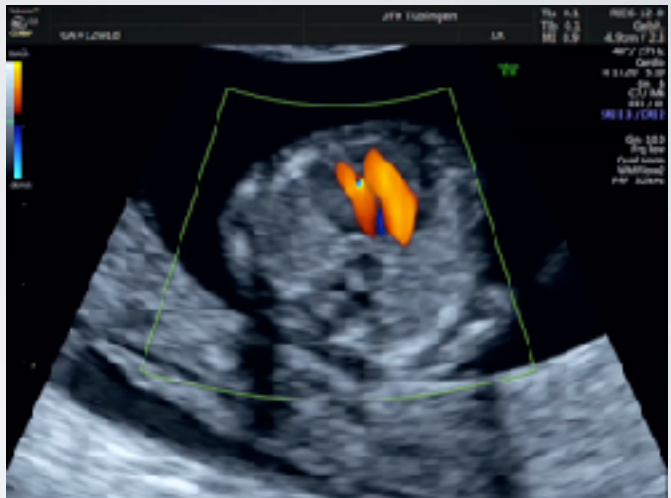


Maternal serum placental growth factor at 11–13 weeks' gestation and fetal cardiac defects

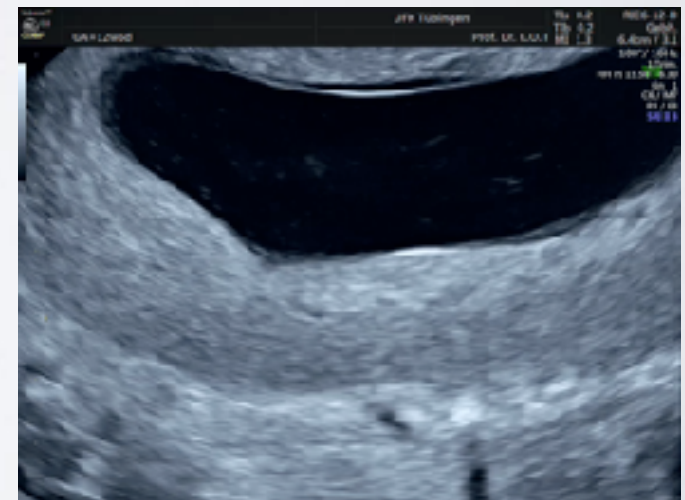
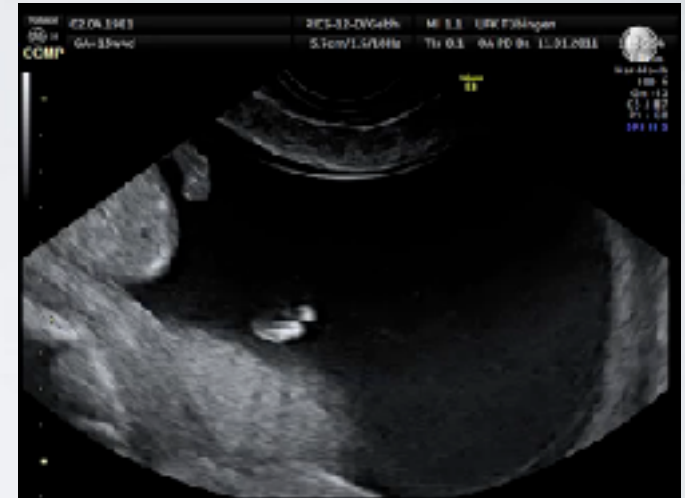
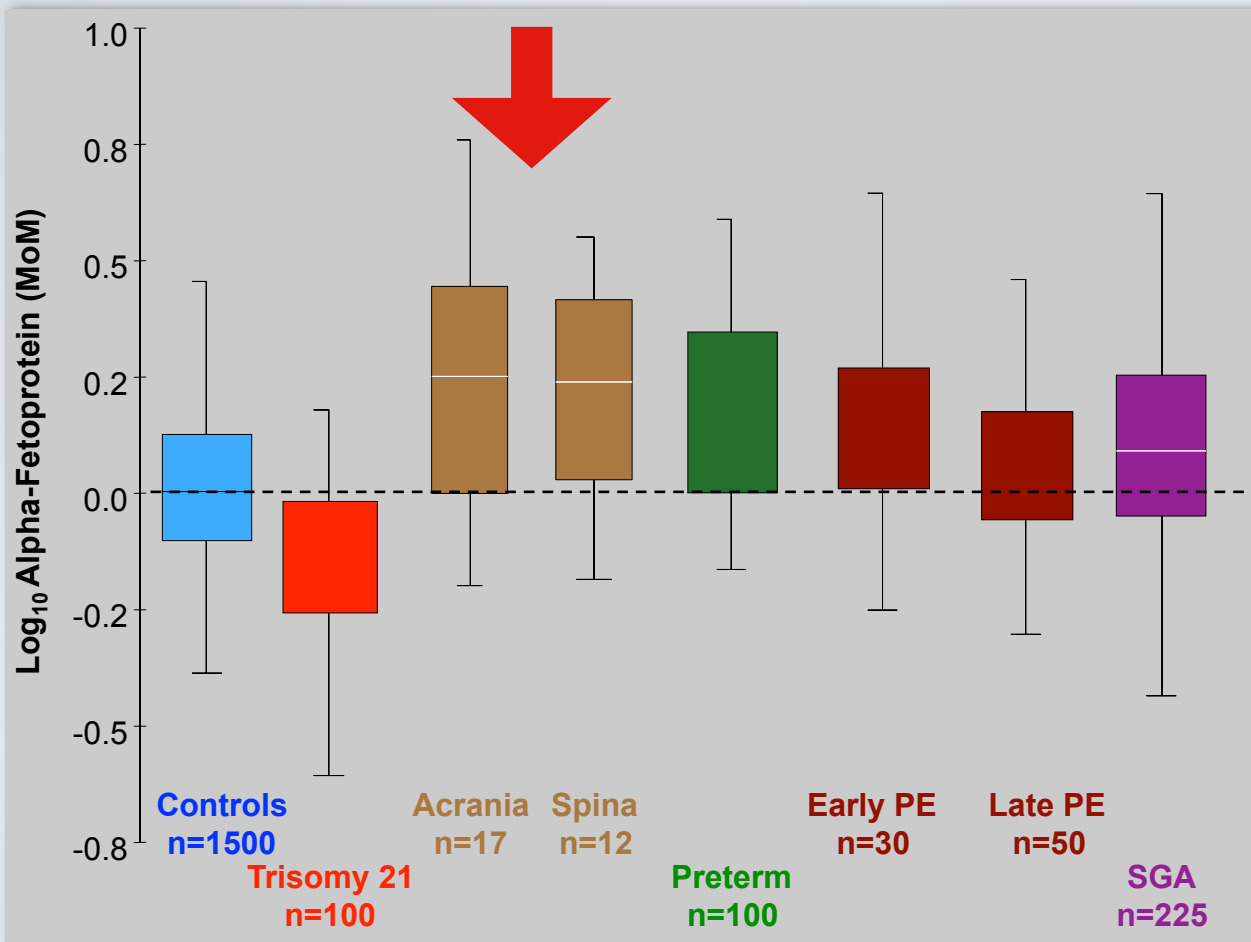
E. LLURBA*†, A. SYNGELAKI‡§, O. SÁNCHEZ†, E. CARRERAS*, L. CABERO* and K. H. NICOLAIDES‡§



0,8 MoM vs 1,0 MoM



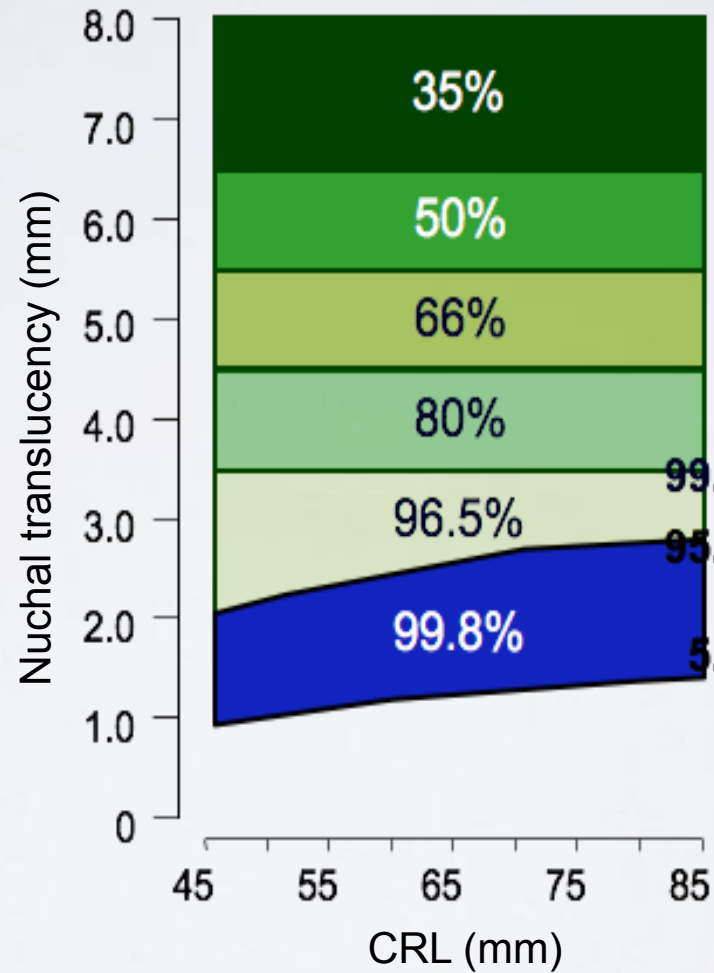
Alpha-Fetoprotein and neural tube defects



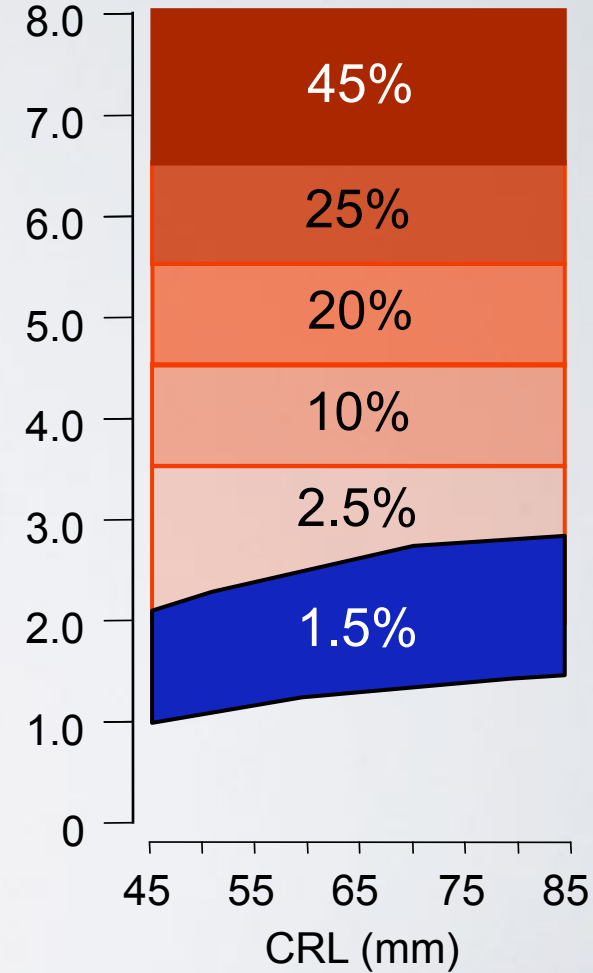
ULTRASOUND MARKERS: NT



Euploid



Major defects



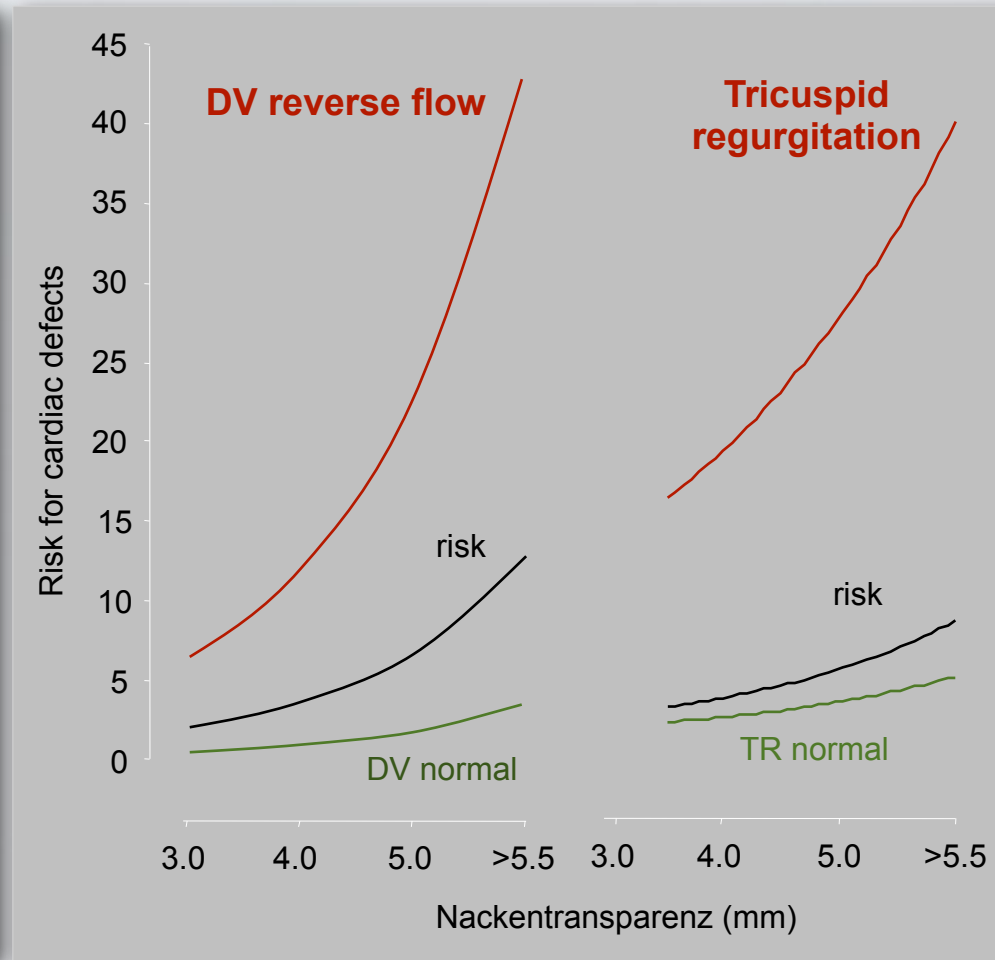
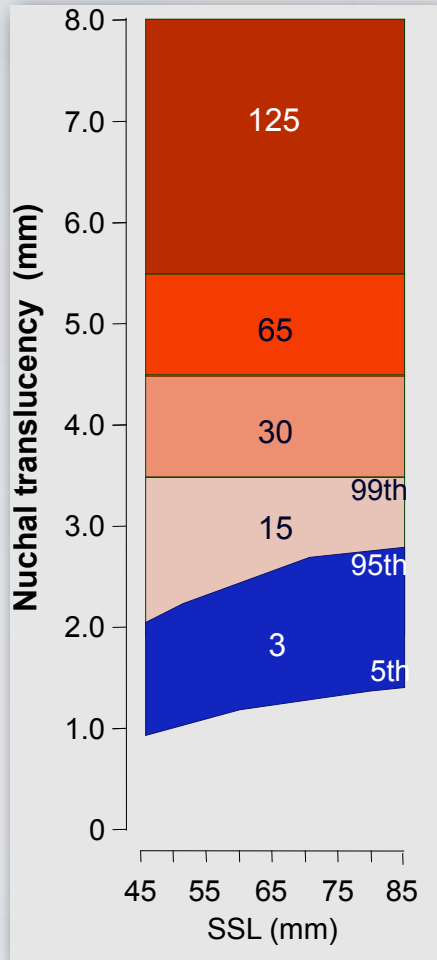
Nuchal translucency and cardiac defects



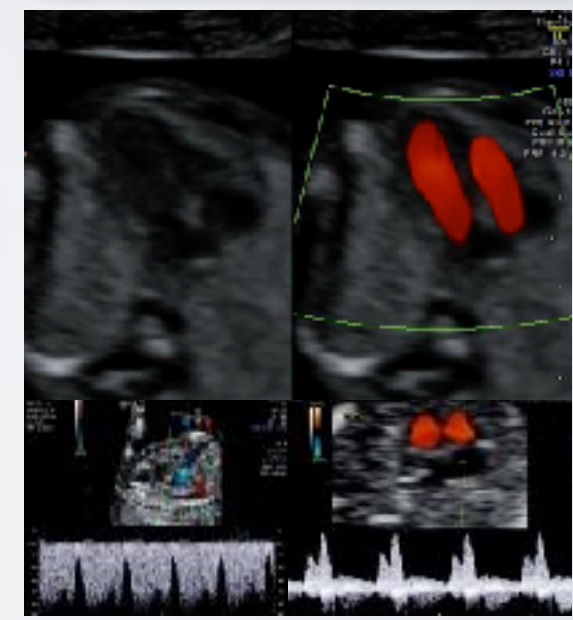
Autor	TOTAL	CHD	DR	FPR
	n	n	%	%
Josefsson et al. 1998	1460	13	38	8.9
Hafner et al. 1998	4214	14	28	1.4
Schwärzler et al. 1998	4474	9	11	2.4
Hyett et al. 1999	29154	50	56	6.1
Michailides et al. 2001	6606	11	36	3.5
Mavrides et al. 2001	7339	26	15	3.4
Bahado-Singh et al. 2005	8167	21	14	4.6
Westin et al. 2006	16383	52	14	2.6
Müller et al. 2007	4181	13	15	2.4
TOTAL	81978	209	28	4.2

Nackentransparenz (mm)

