ST Segment Analysis (STAN) of FHR: Is it the Future of EFM?

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- Consulting fees*
  - Obix

* Paid to UT Health

Objectives

- To understand physiological basis for ST monitoring
- To discuss STAN guidelines and techniques for utilization
- To review clinical trial data of ST analysis
- To review design and progress of *NICHD* MFMU RCT of STAN

ST analysis and Fetal Hypoxia

Hypoxia leading to Ischemia

Lactate accumulation

ATP depletion

Creatine phosphate depletion

Metabolic acidosis

Detected with EFM

Anaerobic metabolism

Glycogenolysis and glycolysis

Change in membrane potential due to liberation of potassium

ST segment elevation & high T waves

Detected with Fetal ECG

ST analysis and Adjunct to EFM

- Additional information from ST analysis will:
- Decrease unnecessary interventions
  - Reduce false (+) rate
  - Lower operative delivery rate
- More timely intervention
  - Reduce false (-) rate
  - Reduce neo morbidity & mortality

Data from clinical trials

Clinical Trials

- Randomized trials on CTG+ST vs. CTG alone
  - Plymouth trial: Westgate et al. (1993)
  - Swedish trial: Amer-Wahlin et al. (2001)
  - Finnish trial: Ojala et al. (2006)
  - French trial: Vayssière et al. (2007)
  - Dutch trial: Westerhuis et al. (2010)
  - Total subjects = 15, 338 women
- 5 Meta-analyses

Data from Meta-analysis

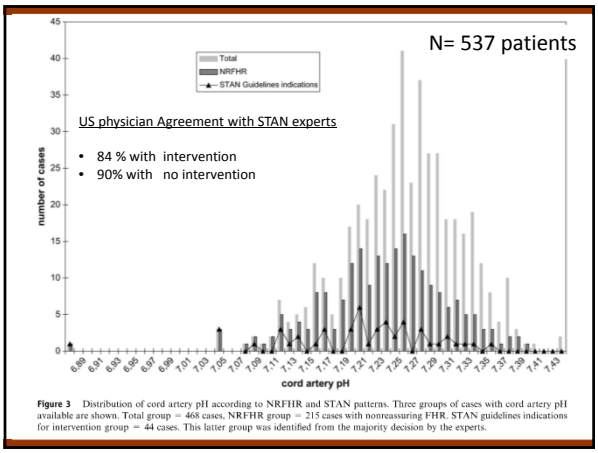
	Cochrane MA - Neilson (2012)	IPD MA - Schuit et al. (2013)	Becker et al. (2012)	Salmelin et al. (2012)	Potti & Berghella (2012)	P. Olofsson review (2013)
Fetal Blood Sampling	**39 %** reduction (RR 0.61, 95% CI 0.41-0.91)	**51 %** reduction (RR 0.49, 95% CI 0.44-0.55)	**41 %** reduction (RR 0.59, 95% CI 0.44-0.79)	**45 %** reduction (RR 0.55, 95% CI 0.40-0.76)		**36 %** reduction (RR 0.64, 95% CI 0.47-0.88)
Admission to special care unit	**11 %** reduction (RR 0.89, 95% CI 0.81-0.99)					
Instrumental vaginal deliveries		**10 %** reduction (RR 0.90, 95% CI 0.83-0.99)				
Admission to neonatal ICU*		**39 %** reduction (RR 0.61, 95% CI 0.39-0.95)				
Metabolic Acidosis						**39 %** reduction (RR 0.61, 95% CI 0.41-0.91)
Total operative deliveries			**6 %** reduction (RR 0.94, 95% CI 0.89-0.98)			**7 %** reduction (RR 0.93, 95% CI 0.88-0.98)
Vaginal operative deliveries			**12 %** reduction (RR 0.88, 95% CI 0.80-0.97)		**11 %** reduction (RR 0.89, 95% CI 0.83-0.97)	**12 %** reduction (RR 0.88, 95% CI 0.81-0.95)

United States Multicenter Clinical Usage Study of the STAN 21 Electronic Fetal Monitoring System

Lawrence D. Devoe, MD,[a,*] Michael Ross, MD,[b] Clayton Wilde, MD,[c] Maureen Beal, MD,[b] Andrej Lysikewicz, MD,[d] Jeffrey Maier, MD,[e] Victor Vines, MD,[f] Isis Amer-Wåhlin, MD,[g] Håkan Lilja, MD,[h] Håkan Norén, MD,[h] Dev Maulik, MD[d]

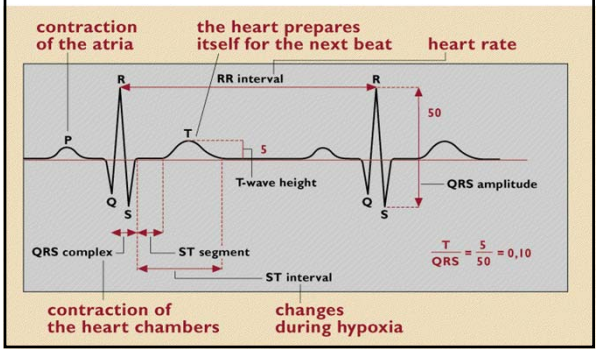
American Journal of Obstetrics and Gynecology (2006) 195, 729–34

- 6 medical centers in US
  - 3 academic and 3 community
  - 39 providers
- Prospective non randomized clinical trial using ST analysis and STAN guidelines
- Compare management and outcomes of US physicians to “STAN experts”



ST Analysis: How does it work?

The ECG complex



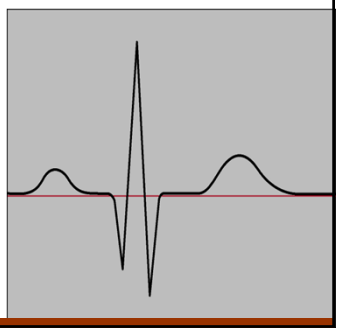
ST - wave forms

Normal ST

aerobic myocardial metabolism

positive energy balance –
Isoelectric line – T wave

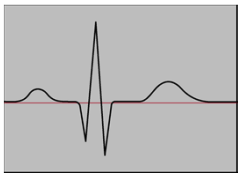
STAN only detects changes in these parameters – MUST have a period of normal ST segment and T wave recording



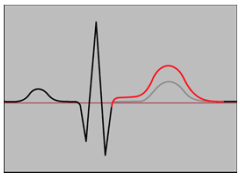
Changes in fetal ECG

Effect of hypoxia

Normal ST
- aerobic metabolism
- positive energy balance

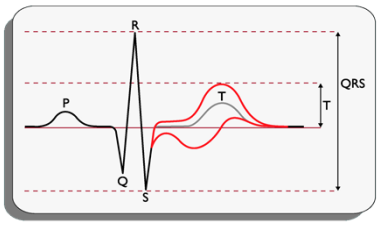


Increased T-wave amplitude
- hypoxia
- adrenalin surge
- anaerobic metabolism



Changes in the ST segment & T wave