Screening for cardiac defects with NT, ductus venosus and tricuspid blood flow

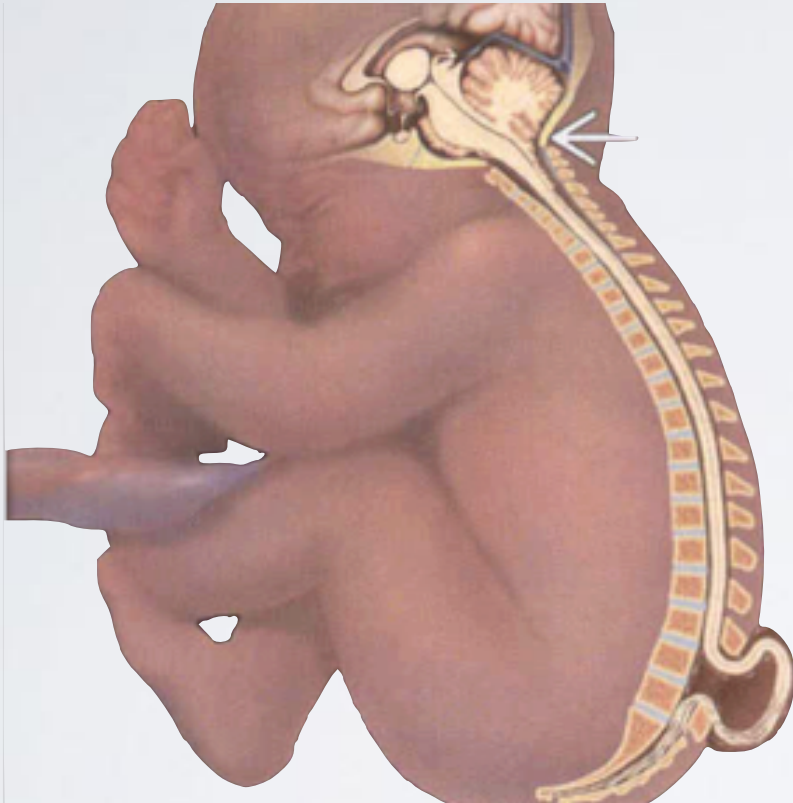


	DR	FPR
NT >95.P	35%	4.8%
TR	33%	1.3%
DV	28%	2.1%
1 of 3	58%	8.0%



40,905 normal fetuses and 85 CDHs

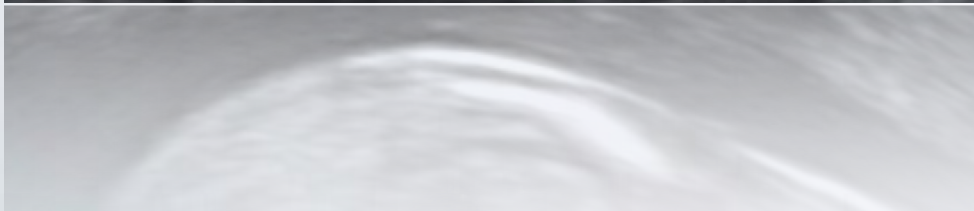
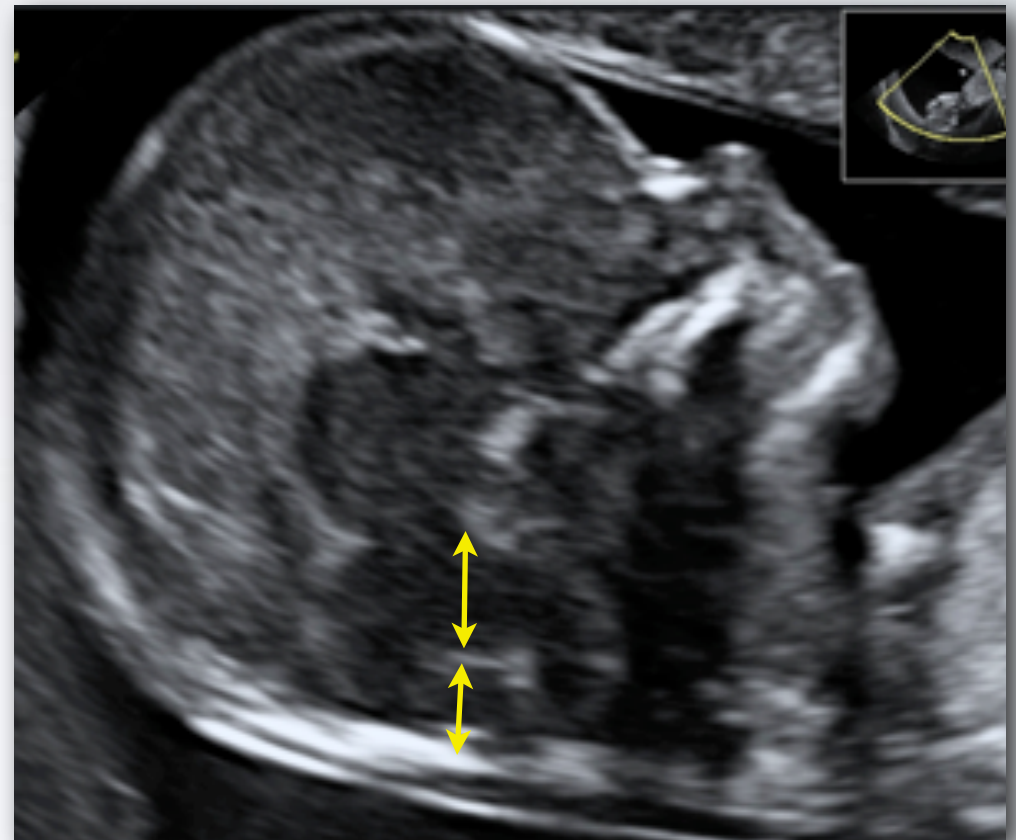
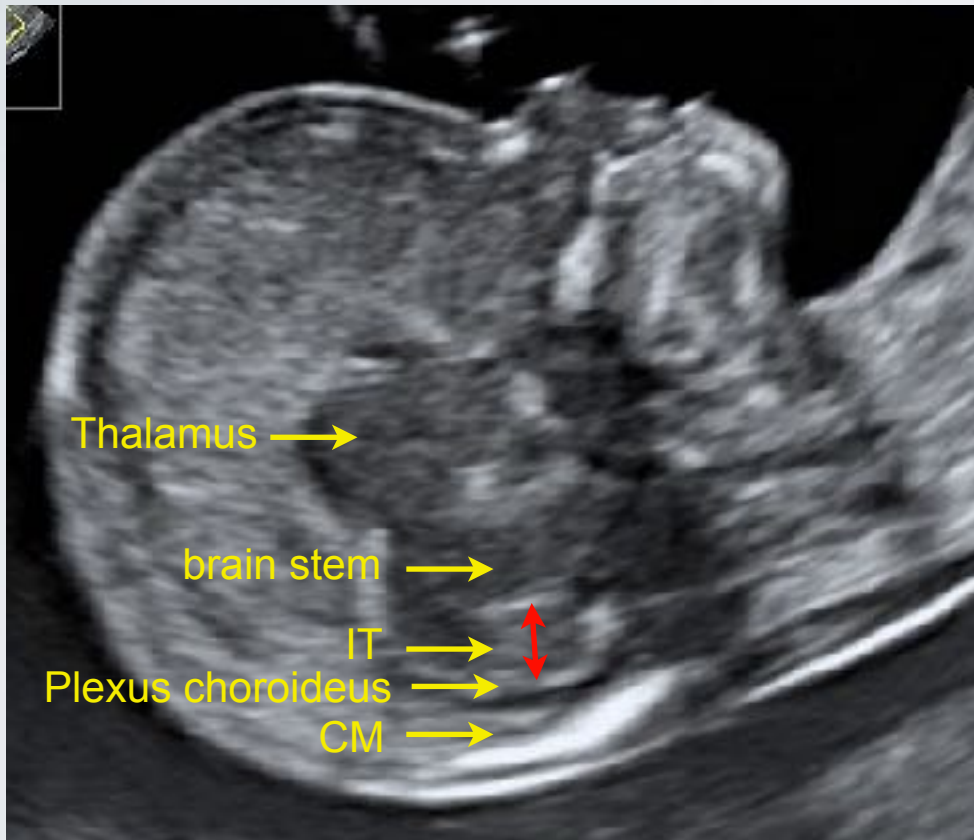
Screening for Spina bifida



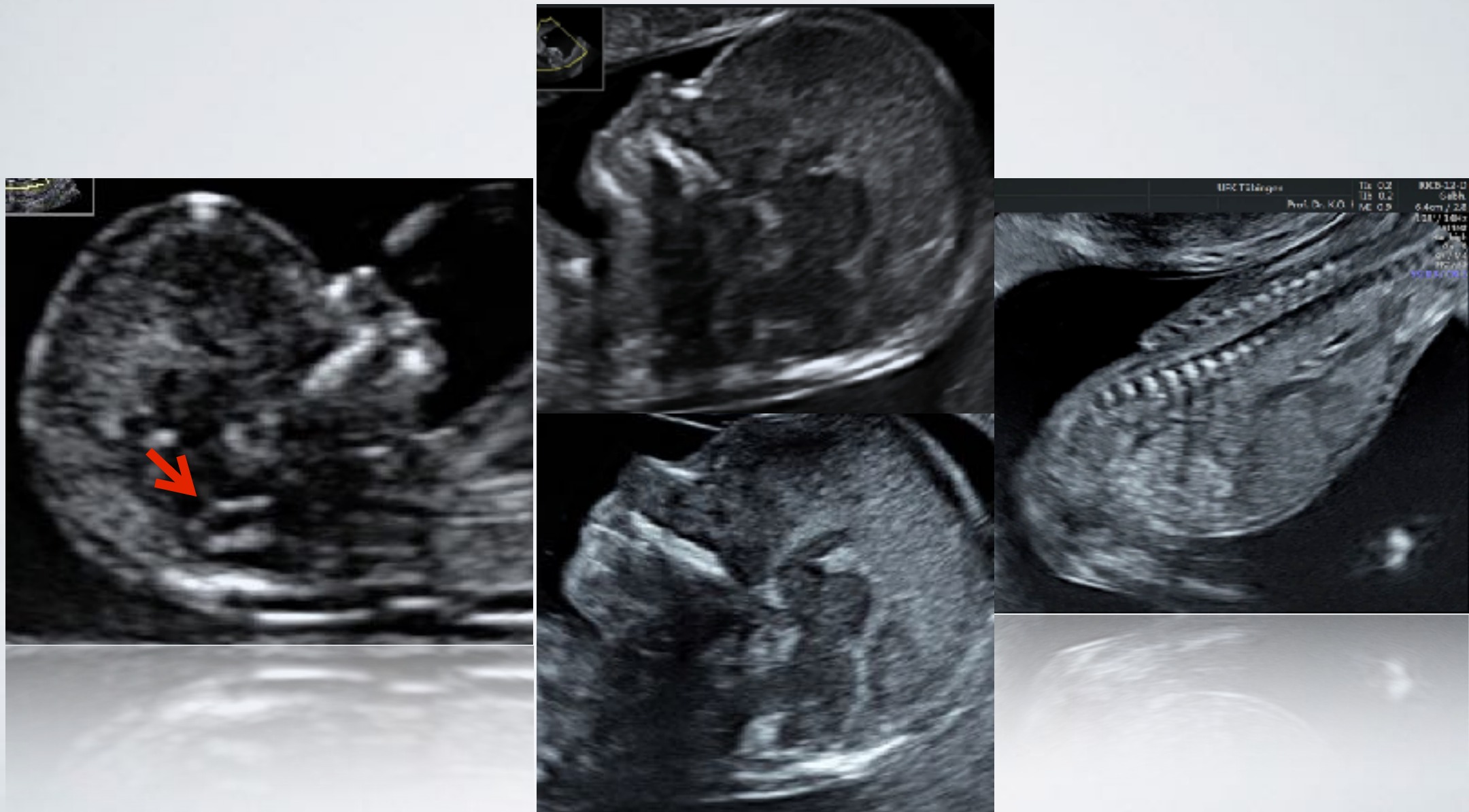
First trimester detection rate
10 - 15%



Screening for Spina bifida



Screening for Spina bifida



Detection of Spina Bifida by First Trimester Screening – Results of the Prospective Multicenter Berlin IT-Study

Früherkennung einer Spina bifida im Ersttrimester-Screening – Ergebnisse der prospektiven, multizentrischen Berliner IT-Studie

Authors

Frank Chih-Kang Chen¹, Janine Gerhardt¹, Michael Entezami²,
Rabih Chaoui³, Wolfgang Henrich¹

Affiliations

- 1 Department of Obstetrics, Charité Universitätsmedizin Berlin, Campus Virchow-Klinikum, Berlin, Germany
- 2 Kudamm-199, Center for antenatal diagnostics and human genetics, Berlin, Germany
- 3 Friedrichstrasse 147, Prenatal Diagnosis and Human Genetics, Berlin, Germany



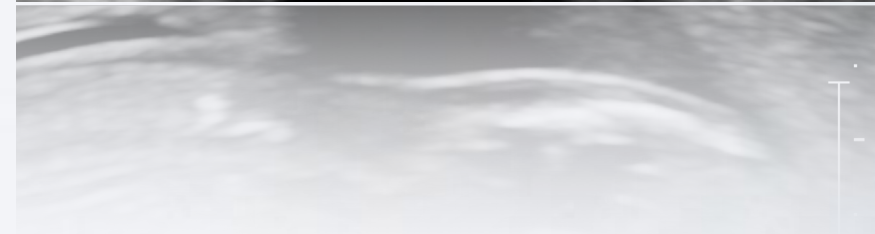
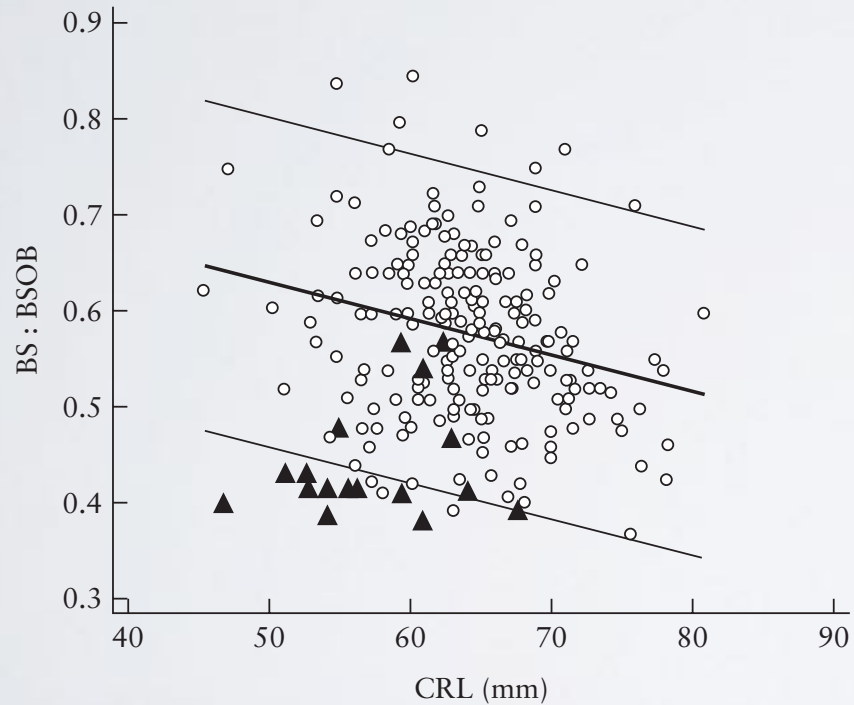
Multicenter study in Berlin
Normal pregnancies n= 15.526
Fetuses with spina bifida n= 11

Detected or suspected cases
in the first trimester 100%

Appearance of fetal posterior fossa at 11–14 weeks in fetuses with Dandy–Walker malformation or chromosomal anomalies

P. VOLPE*, E. CONTRO†, T. FANELLI*, B. MUTO*, G. PILU† and M. GENTILE‡

*Fetal Medicine Unit, Di Venere and Sarcone Hospitals, ASL BA, Bari, Italy; †Department of Obstetrics and Gynecology, University of Bologna, Bologna, Italy; ‡Medical Genetics Unit, Di Venere Hospital, ASL BA, Bari, Italy



FACIAL DEFECTS



First trimester detection rate
for cleft lip and palate 5%



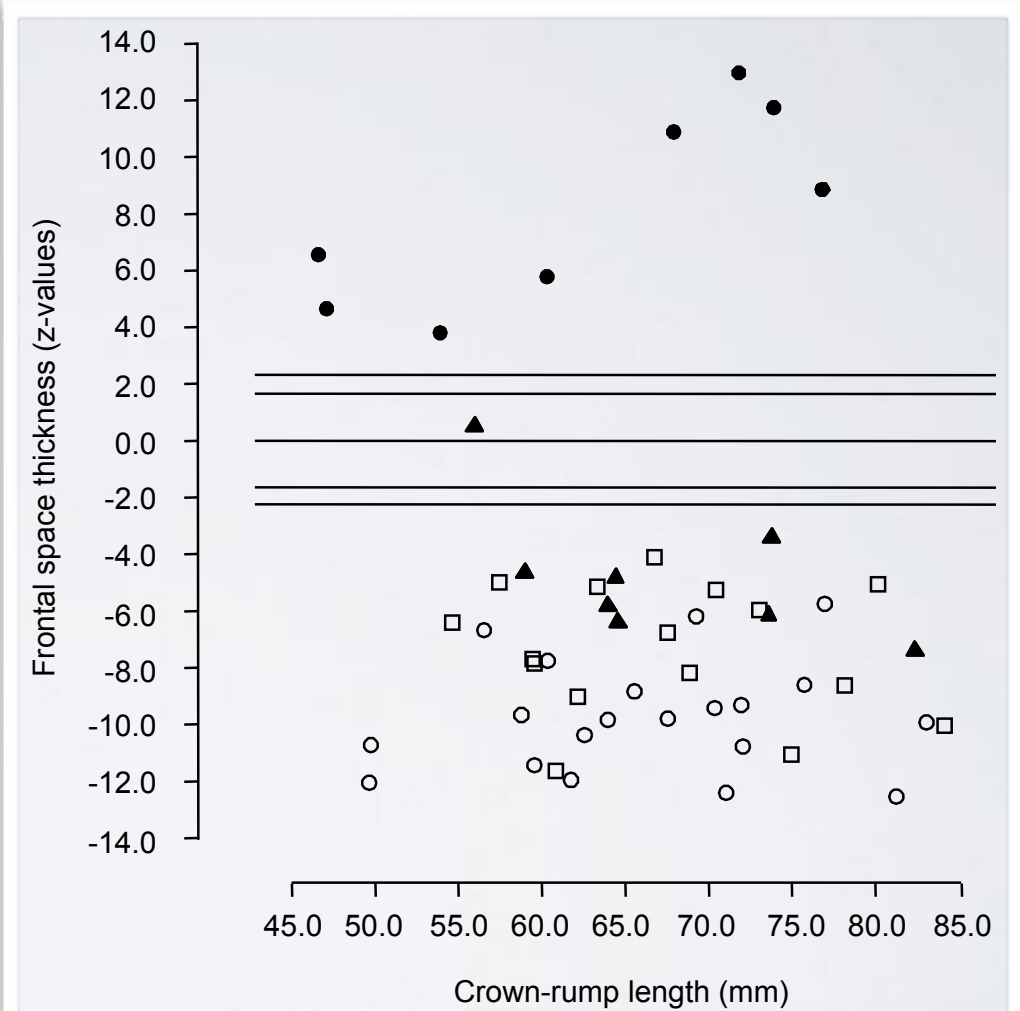
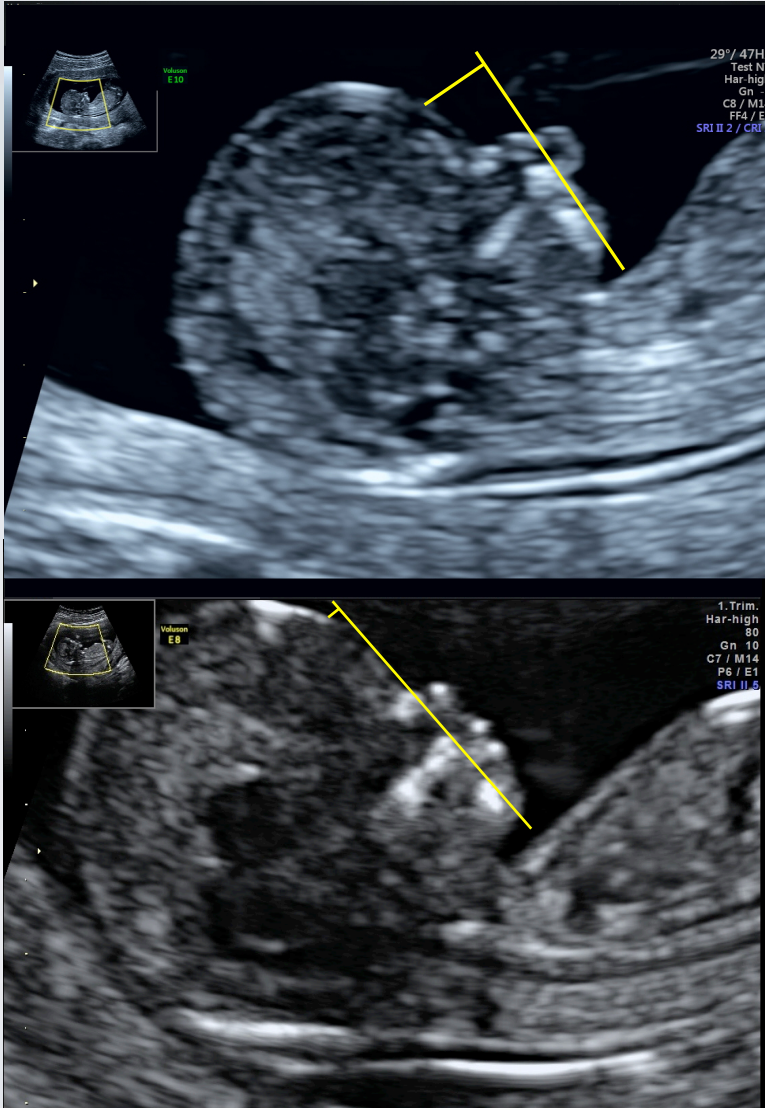
Retronasal triangle

Cleft lip and Palate „Mind the Gap“



Cleft lip and palate

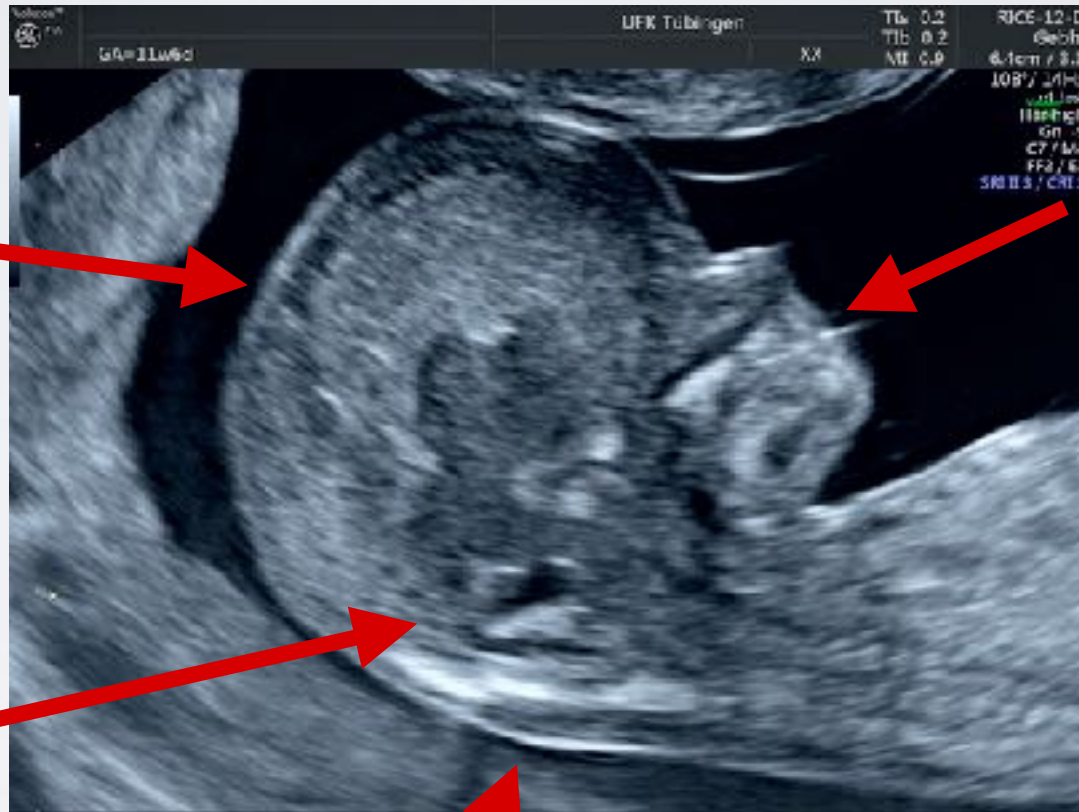
Frontal Space Measurement



- Bilateral cleft lip and palate
- ▲ Unilateral cleft lip and palate
- Median cleft lip and palate
- Retrognathia

The fetal profile

All in one - image



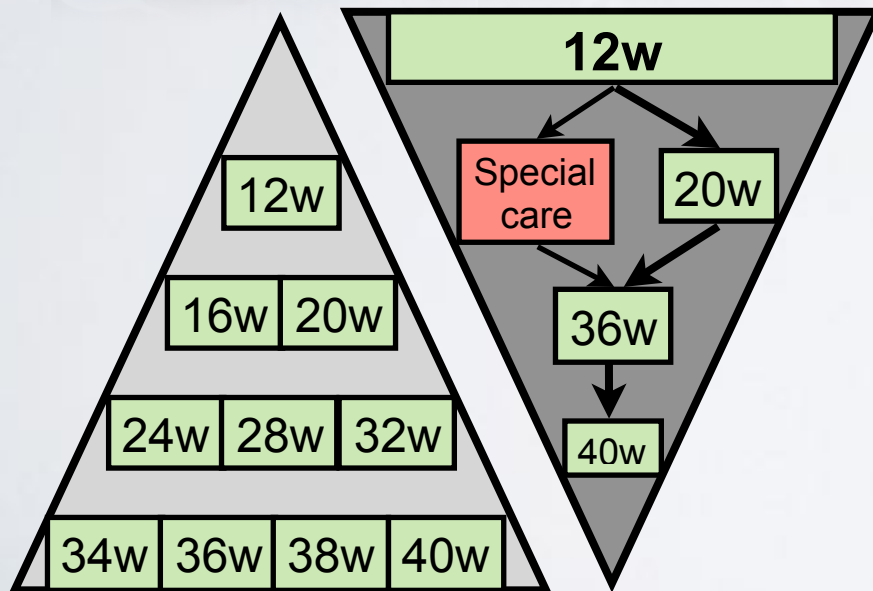
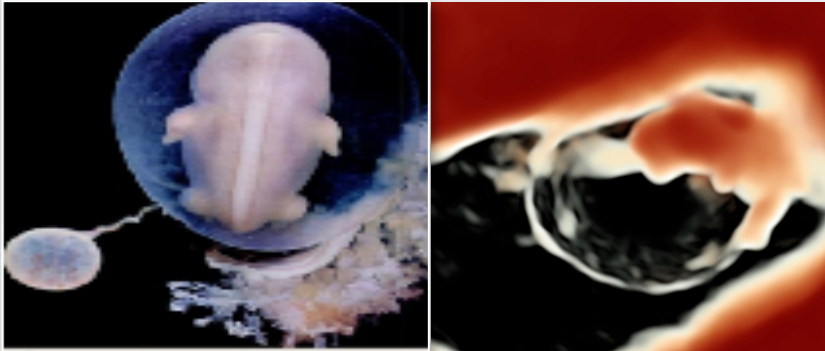
Facial clefts
Retrognathia

Nuchal translucency

Anencephaly
Holoprosencephaly

Spina bifida
Cerebelar anomalies

Contemporary First Trimester Screening



	DR	FPR
• ANEUPLOIDY	90 - 99%	1 - 5%
• FETAL DEFECTS	50%	?
• PREECLAMPSIA	>90%	10 %
• IUGR / SGA	50%	10 %
• PRETERM DELIVERY	60%	10 %
• GESTATIONAL DIABETES	85%	40 %

+ + + + +

GEHIRN



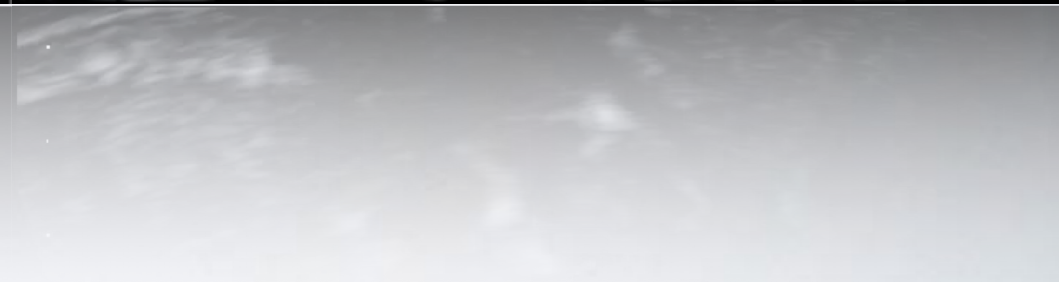
Detektionsrate
für Exen- und Holo-
prosencephalie fast 100%



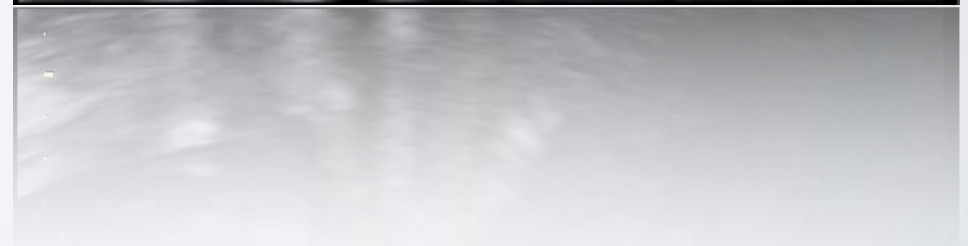
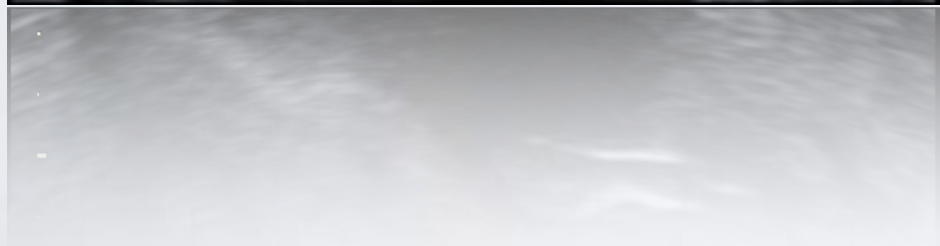
GEHIRN



GEHIRN



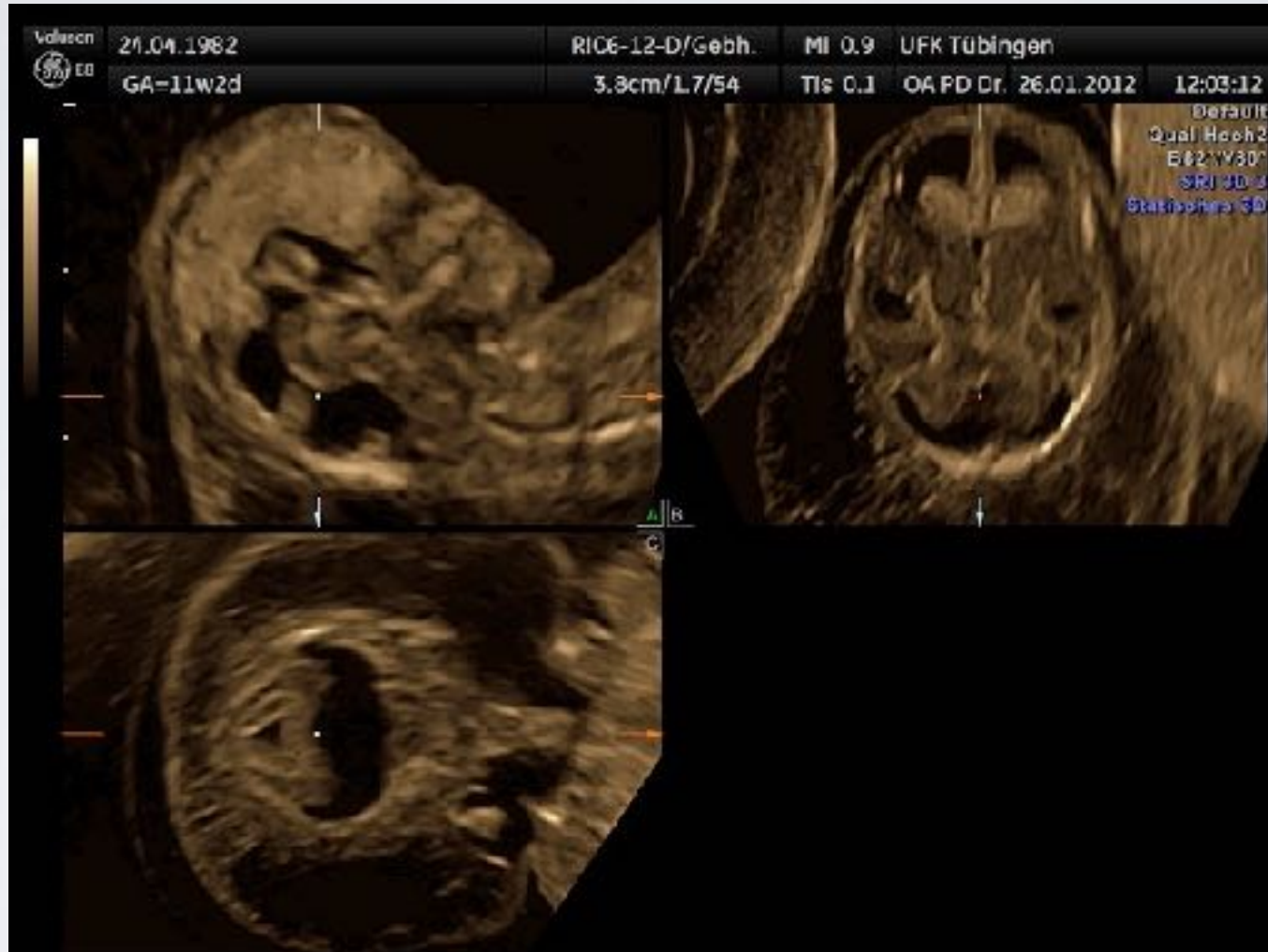
GEHIRN



GESICHT



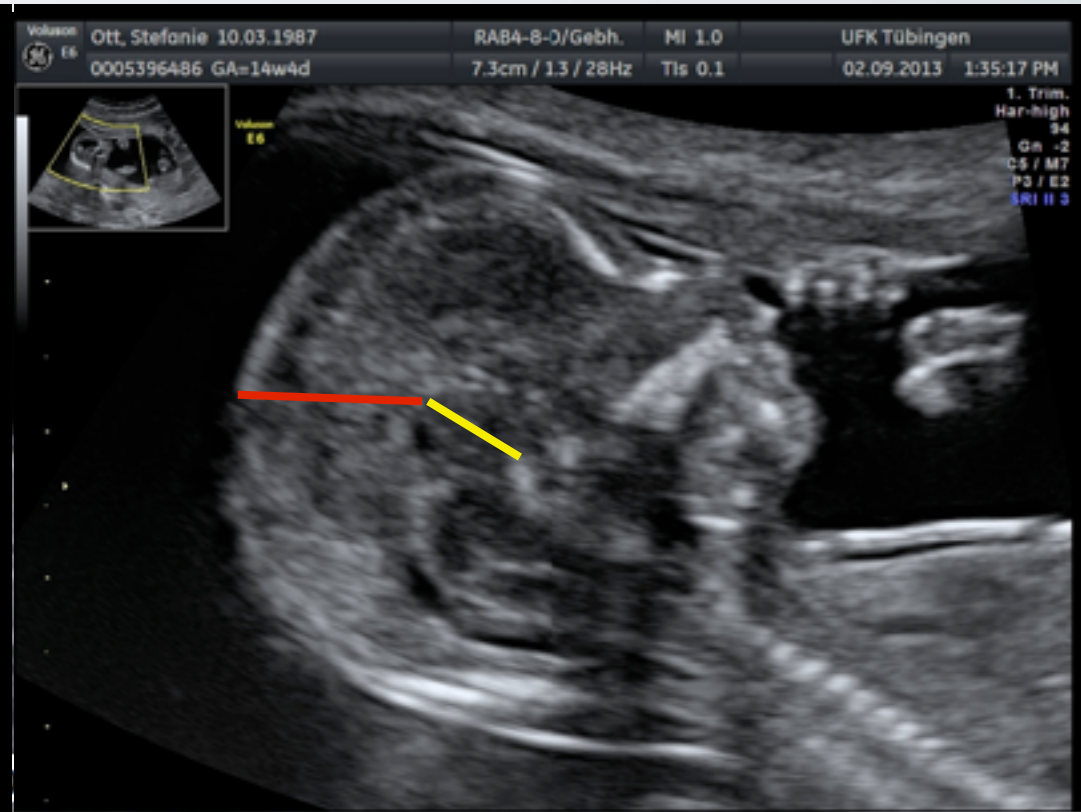
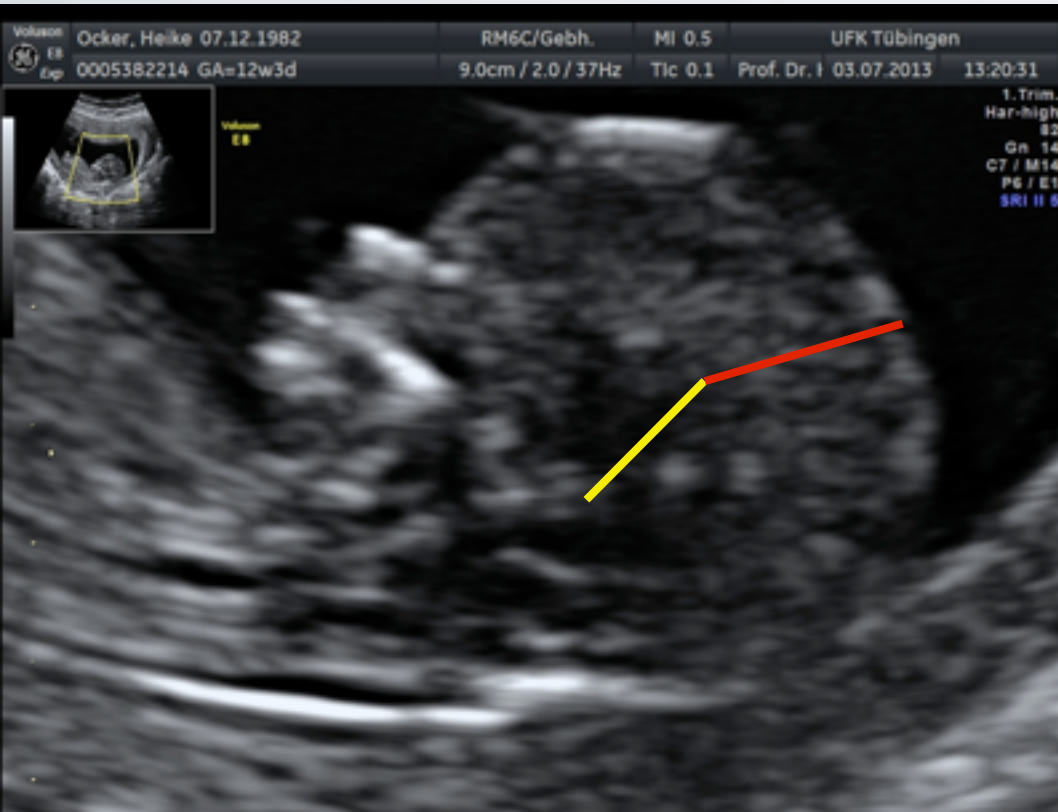
FOSSA POSTERIOR - DANDY WALKER?



BALKENAGENESIE

Normal

Balkenagenesie



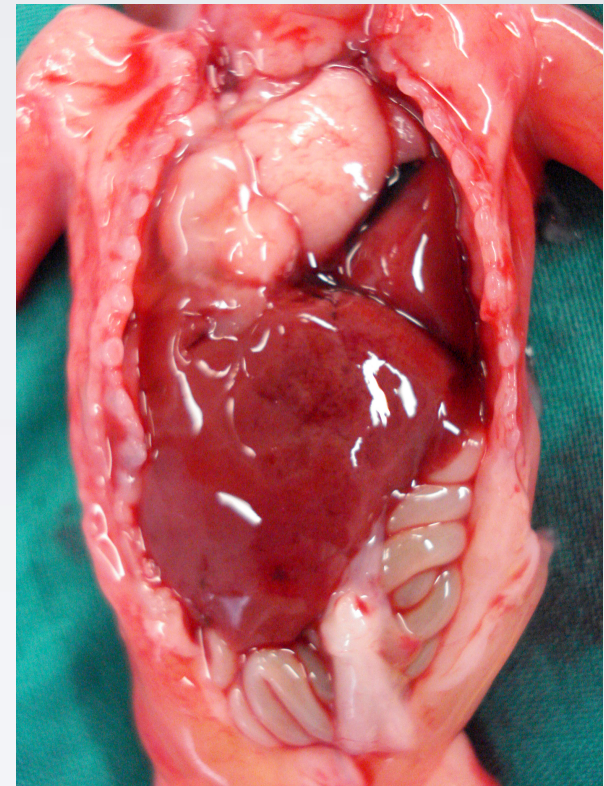
GEHIRN



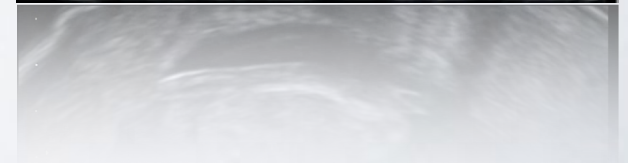
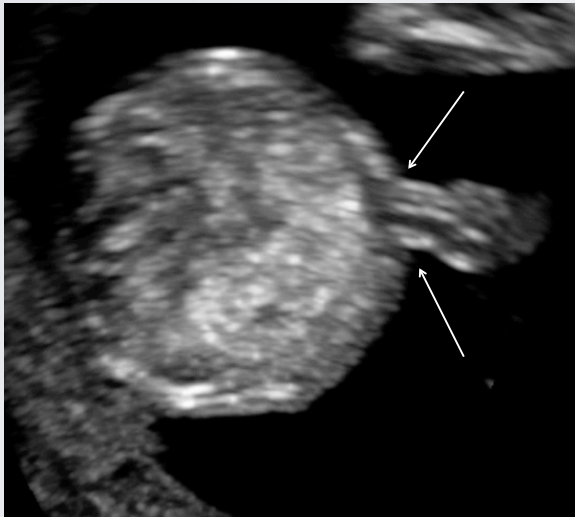
GEHIRN



ZWERCHFELL



ABDOMEN

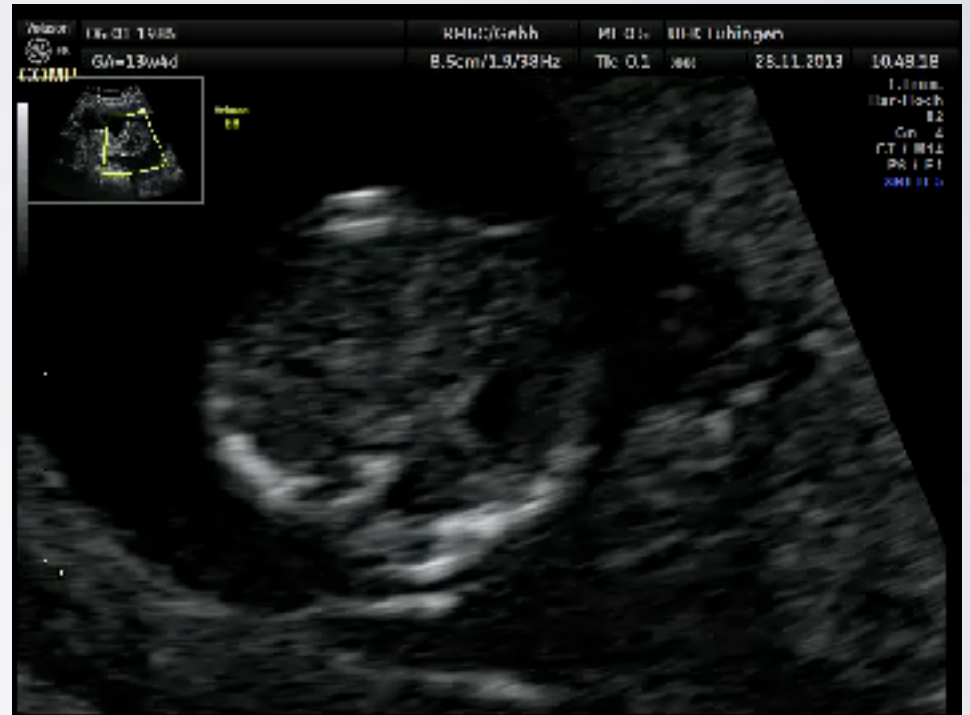


OMPHALOZELE UND ANEUPLOIDIE



SSL	n	Aneuploidie
45-55mm	102	60 %
56-65mm	35	57 %
>65mm	13	46 %
Leber	17	53 %

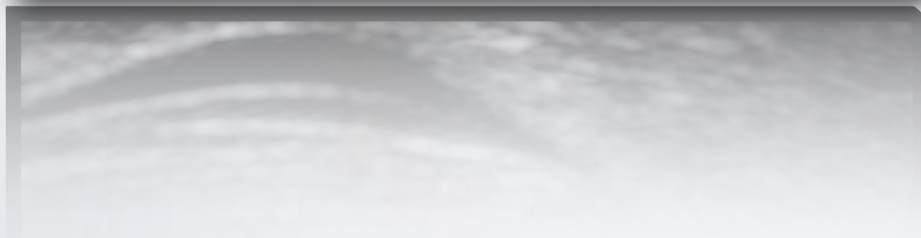
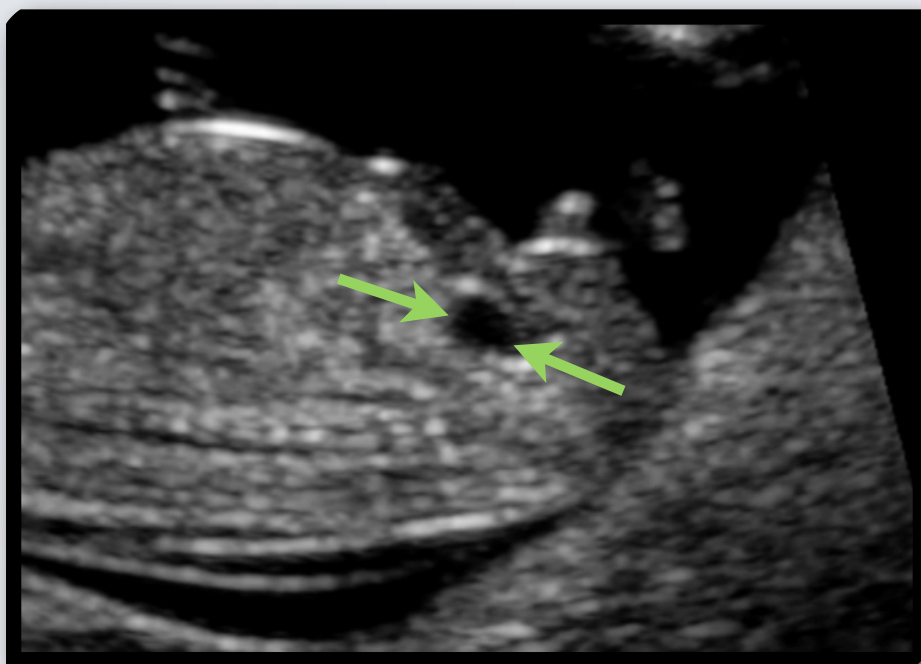
GASTROINTESTINALTRAKT



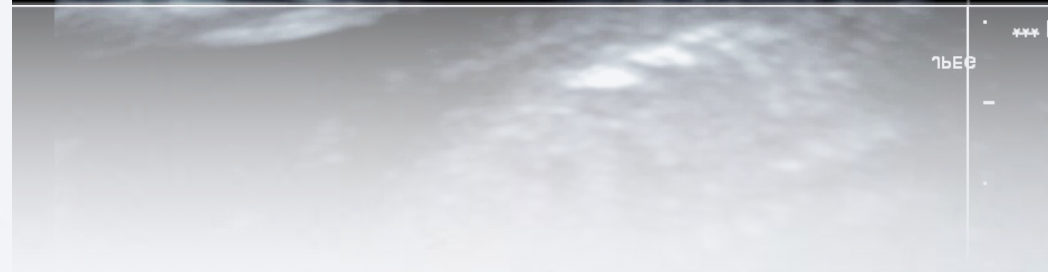
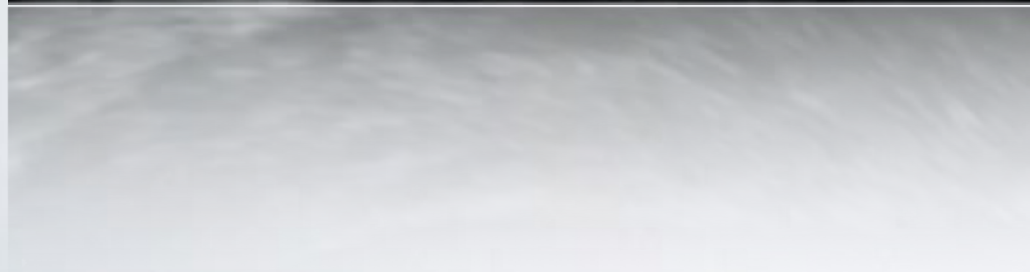
GASTROINTESTINALTRAKT



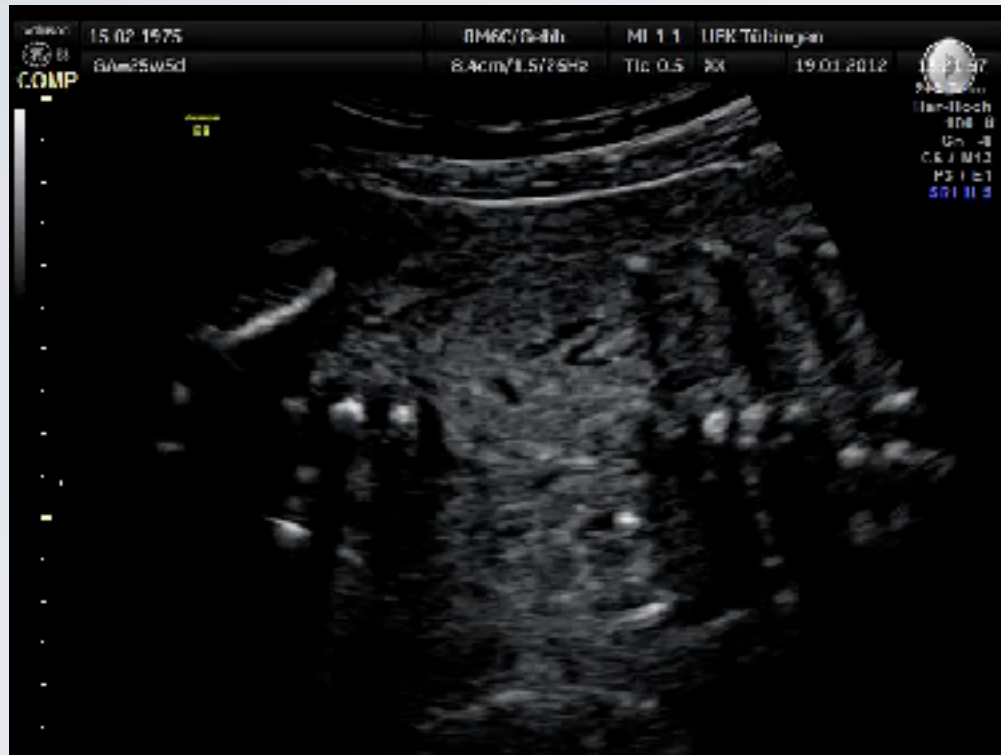
NIERE UND BLASE



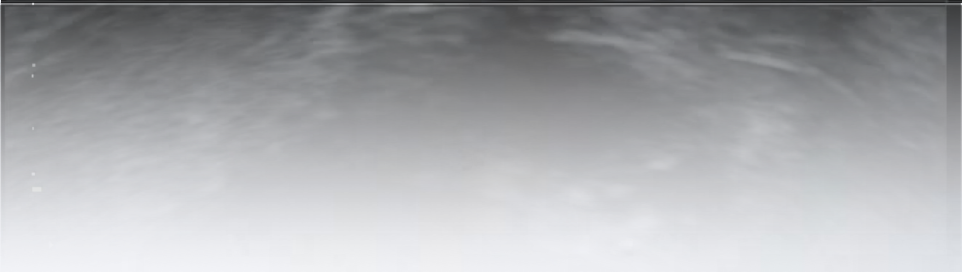
NIERE UND BLASE



NIERE UND BLASE



EXTREMITÄTEN



KOMPLEXE FEHLBILDUNGEN



KOMPLEXE FEHLBILDUNGEN



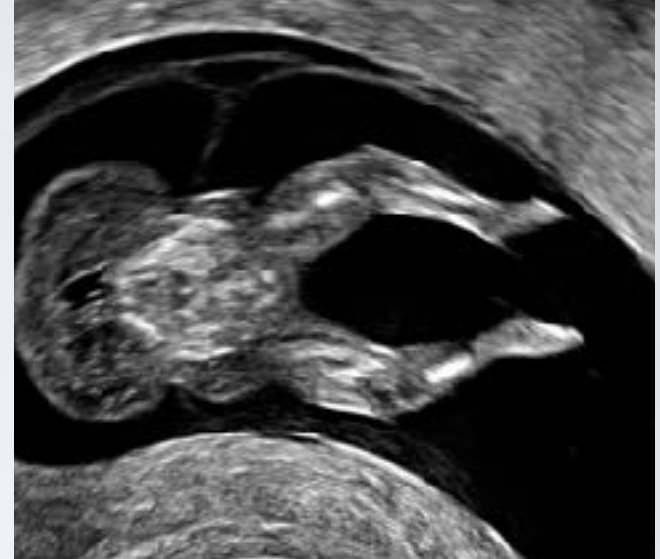
KOMPLEXE FEHLBILDUNGEN



KOMPLEXE FEHLBILDUNGEN



SONSTIGE





Tübinger Pränataltage 13 - 15 Februar 2014

**Mit Kursen zum
Fehlbildungskurs, Echokardiographie, Gyn-US,
Perinatologisches Management**

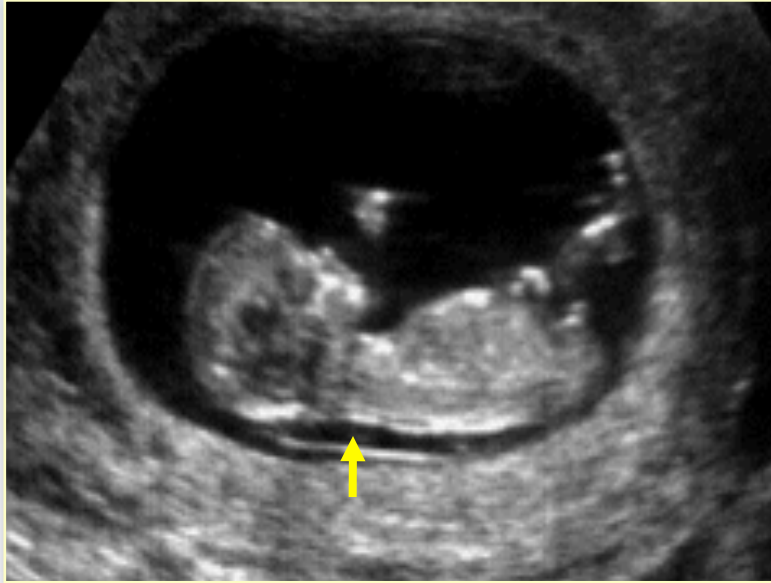
Referenten: u.a.

Arabin, Berg, Chaoui, Dürr, Eiben, Fischer, Geipel, Gonser, Hackelöer,
Hildebrandt, Kainer, Kalache, Kozlowski, Maul, Meuli, Mielke, Poets,
Prömpeler, Schleussner, Schmidt, Schramm, Stressig, Tekesin,
Verlohren, Wacker, Vetter

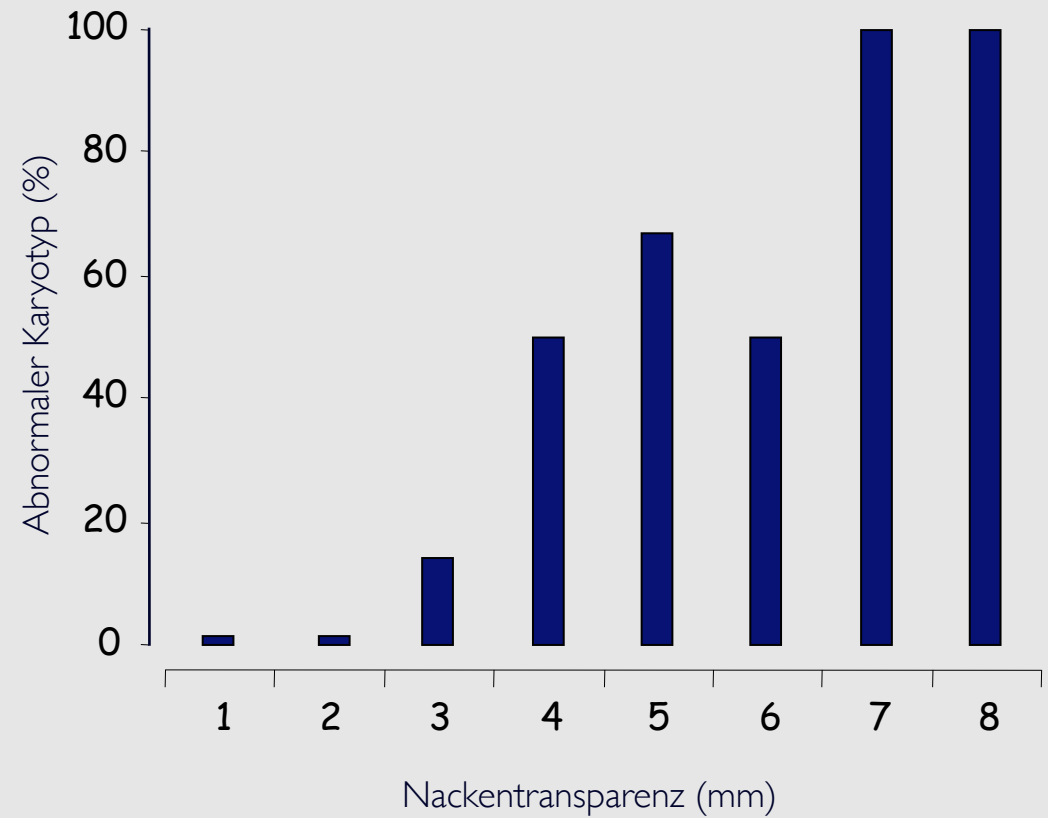
EINSATZ VON COMBINED TESTS, ZUSATZMARKERN UND NIPT



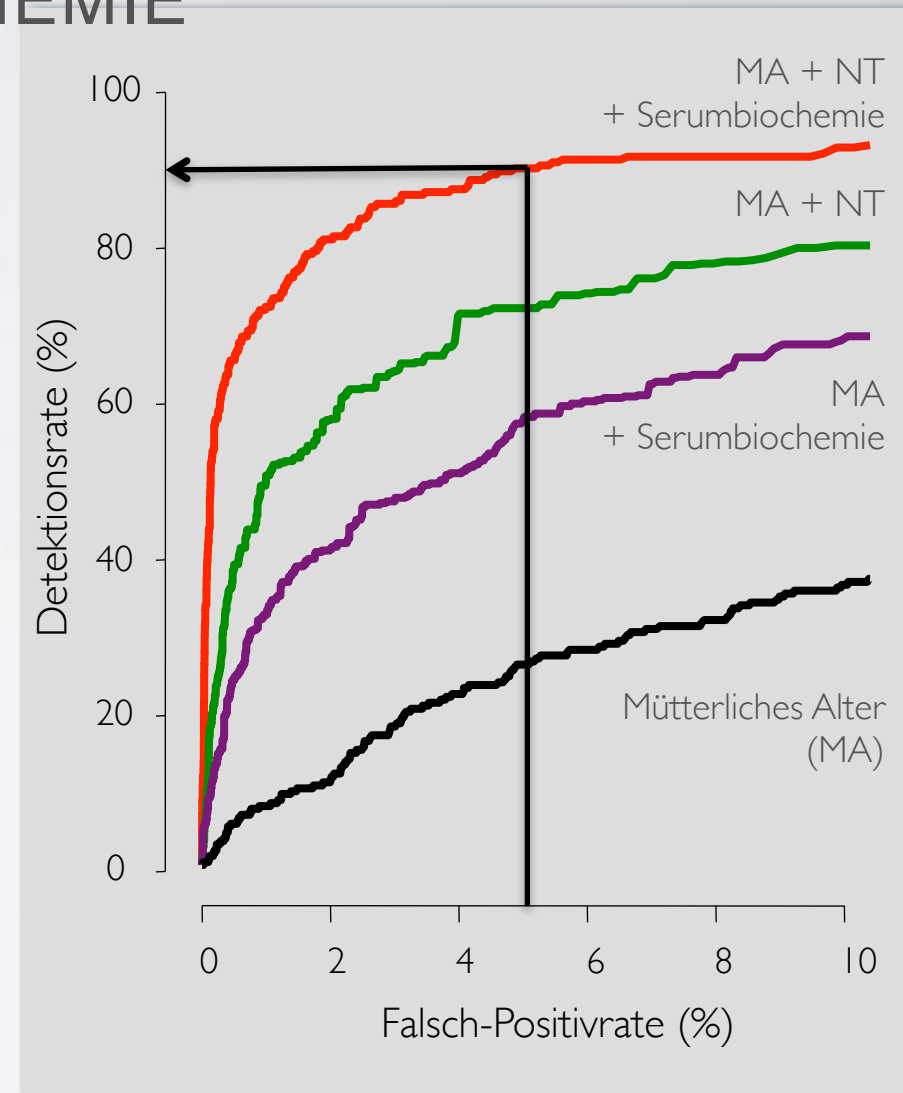
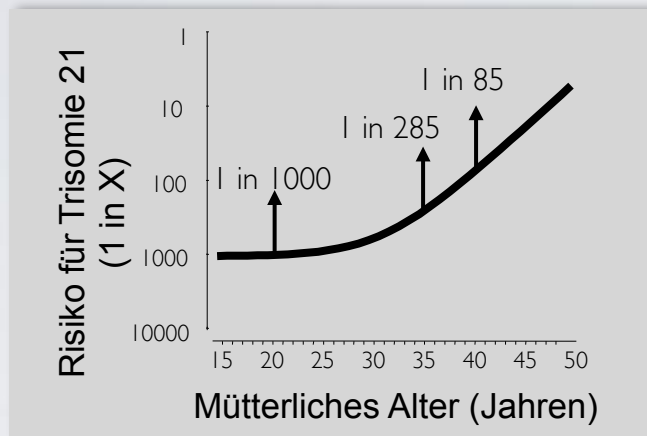
ERSTTRIMESTERSCREENING 1992



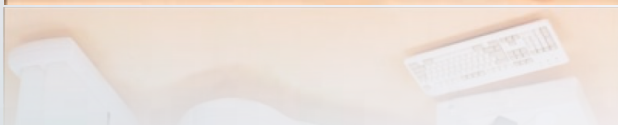
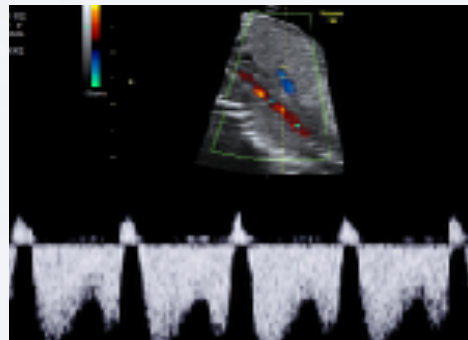
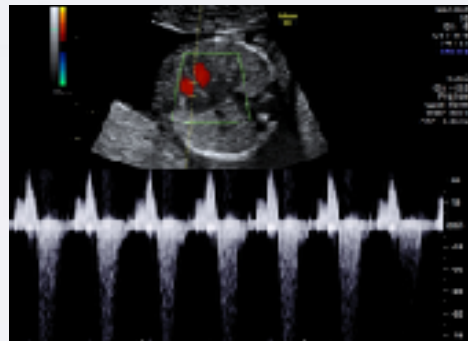
NT	Aneuploidie
<3mm	1% (10/776)
>3mm	35% (18/51)



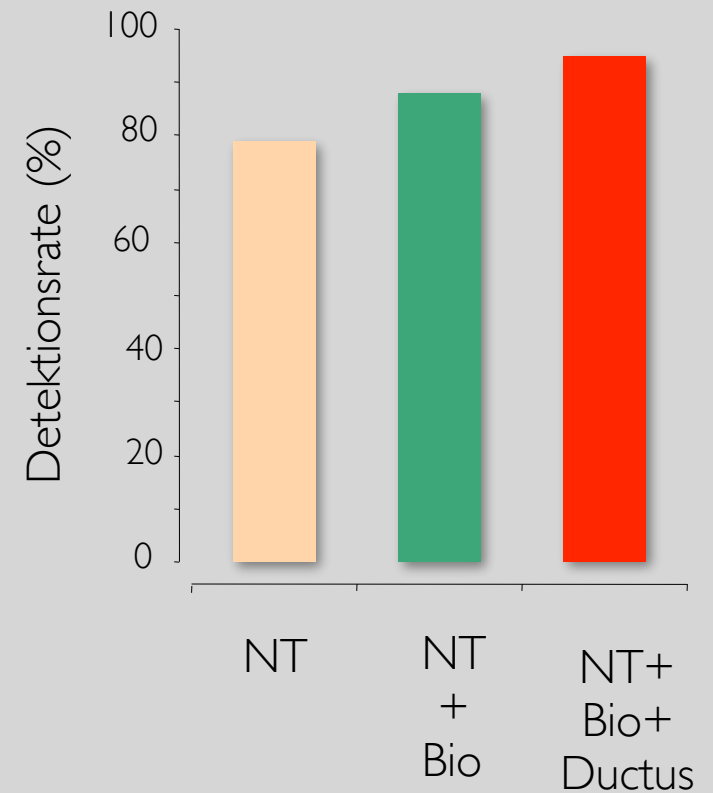
KOMBINIERTES ERSTTRIMESTER-SCREENING – MÜTTERLICHES ALTER, FETALE NT UND SERUMBIOCHEMIE



ERSTTRIMESTER-SCREENING HEUTE



DR 95% für 2-3% FPR !



KOMBINIERTES RISIKO ODER EINZELRISIKOBETRACHTUNG

Risiko für Trisomien im 1. Trimenon basierend auf der

FMF Benutzer: LizenzInformation

Chromosomenaberration, frühere Schwangerschaft: Tr 21 Tr 18

	Trisomie 21:	Trisomie 18:
Hintergrundrisiko	1 : 221	1 : 534
Risiko nach Ultraschall	1 : 1107	1 : 1619
Risiko nach Biochemie	1 : 208	1 : 3809
Adjustiertes Risiko	1 : 1055	1 : 10684

	Trisomie 21 DR (95% CI)	Euploid FPR (95% CI)
Kombiniertes Risiko ≥1:250	90,2% (86,1 - 93,5)	5,0% (4,8 - 5,2)
NT u/o Bio- Risiko ≥1:250	94,5% (92,7 - 97,5)	15,3% (15,0 - 15,6)

ÜBERPRÜFUNG MÖGLICHER FEHLERQUELLEN

Ultraschall

Bildqualität?



Biochemie

Einflussfaktoren
berücksichtigt?



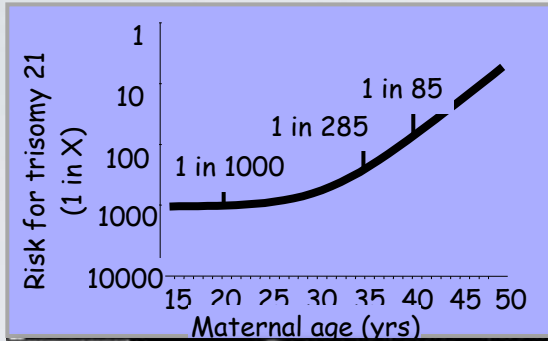
weiß, 69kg,
Nichtraucher **1:450**
Spontane Konzeption
65mm



55mm **1:1500**
75mm **1:150**

Referenzpatientin:
Aberrisiko 1:250,
b hCG 1,44 MoM
PAPP-A 0,95 MoM

ERSTTRIMESTER-SCREENING AUF TRISOMIE 21 IN DEUTSCHLAND

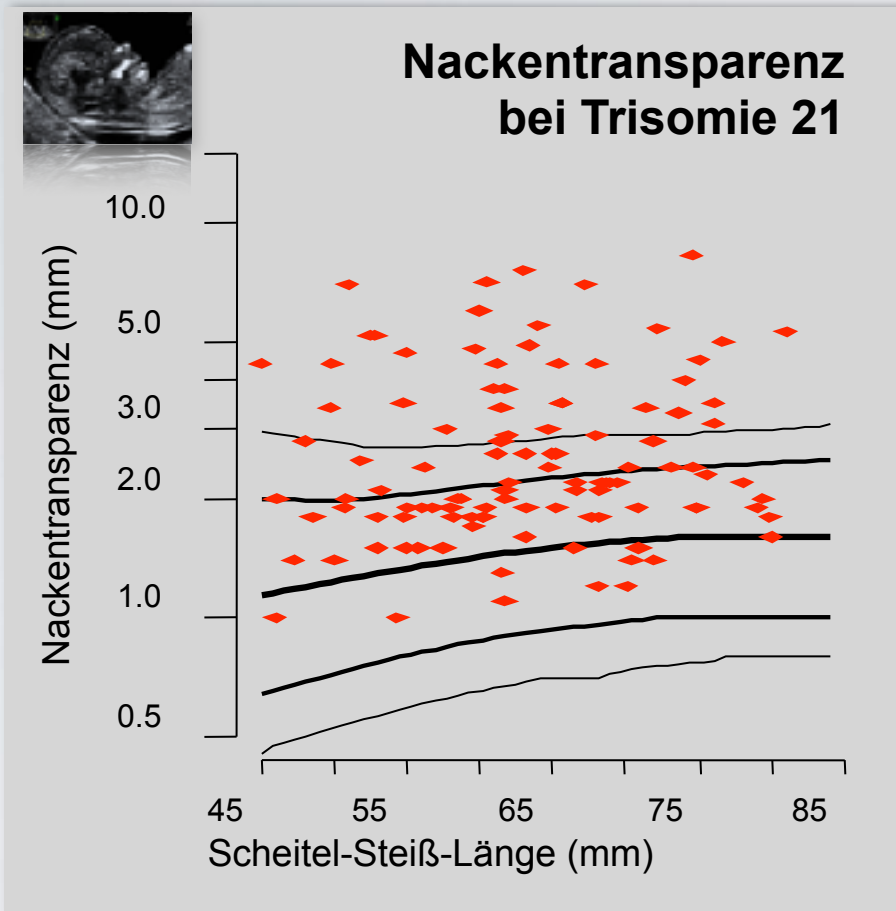


Screening-Methode DR bei FPR 5%

MA + NT	48%
MA + Biochemie	65%
MA + NT + Biochemie	80%

Euploid n=38.751
Trisomie 21 n=109

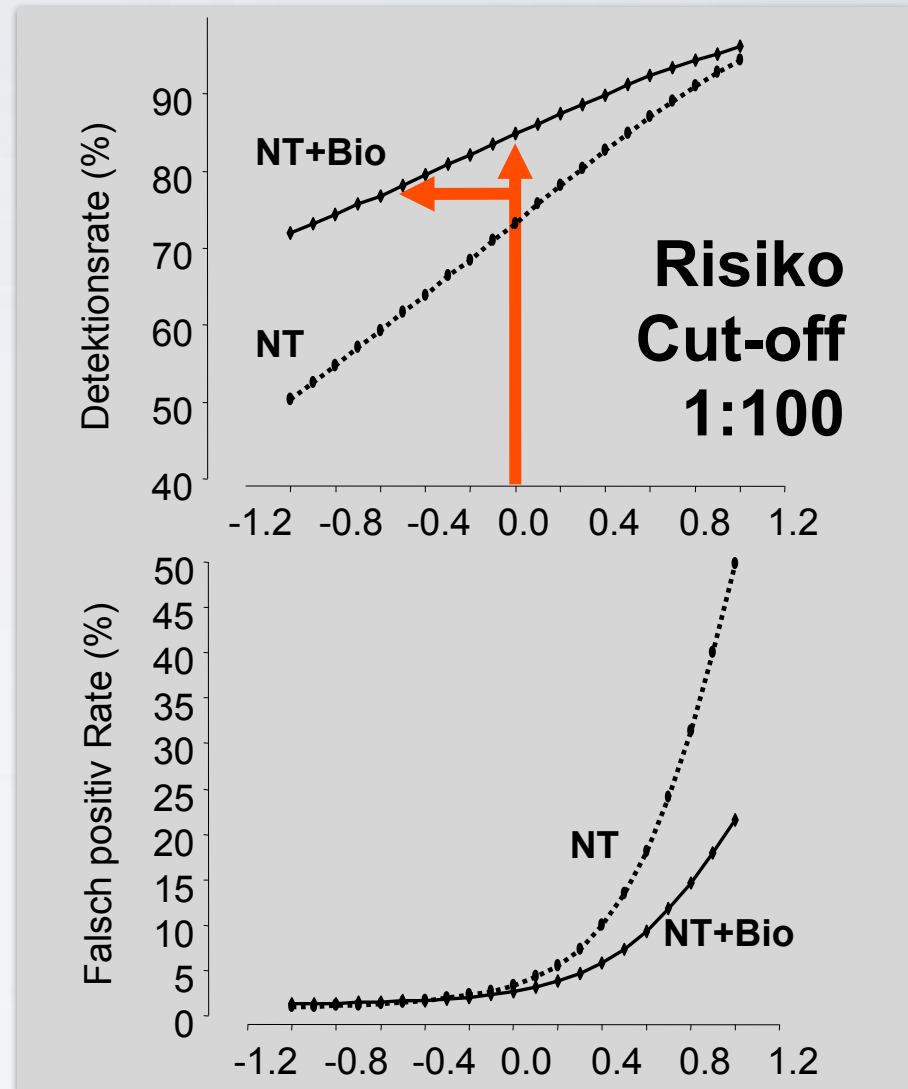
NACKENTRANSPARENZMESSUNG BEI TRISOMIE 21



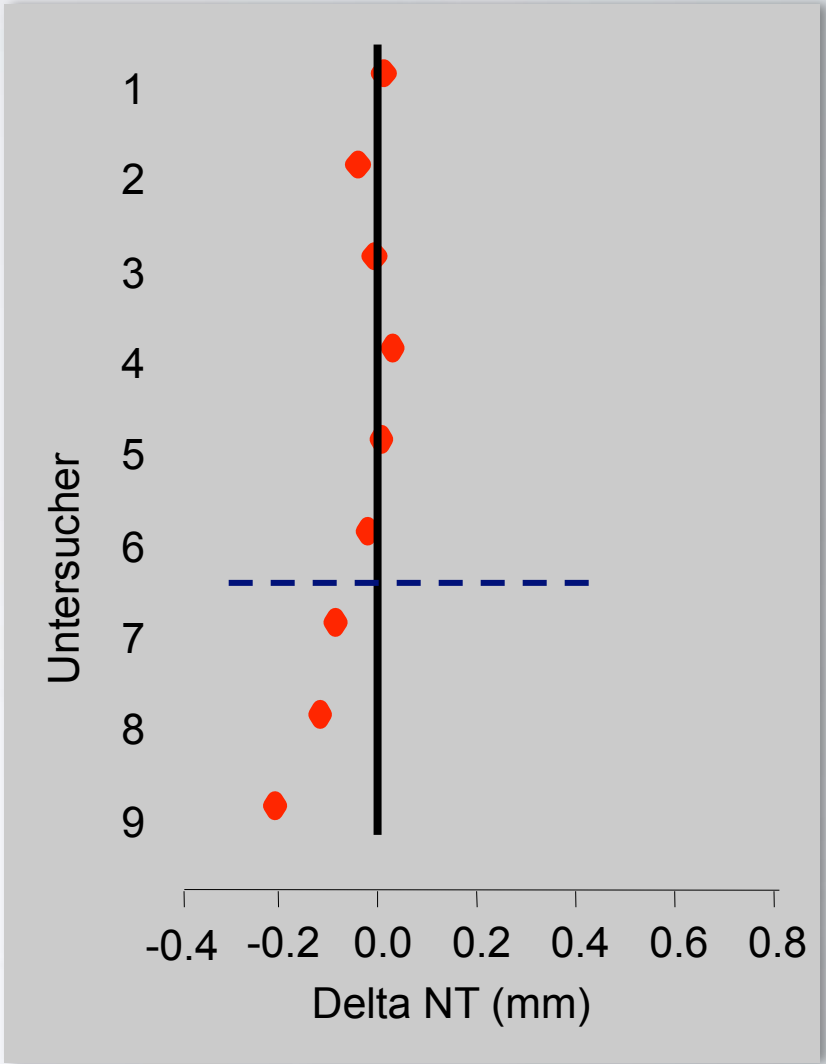
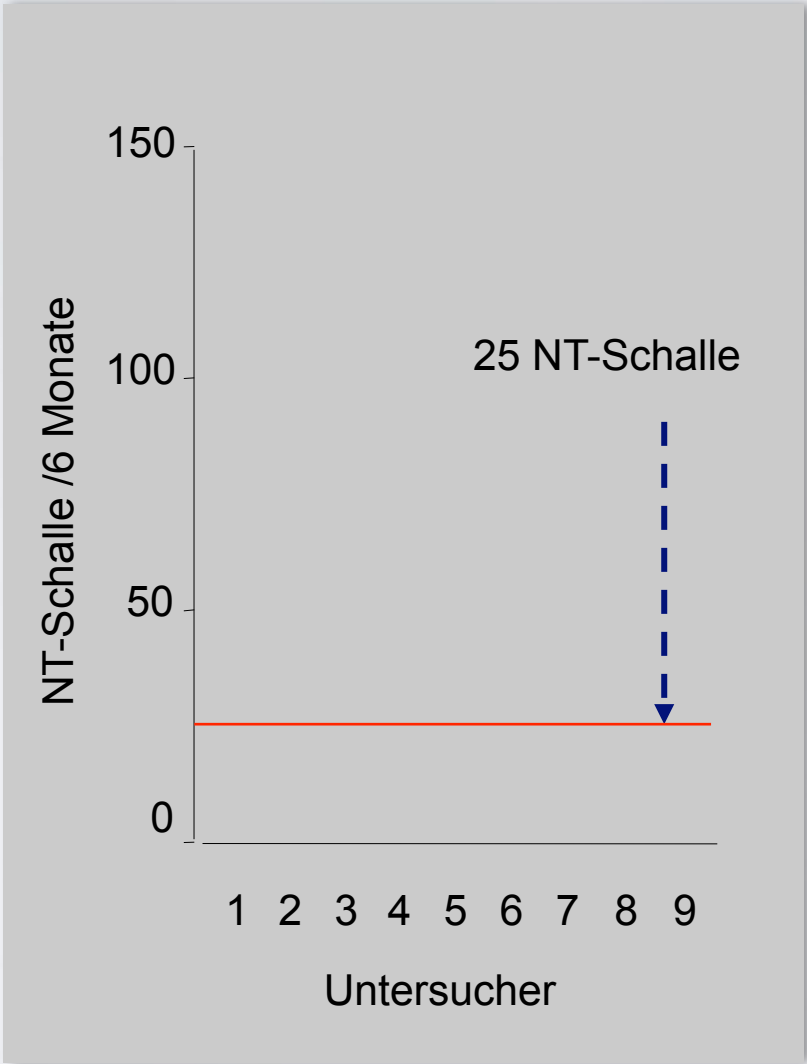
DeltaNT bei Trisomie 21

Degum 0/1: +0,55 mm

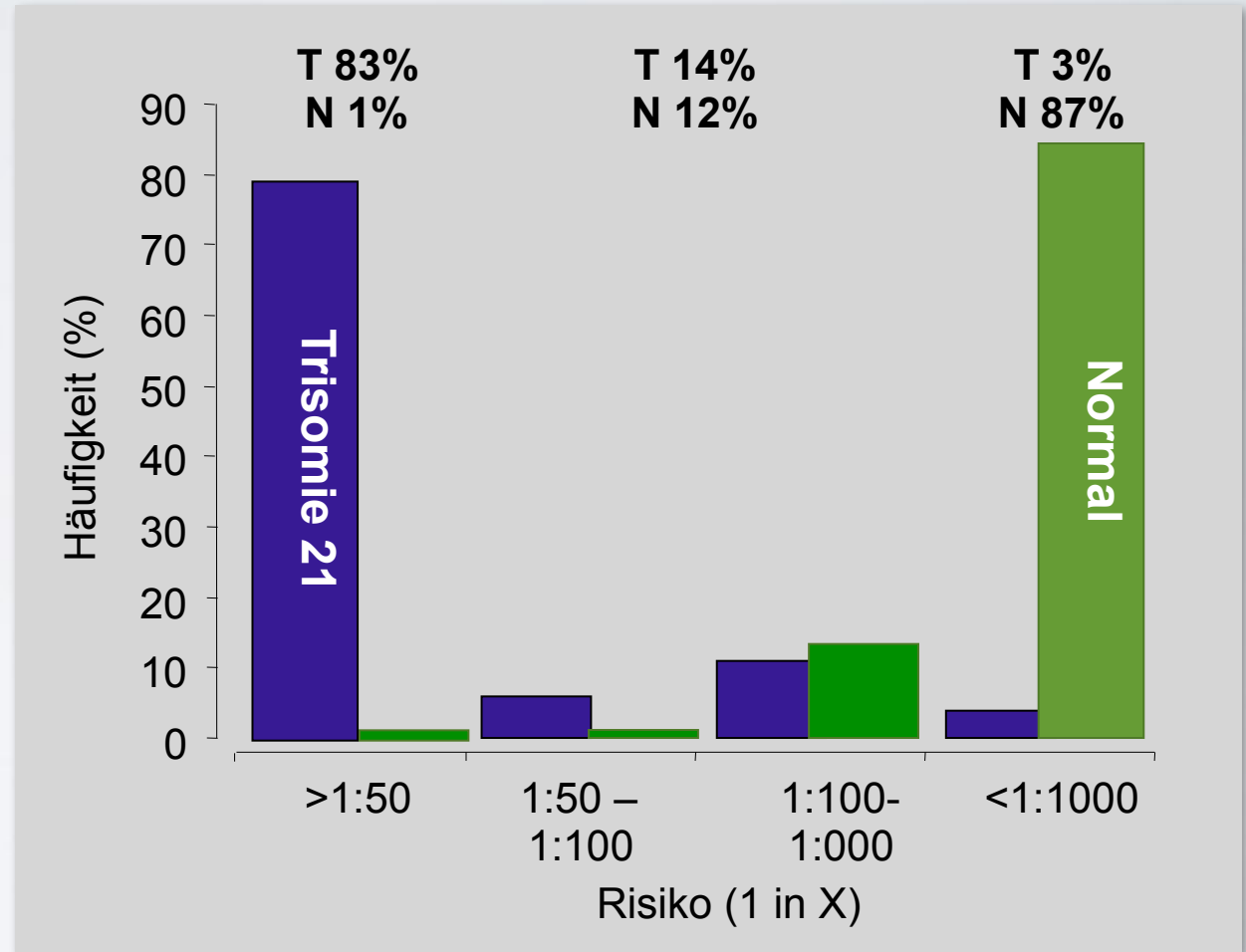
Degum 2/3: +0,97 mm



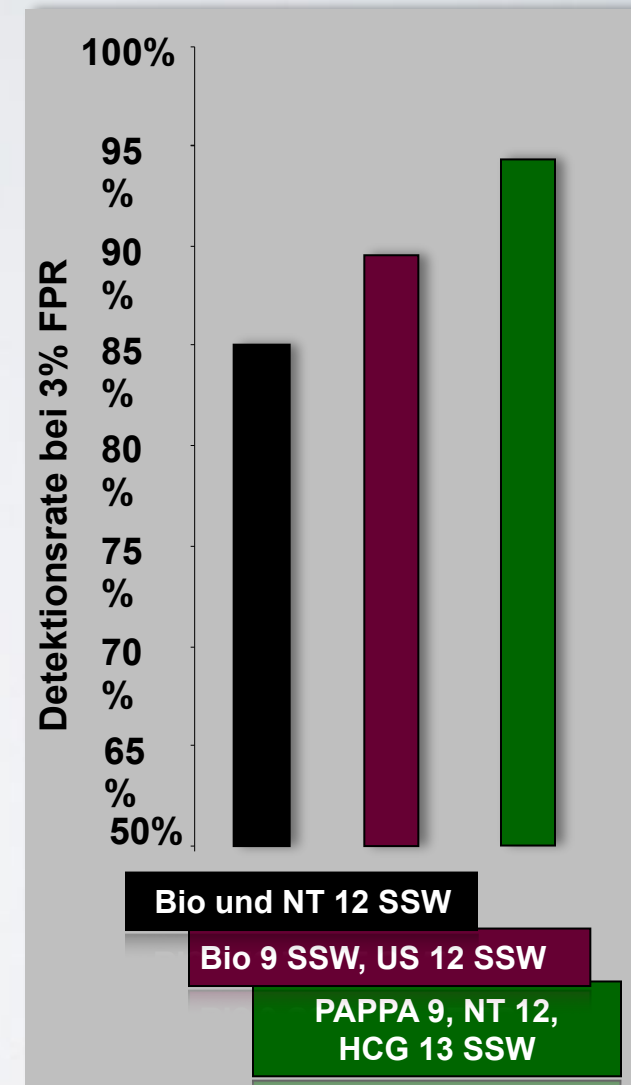
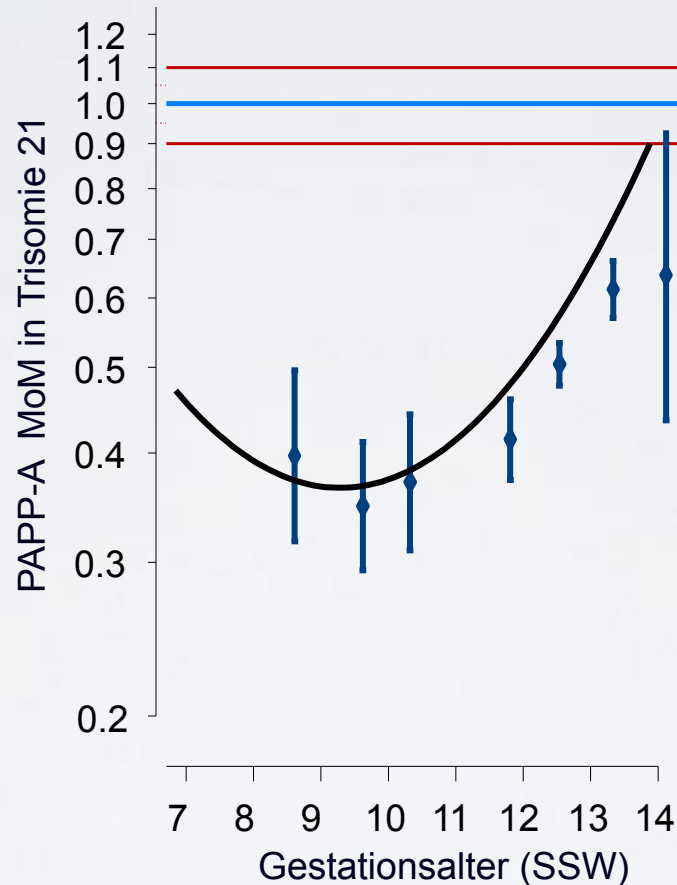
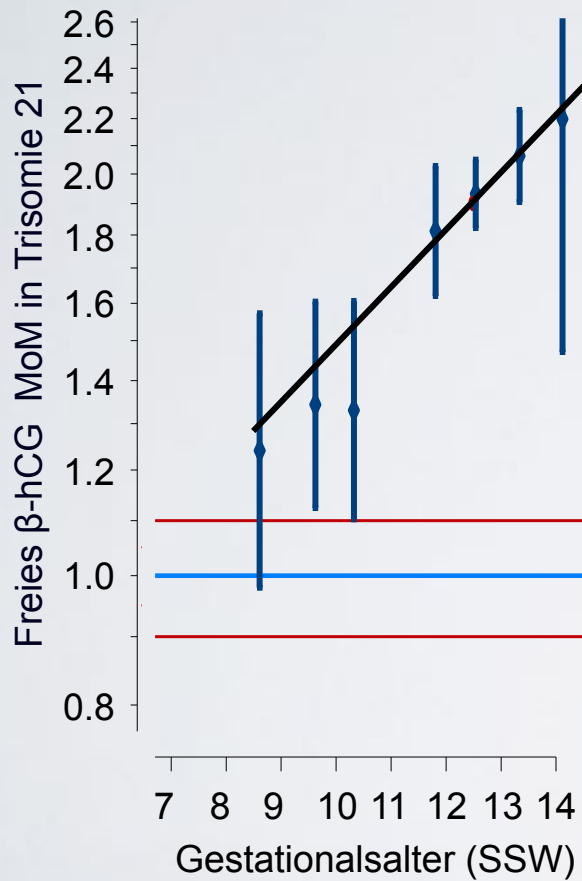
UNTERSUCHUNGSFREQUENZ UND QUALITÄT (DQAAS)



VERTEILUNG DER RISIKEN BEI ADÄQUATEM ETS



ZWEIZEITIGES ERSTTRIMESTER-SCREENING



222,821 normale SS und 886 mit Trisomie 21 aus UK, Dänemark and Zypern

ANPASSUNG DER SERUMBIOCHEMIE AN WERTE DER VORSCHWANGERSCHAFT

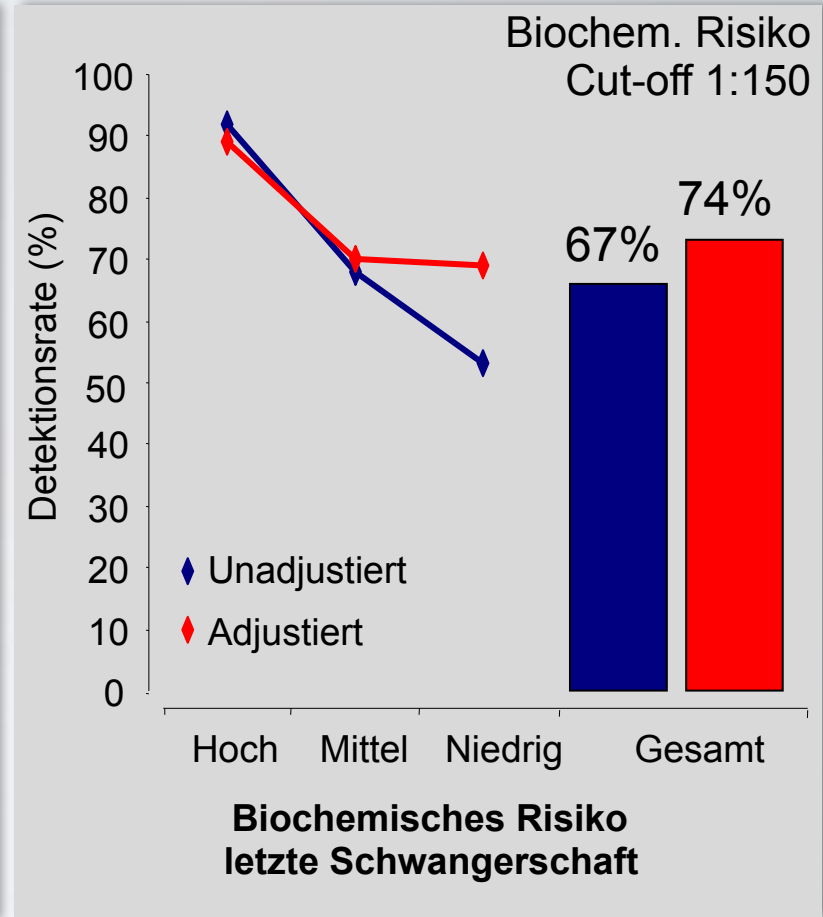
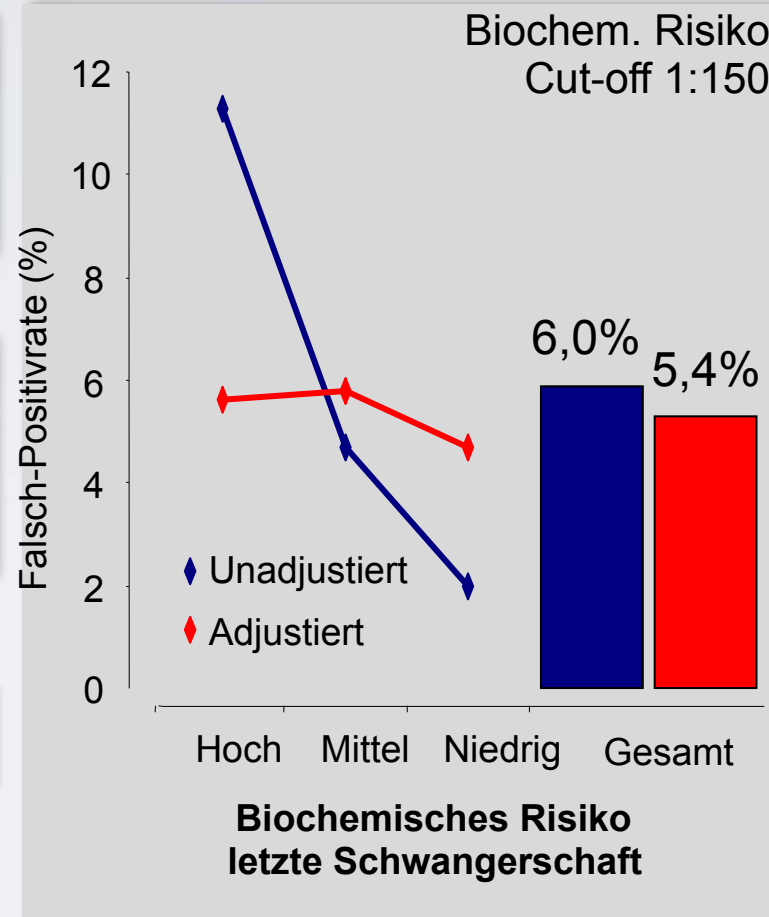
Folge-
schwangerschaften
Euploid n=8.499
Trisomie 21 n=49

Einteilung nach
Biochemie der
ersten
Schwangerschaft

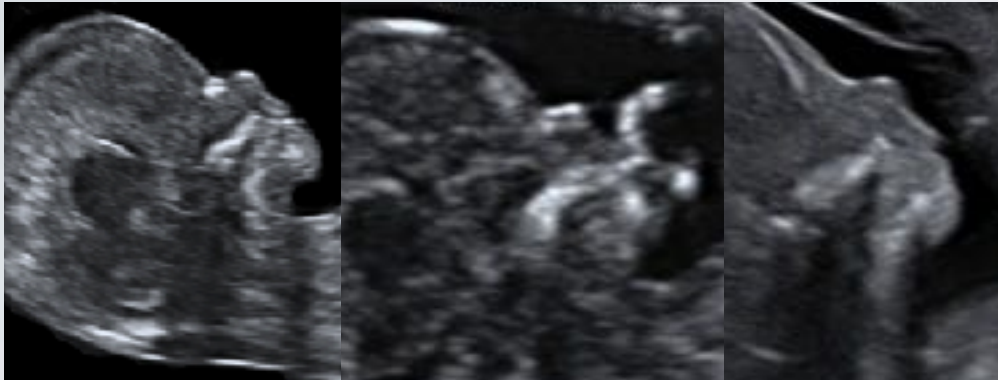
Hoch

Niedrig

Mittel

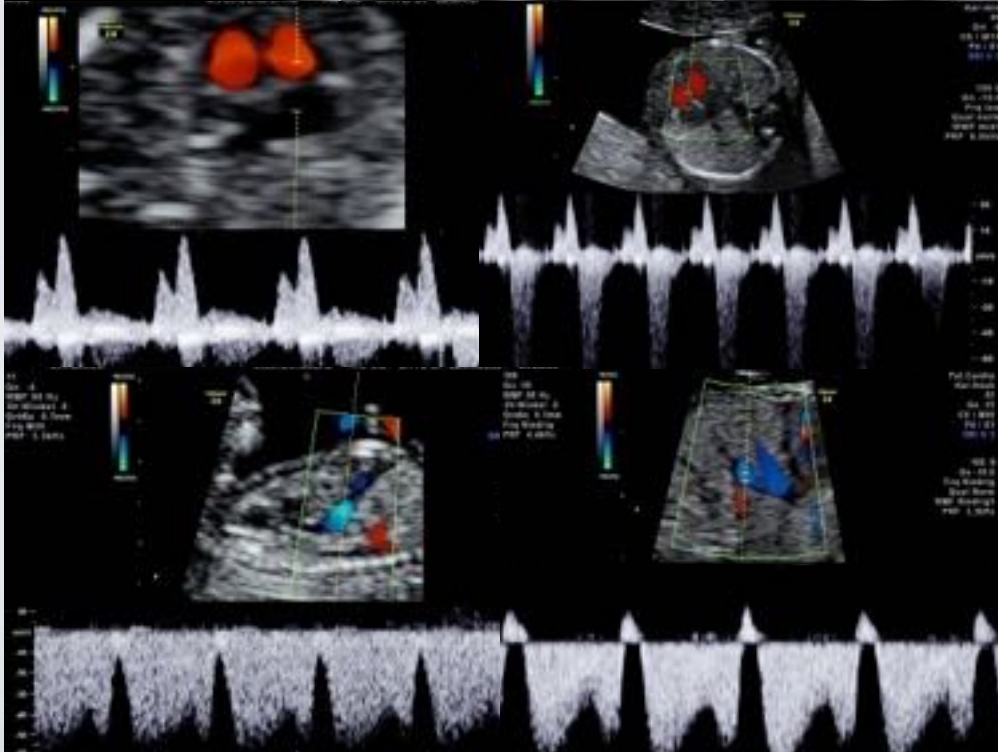


NEUE ULTRASCHALLMARKER



Nasenbein

DR 60% und FPR 1-3%



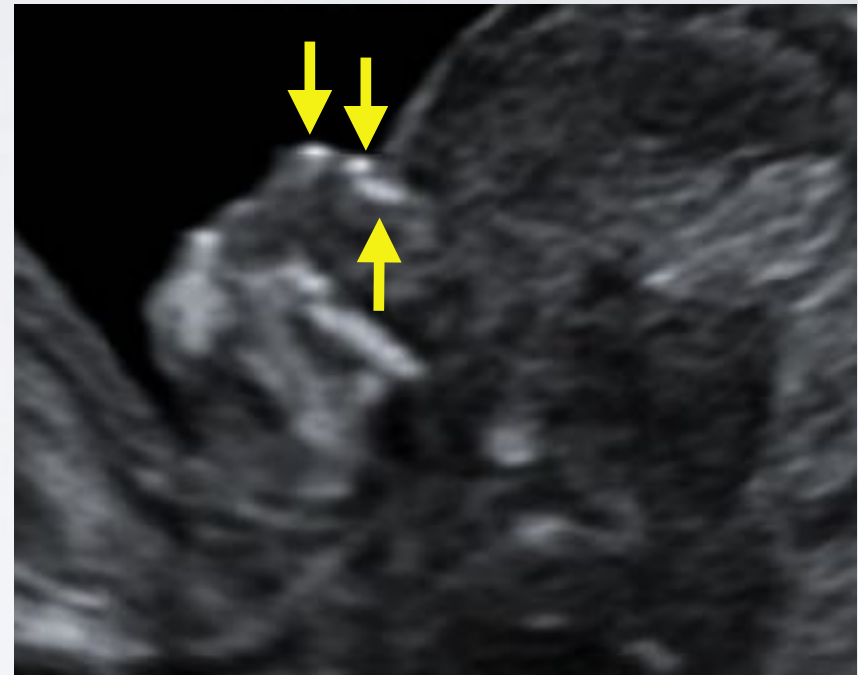
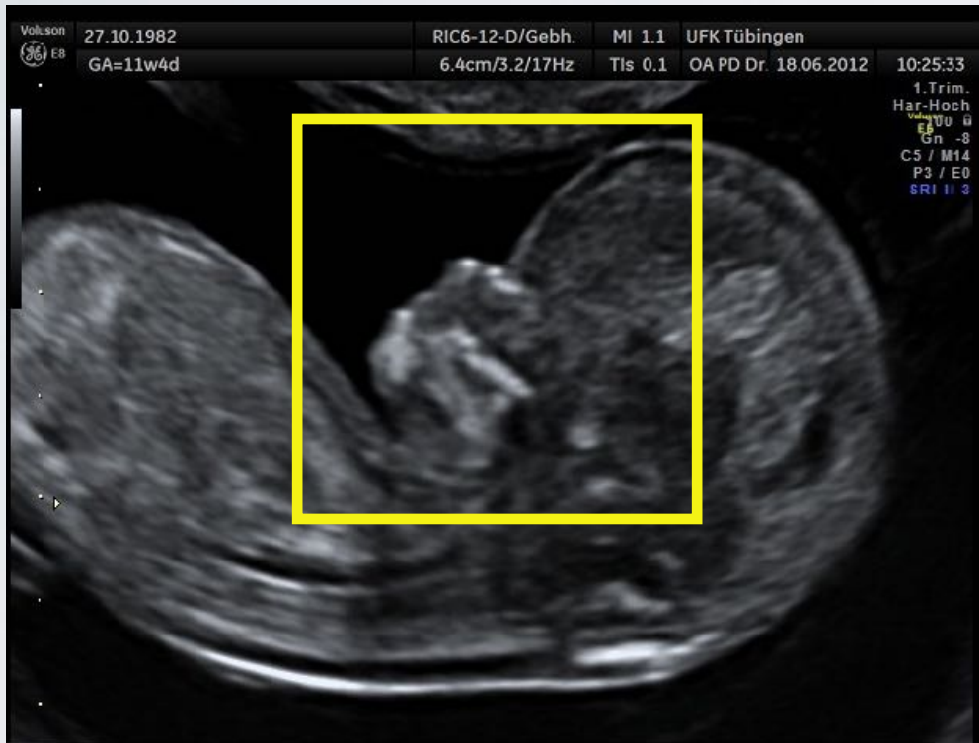
Trikuspidalklappenfluss

DR 56% und FPR 1%

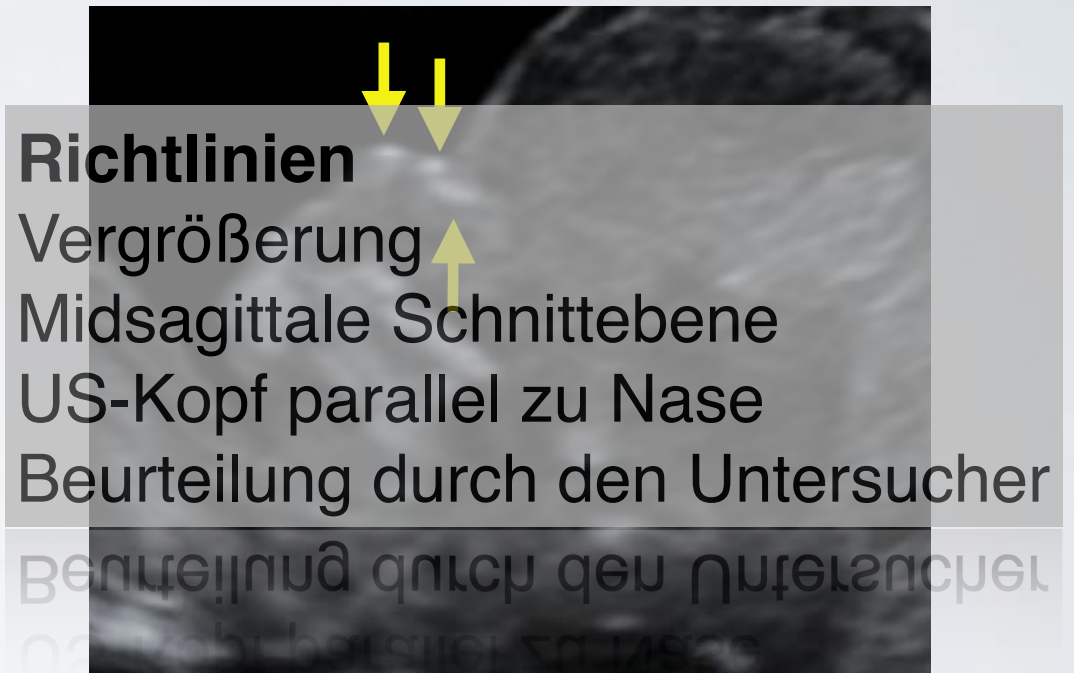
Ductus venosus

DR 66% und FPR 3%

NASENBEIN



NASENBEIN



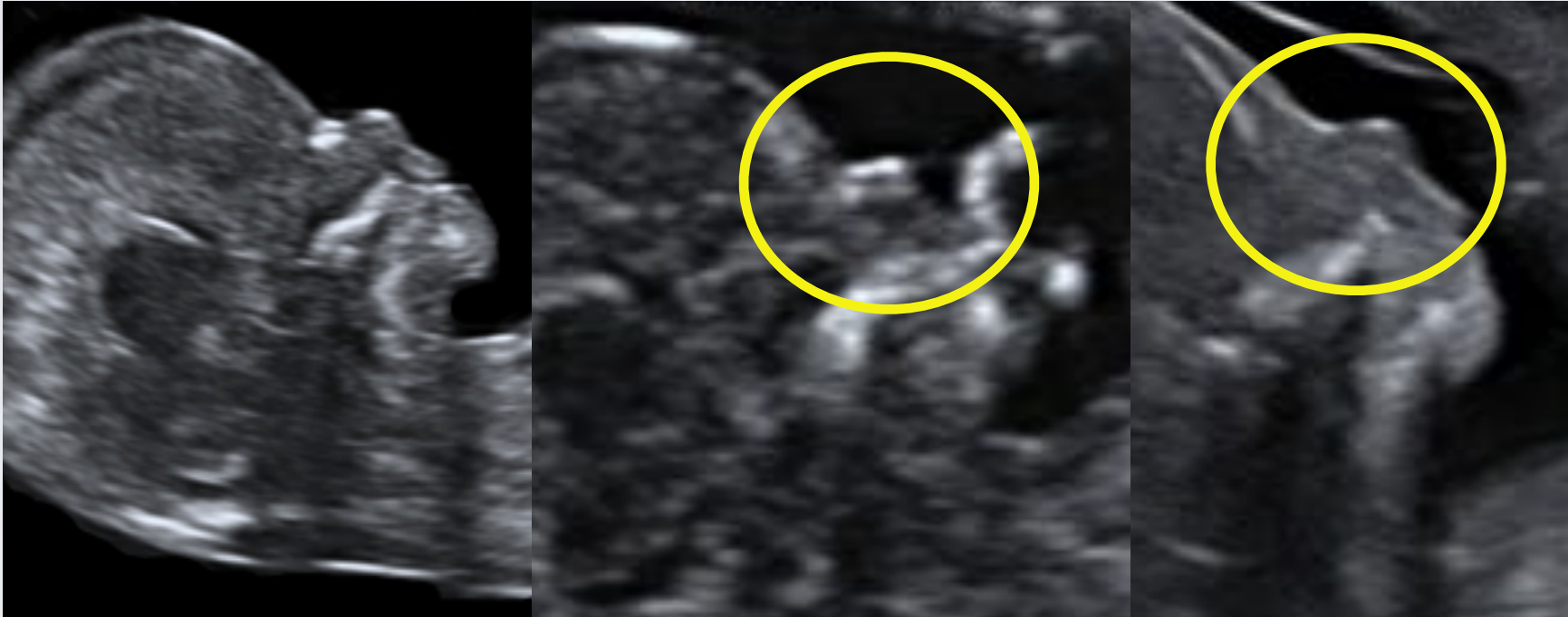
NASENBEIN



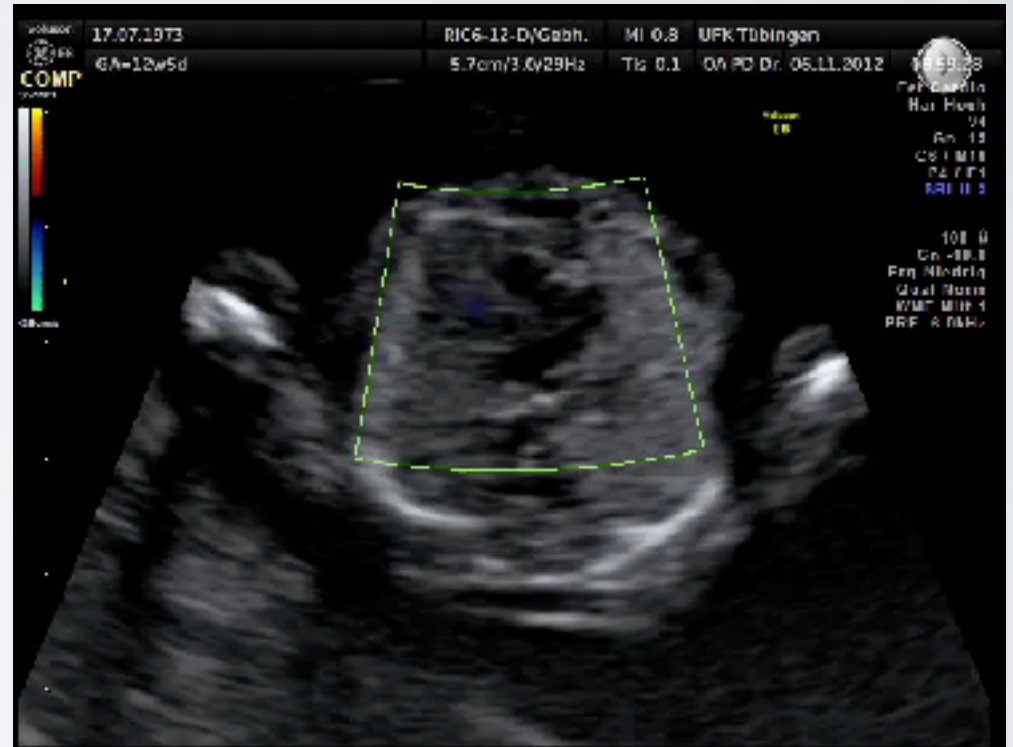
Detektionsrate bei Trisomie 21: 60%
Falsch-Positivrate bei normalen Feten: 1-3%

FALSCH-POSITIVRATE BEI NORMALEN FETEN: 1-3%

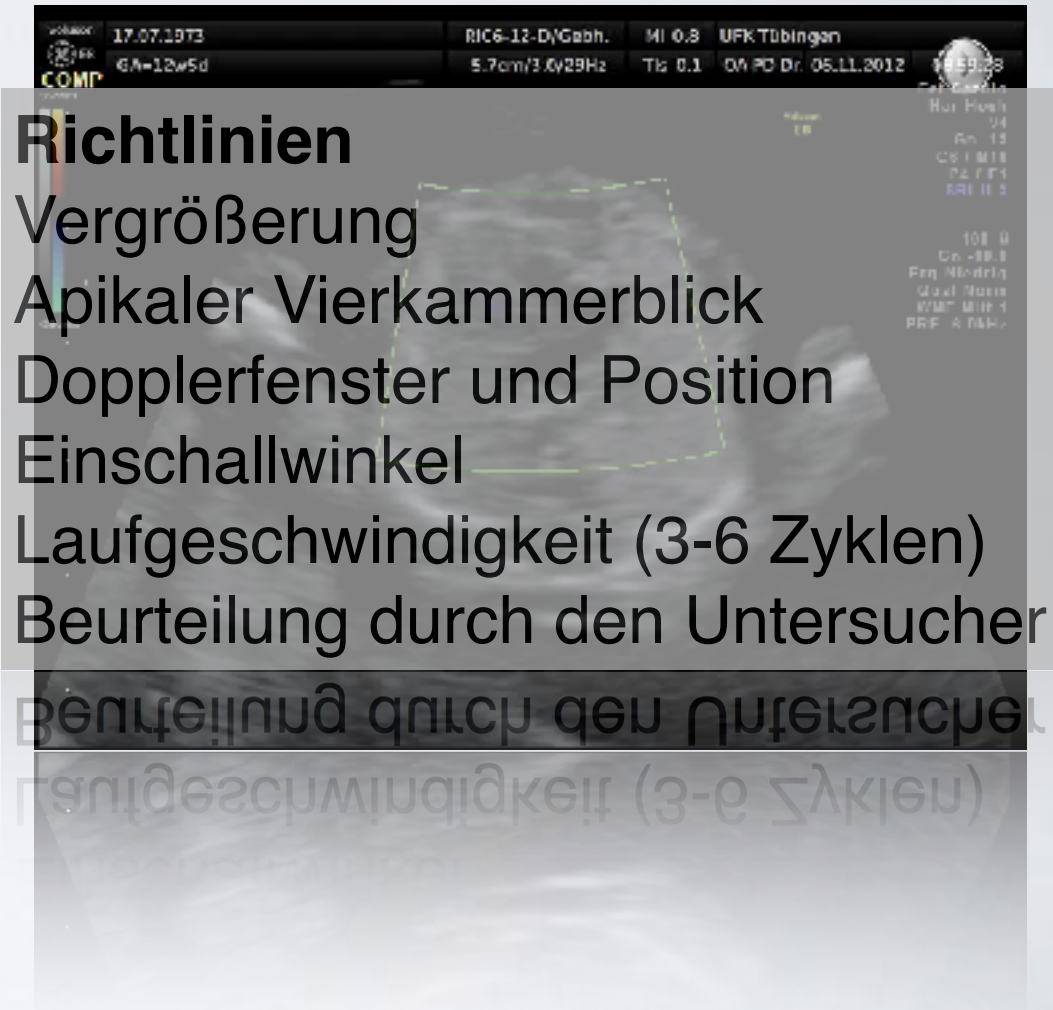
NASENBEIN



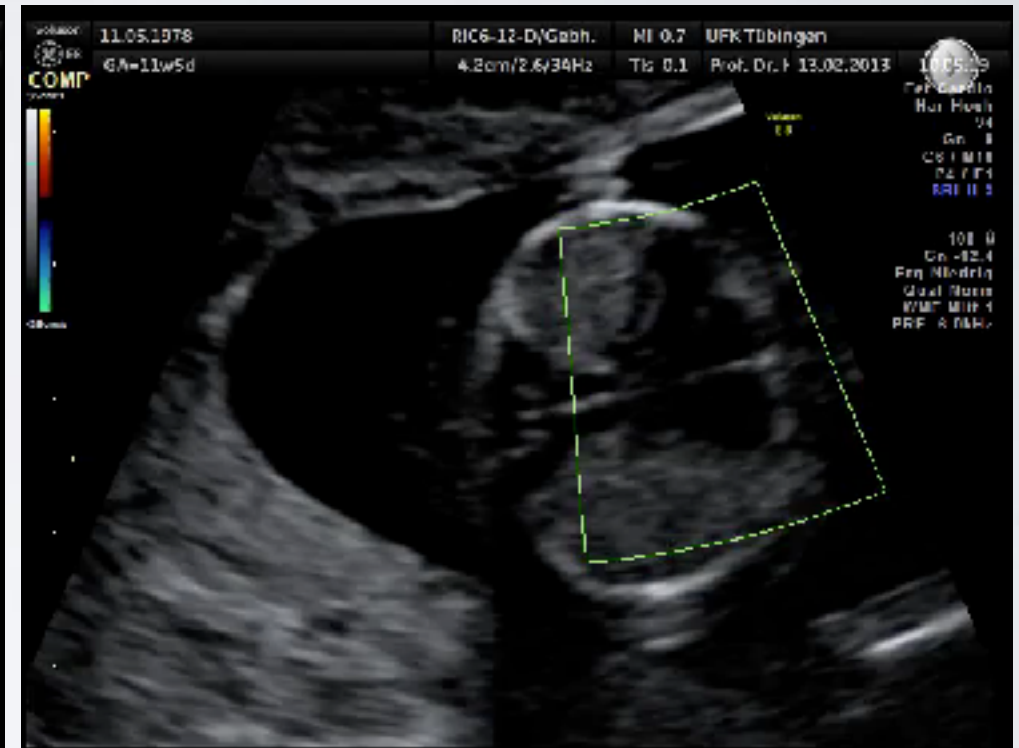
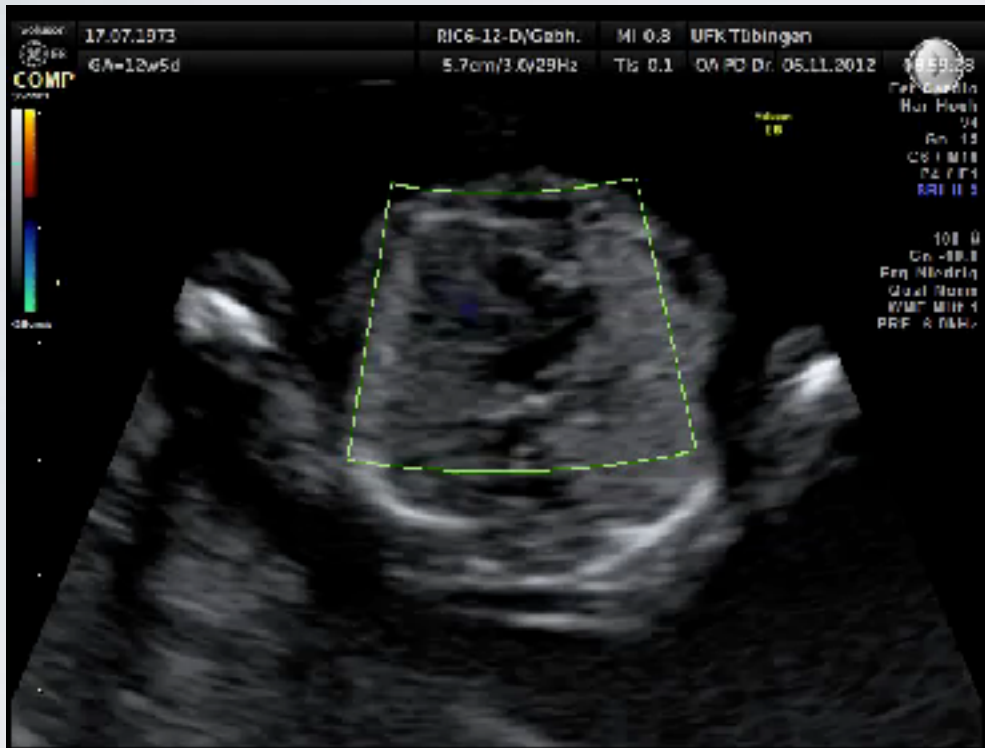
TRIKUSPIDALKLAPPENFLUSS



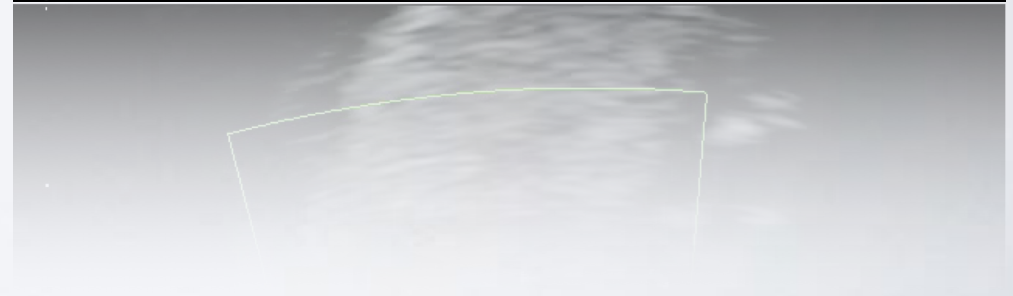
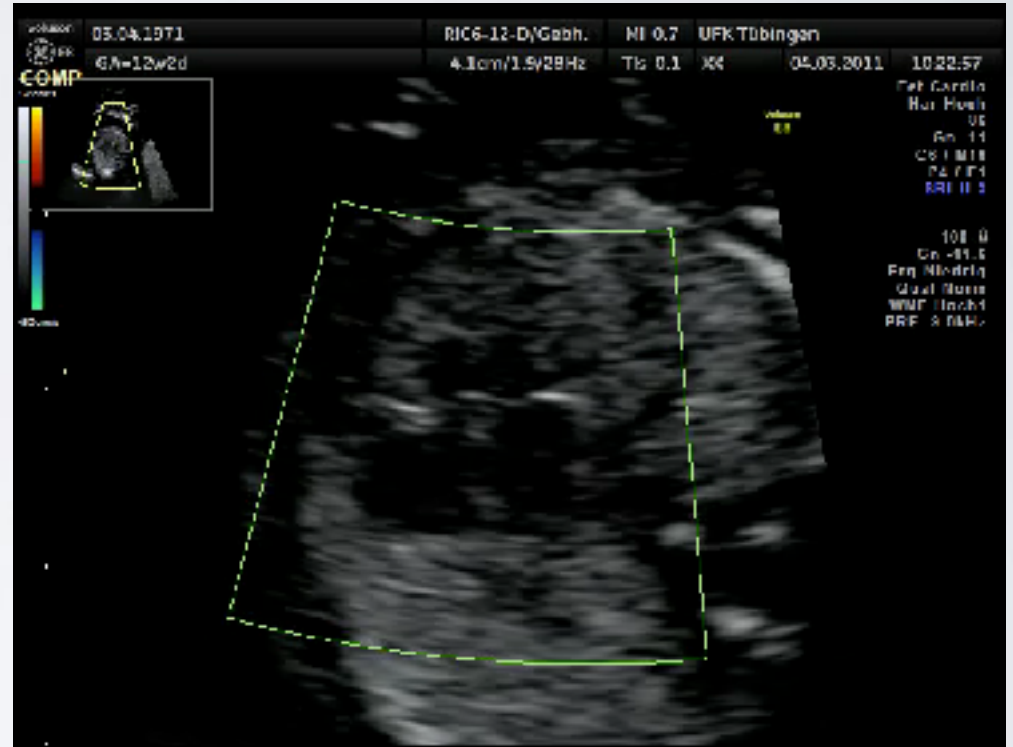
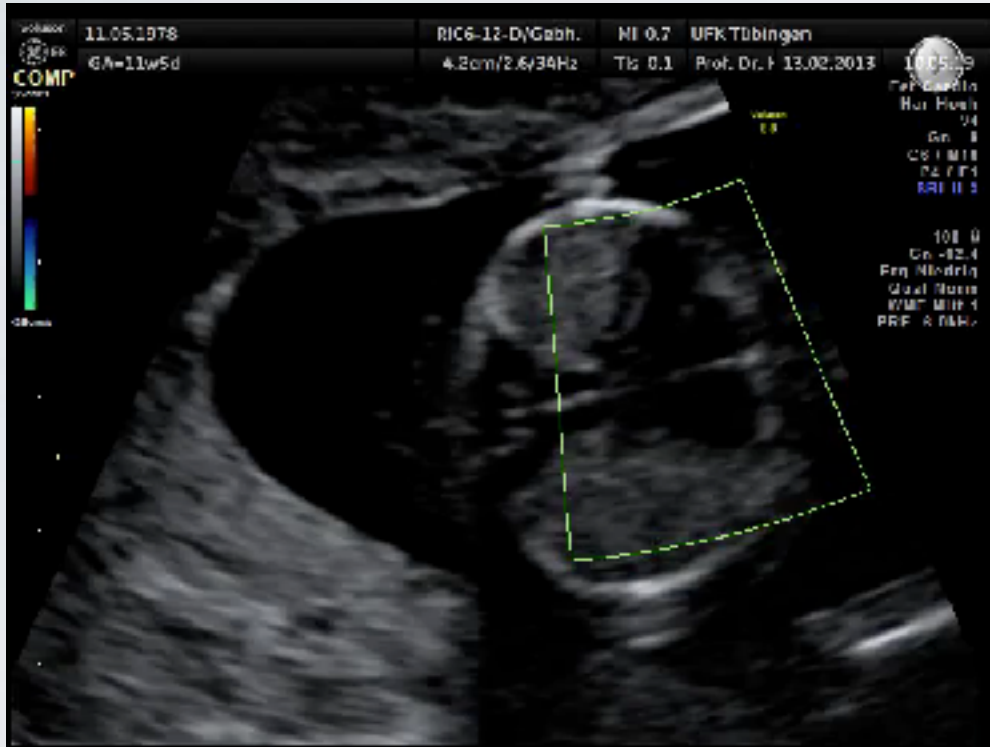
TRIKUSPIDALKLAPPENFLUSS



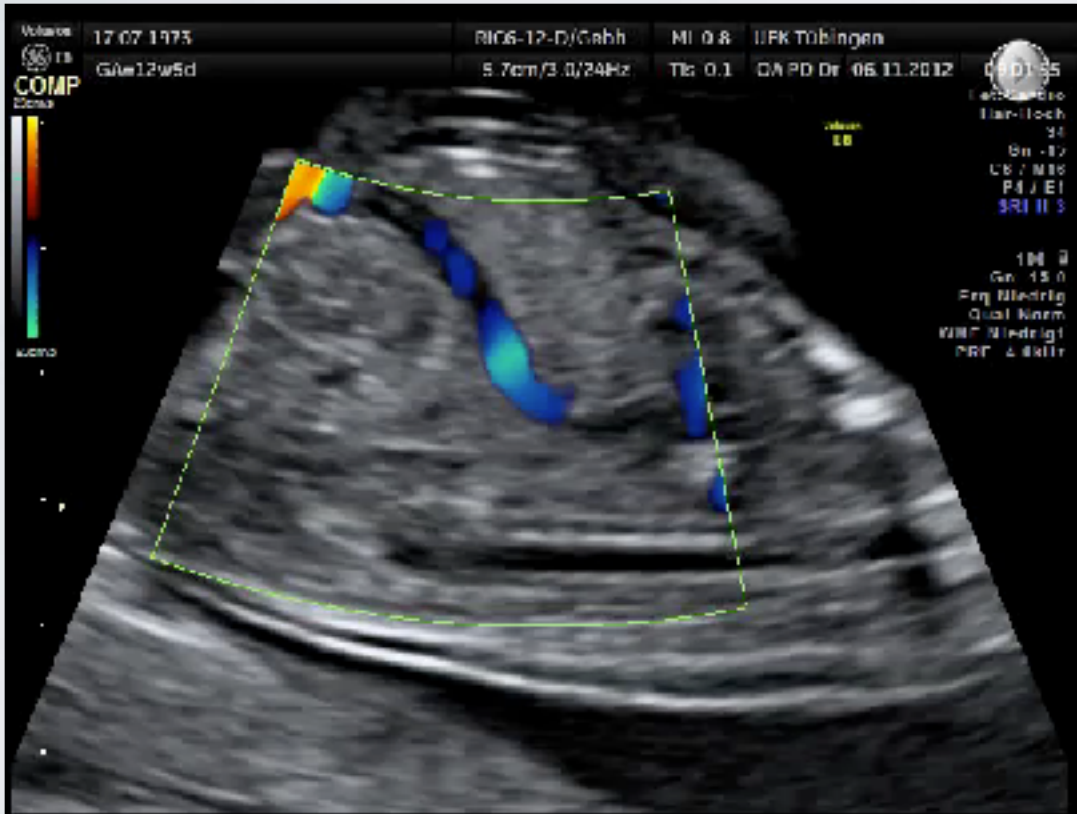
TRIKUSPIDALKLAPPENFLUSS



TRIKUSPIDALKLAPPENFLUSS

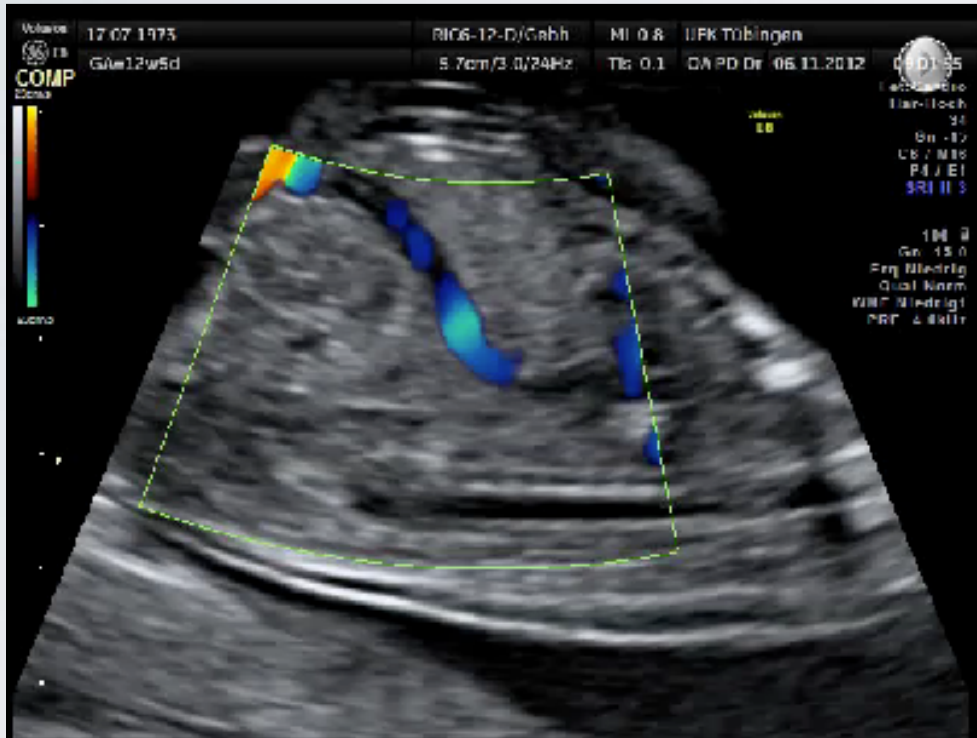


DUCTUS VENOSUS



- Midsagittaler Schnitt
- Dopplerwinkel $<30^\circ$
- Filter auf Minimum

DUCTUS VENOSUS



Richtlinien

Vergrößerung

Midsagittale Schnittebene

Dopplerfenster und Position

Einschallwinkel $<30^\circ$

Filter 50-70 Hz

Laufgeschwindigkeit (3-6 Zyklen)

Beurteilung durch den Untersucher

Beurteilung durch den Untersucher

Laufgeschwindigkeit (3-6 Zyklen)

Filter 50-70 Hz

Richtlinien

TRIKUSPIDALKLAPPENFLUSS

Detektionsrate bei Trisomie 21: 56%
Falsch-Positivrate bei normalen Feten: 1%

Falsch-Positivrate bei normalen Feten: 1%



Welcome to the Fetal Medicine Foundation

The Fetal Medicine Foundation is a Registered Charity that aims to improve the health of pregnant women and their babies through research and training in fetal medicine.

The Foundation, with the support of an international group of experts, has introduced an educational programme both for healthcare professionals and parents and a series of certificates of competence in different aspects of fetal medicine.

In the last 17 years, The Foundation has supported research and training in the following areas through grants to a total of more than £15 million:

- Early diagnosis of fetal abnormalities
- Screening for chromosomal defects
- Development of safer techniques for prenatal diagnosis
- Intrauterine fetal surgery
- Prediction and prevention of stillbirth
- Prediction and prevention of pre-term birth
- Preeclampsia and fetal growth restriction
- Problems of multiple pregnancies

If you are a health care professional and you want to go to the [FME](#) page please login below:

Name: Password:

Advances in Fetal Medicine

L o n d o n - 2 0 1 3

Dates: 14th and 15th of December

Venue: Institute of Education, London University

Address: 20 Bedford Way, WC1H 0AL, London

Online registration is open, please [click here](#)

Programme is available, please [click here](#)

Videos of fetal echocardiography

This is a new internet-based course by Dr Fred Ushakov and is based on videos of first trimester cardiac defects.

Please [click here](#) to go to the course main page



Centre **Foundation** Courses & Congress Training & Certification Online Education Research Look for Life Contact us

Own page Logout

Welcome to your personal FMF page

Personal details

Name: Karl Oliver **Kagan** FMF ID number: **31444**

View or edit your [contact details](#) Change your [password](#)

FMF Certificates of competence in the 11-13 weeks scan

Theoretical course: completed on **Feb 13, 2009** - if you want to review the 11-13 weeks course please select: [Patient](#) / [Medical practitioner](#)

Certified: **Apr 04, 2008**

Certification	Certificate of competence	Last audit	Report	License
NT scan	Apr 04, 2008	View images	Mar 26, 2013	expires on Mar 26, 2014
Nasal bone	Nov 30, 2008	View images	Mar 26, 2013	yes
Ductus venosus	Nov 30, 2008	View images	Mar 26, 2013	yes
Tricuspid flow	Nov 30, 2008	View images	Mar 27, 2013	yes
Facial angle	Nov 30, 2008	View images	Apr 23, 2009	no
Uterine Doppler (PET)	Nov 30, 2008	View images	Mar 26, 2013	yes

Audit / licensing

If you want to obtain a Certificate of competence in the 11-13 weeks scan, or to submit your audit please click [here](#)

To download the FMF software (2.8) and obtain or renew your license for risk calculation please click [here](#)



[Centre Foundation](#) [Courses & Congress](#) [Training & Certification](#) [Online Education](#) [Research](#) [Look for Life](#) [Contact us](#)

[Own page](#) [Logout](#)

New - In order to obtain the Certificate of competence in assessment of the nasal bone, tricuspid flow and ductus venosus flow or to renew your license for these markers you are no longer required to upload 1 image with an abnormal finding. Instead, you will be asked to do a quick online test and then upload 3 images, specifying whether the finding shown in each image is normal or abnormal.

Step 1: select audit type

Audit type:

Step 2: select three images

Select three images of nuchal translucency showing the calliper placement.

Images must be in JPEG, PNG or GIF format. The resolution should be the original size, if possible, but at least 540 x 430. You should upload three images.

First image file: Keine Datei ausgewählt

Second image file: Keine Datei ausgewählt

Third image file: Keine Datei ausgewählt

Step 3: add a data file

Here you can upload a data file containing NT measurements. A good distribution of measurements is a condition for being included on the list of sonographers with a satisfactory audit.

Click [here](#) for details of exporting your data from Astraia or the FMF software. Instructions for ViewPoint are [here](#). If you want to know how to submit data from Excel or another program, click [here](#).

- I have a file to upload
 I don't have any data
 I have less than 30 cases



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Own page Logout

FMF Audit details

Karl Oliver Kagan

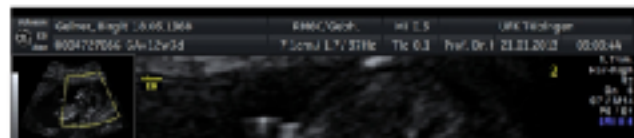
NT scan , Mar 25, 2013, *NT2.jpg*



- Magnification ✓
- True mid-sagittal section ✓
- Neutral fetal position ✓
- Calipers "ON-to-ON" ✓
- Maximum lucency ✓
- Thin nuchal membrane ✓

Examiner: Olga Torres Khoury

NT scan , Mar 25, 2013, *nt3.jpg*



- Magnification ✓
- True mid-sagittal section ✓
- Neutral fetal position ✓

Mar 26, 2013

FMF ID: 31444

Measurement of nuchal translucency

Dear Karl Oliver Kagan,

Thank you for submitting your logbook of 3 images. I examined each image for the following criteria: magnification (head and thorax only), mid-sagittal section of the face, neutral fetal position (no flexion or extension), calliper placement, maximum lucency, and thin nuchal membrane (see table below).

Criteria	Image number		
	1	2	3
Magnification	✓	✓	✓
True mid-sagittal section	✓	✓	✓
Neutral fetal position	✓	✓	✓
Calipers "ON-to-ON"	✓	✓	✓
Maximum lucency	✓	✓	✓
Thin nuchal membrane	✓	✓	✓

Legend: ✓ = pass ✗ = fail - = not possible to assess

The distribution of your nuchal translucency measurements

You have examined a total of 309 fetuses. The median of your NT distribution is 0.11 mm above what it should be. The scatter of your results is acceptable.

Assuming you screen by NT alone, your detection rate for a false positive rate (FPR) of 3% will be 74.0%, compared to the expected 72.0%. If you screen by NT and biochemistry, the detection rate for a FPR of 3% will be 88.0%, compared to the expected 86.0%.

In screening by NT and biochemistry at a risk cutoff of 1 in 100 the FPR and detection rate should be 2.7% and 84% respectively. On the basis of your distribution the values would be 2.5% and 86.0%.

Your distribution of NT meets the FMF criteria.

Re-audit schedule

Your images are satisfactory and the distribution of your NT measurements was good. Your name will now be included on the list of certified sonographers with a satisfactory audit on the FMF website. Your license has been extended for one year; your next audit is due in **Feb 26, 2014** and your license expires in **Mar 26, 2014**.

Best wishes,

Olga Torres Khoury

News ScholarOne Manuscripts Archives Web of Know...

select: Patient / Medical practitioner

014

se click here
here

TK

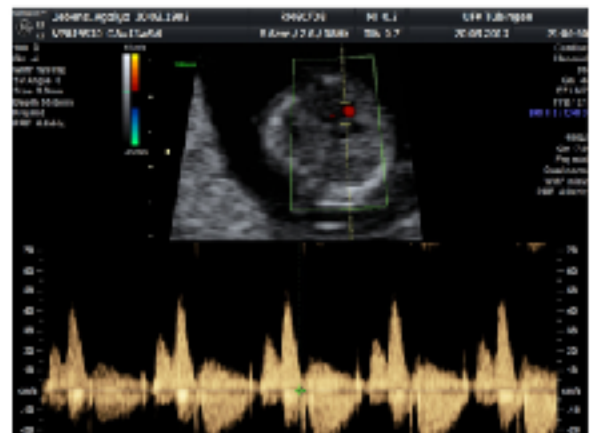


FMF Audit details

Karl Oliver Kagan

Tricuspid flow, Mar 27, 2013, *tr1.jpg*

User's assessment: **Normal flow**



- Magnification ✓
- Apical four chamber view ✓
- Sample volume size and position ✓
- Insonation angle ✓
- High sweep-speed (3-6 waveforms) ✓
- User's assessment ✓

Examiner: Olga Torres Khoury

Tricuspid flow, Mar 27, 2013, *tr2.jpg*

User's assessment: **Normal flow**



- Magnification ✓
- Apical four chamber view ✓



137 Harley Street, London W1G 6BG
 Tel: +44 20 7034 3070 Fax: +44 20 7034 3071
 Email: fmcertification@fetalmedicine.com

Karl Oliver Kagan
 Anne-Frank-Strasse 33
 Reutlingen
 72764
 Germany

Mar 26, 2013

FMF ID: 31444

Assessment of ductus venosus flow

Dear Karl Oliver Kagan,

Thank you for submitting your logbook of 3 images. I examined each image for the following criteria: magnification, mid-sagittal view, sample volume between 0.5 and 1 mm, angle of insonation angle less than 30 degrees, low filter: 50-70 Hz, high sweep-speed (3-6 waveforms), and your assessment (see table below).

Criteria	Image number		
	1	2	3
Magnification	✓	✓	✓
Mid-sagittal view	✓	✓	✓
Sample volume 0.5-1 mm	✓	✓	✓
Insonation angle less than 30°	✓	✓	✓
Low filter: 50-70 Hz	✓	✗	✗
High sweep-speed (3-6 waveforms)	✓	✓	✓
User's assessment	✓	✓	✓

Legend: ✓ = pass ✗ = fail -- = not possible to assess

- In 2 of your images the setting of the filter was not correct (should be 50-70 Hz).

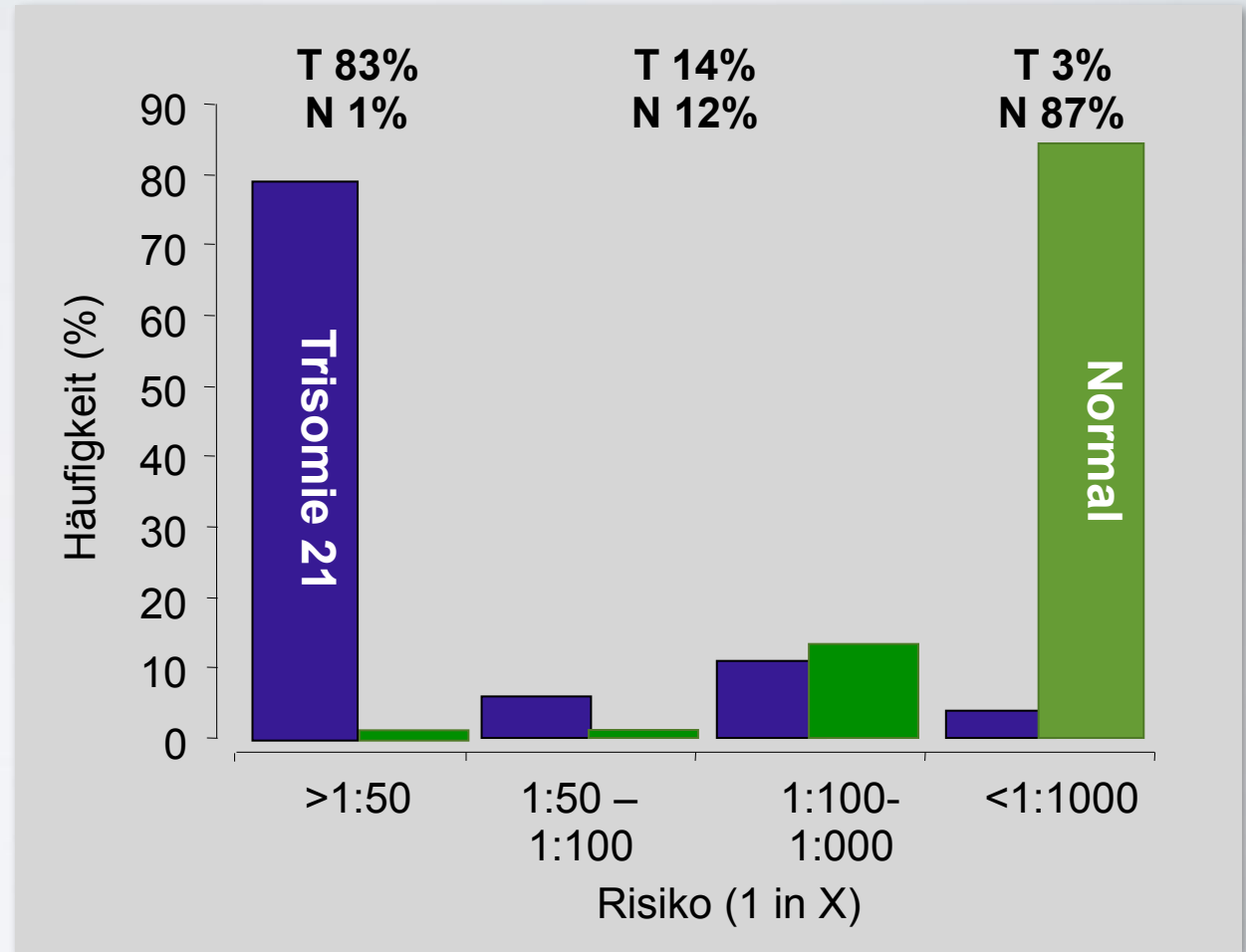
Your images are satisfactory. Your software license will include the assessment of **ductus venosus flow** in the risk calculation for chromosomal abnormalities and your name will appear on the list of sonographers certified for ductus venosus assessment.

select: [Patient](#) / [Medical practitioner](#)

014

[see click here](#)
[here](#)

VERTEILUNG DER RISIKEN BEI ADÄQUATEM ETS



ZWEI-STUFEN-SCREENING

**Kombiniertes
Screening**



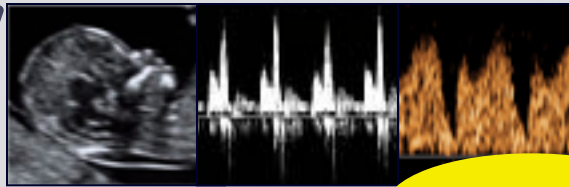
**Hohes Risiko
>1:50 → CVS**

1,5% / 85%

**Niedriges Risiko
<1:1000 → US**

84% / 1,2%

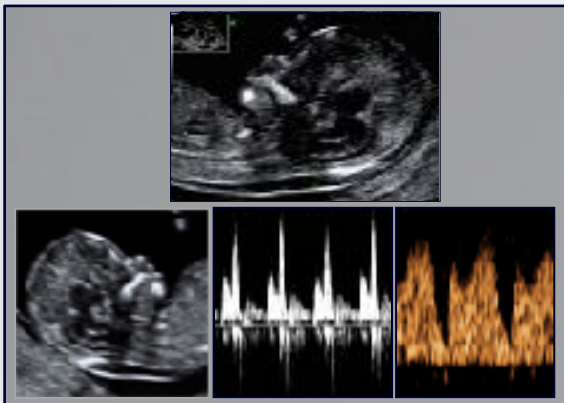
Borderline Risiko



15% / 14%

**Detektionsrate 90-95%
Falsch-positiv Rate 2,5%**

ADDITION DER NEUEN MARKER BEI ALLEN UNTERSUCHUNGEN OHNE BIOCHEMIE



Detektionsrate 83-85%
Falsch-positiv Rate 2,9%
Cut-off 1:100

ZWEI-STUFEN CROSS-TRIMESTER-SCREENING

**Kombiniertes
Screening**



**Hohes Risiko
>1:50 → CVS**

1,5% / 85%

**Niedriges Risiko
<1:1000 → US**

84% / 1,2%



15% / 14%

Meta-analysis of second-trimester markers for trisomy 21

M. AGATHOKLEOUS*, P. CHAVEEVA*, L. C. Y. POON*, P. KOSINSKI* and
K. H. NICOLAIDES*†

*Harris Birthright Research Centre for Fetal Medicine, King's College Hospital, London, UK; †Department of Fetal Medicine, University College Hospital, London, UK●

Marker	DR (%)	FPR (%)	LR +	LR -	LR isoliert
Echogener Fokus	24,4	3,9	5,85	0,8	0,95
Ventrikulomegalie	7,5	0,3	25,78	0,94	3,6
Nackenödem	26,2	1,2	19,18	0,8	3,12
Hyperechogener Darm	16,7	1,1	11,44	0,9	1,65
Hydronephrose	13,7	1,4	7,77	0,92	1,1
Kurzer Humerus	30,3	4,6	4,81	0,74	0,78
Kurzer Femur	27,7	6,4	3,72	0,8	0,61
ARSA	30,7	1,5	21,48	0,71	3,94
Abnormales Nasenbein	59,8	2,8	23,26	0,46	6,58

PARADIGMENWECHSEL IN DER PRÄNATALMEDIZIN



1980er

Alter
DR 50%
FPR 20%



1990er

Biochemie
DR 60-80%
FPR 5%



2000er

Komb. ETS
DR 90%
FPR 5%



2010er

cffDNA
DR 99%
FPR 0,1%



SCREENING MITTELS CFFDNA

	Detektionsrate		Falsch-positiv Rate	
Trisomie 21	n=147*	99 %	n=12.855*	0,1 %
Trisomie 18	n=147	99 %	?	0,1 %
Trisomie 13	n=22	86 %	?	0,5 %

* Screening-Studien

Zusammenfassung der Studien von Nicolaides, Dan, Ashoor, Palomaki und Norton et al.

SCREENING MITTELS CFFDNA



- Nur limitiert verfügbar
- Sehr teuer (> €500)
- Bisher nur Screening auf Trisomie 21,18,13,X
- Bisher keine ausreichend großen Screening-Studien
- Bisherige Studien fast nur Hochrisiko-Kollektiv

IMPLEMENTIERUNG VON NIPT

Nur NIPT (wenn kein Befund ETS Cut-off 1:50)

Contingent Ansatz (erst ETS, borderline Risiko NIPT)

Nur ETS (Cut-off 1:250)

IMPLEMENTIERUNG VON NIPT

Labor pränatal.de Düsseldorf 2000 - 2012
21052 ETS-Untersuchungen

212 aneuploide Schwangerschaften
189 (89%) T21, T18, T13, X - Aneuploidie
23 (11%) sonstige mit adverssem Outcome

ETS €150
NIPT €500
Karyotypisierung €1000

DR T21 99%
DR T18 98%
DR T13 90%
DR Sex 99%
FPR 0,5%

IMPLEMENTIERUNG VON NIPT

Nur NIPT

Detektionsrate Trisomie 21: 126 (99%)

Detektionsrate alle Aneuploidien: 186 (88%)

Invasive Diagnostik: 305 (1,5%)

Kosten: €10,937,600

Nur ETS (Cut-off 1:250)

Detektionsrate Trisomie 21: 116 (91%)

Detektionsrate alle Aneuploidien: 193 (91%)

Invasive Diagnostik: 2006 (9,5%)

Kosten: €5,158,250

IMPLEMENTIERUNG VON NIPT

Contingent Model

Erst ETS (borderline Risiken NIPT)

Detektionsrate Trisomie 21: 124 (98%)

Detektionsrate alle Aneuploidien: 200 (94%)

Invasive Diagnostik: 706 (3.4%)

Kosten: €6,445,750

STRATEGIE „LATE NIPT“: ETS ALS TRIAGE-TEST

I.Screen MuRi 8+1 bis 10+6

Beratung
über cff DNA

ETS 11+1 - 13+6 SSW
Aneuploidie-Screening
Frühe Organdiagnostik
PE-Screening etc.

Fehlbildung

NT >>95.Perz.
PAPP-A << 5.Perz

ETS
pos

ETS
interm

ETS
neg

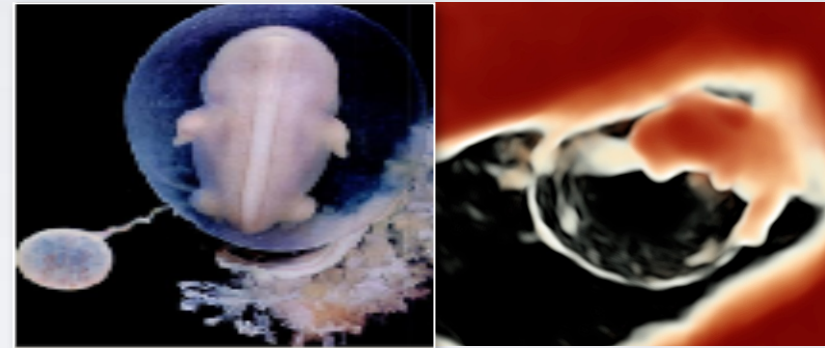
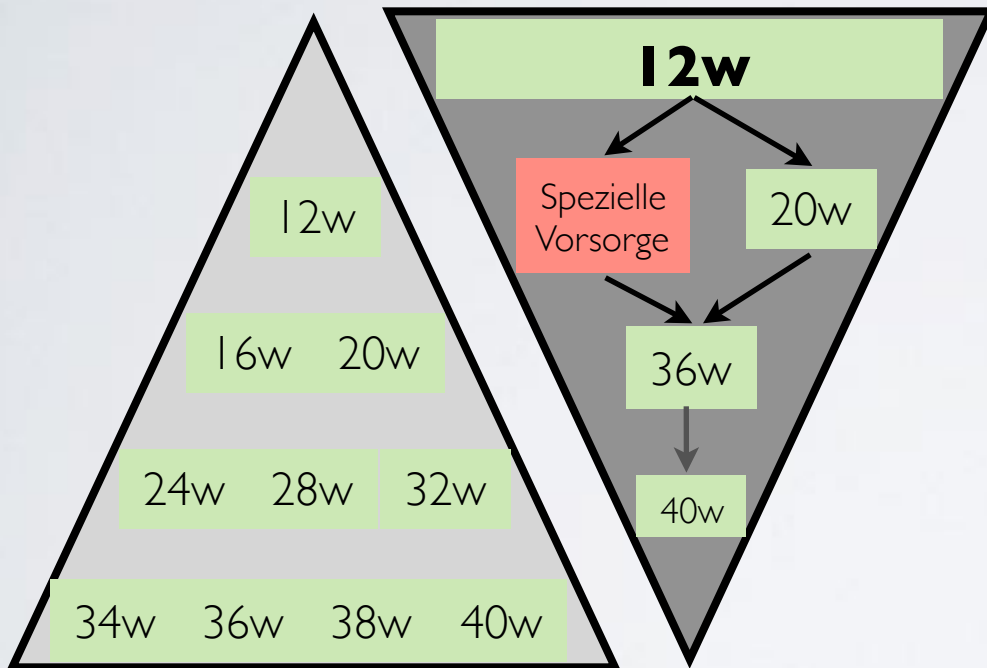
Angst

CVS +/-
microarray

cff DNA

RISIKOADAPTIERTE SCHWANGERSCHAFTSBETREUUN

G



- ANEUPLOIDIE
- FEHLBILDUNGEN
- PRÄEKLAMPSIE
- IUGR / SGA
- FRÜHGEBURT
- GESTATIONSDIABETES ..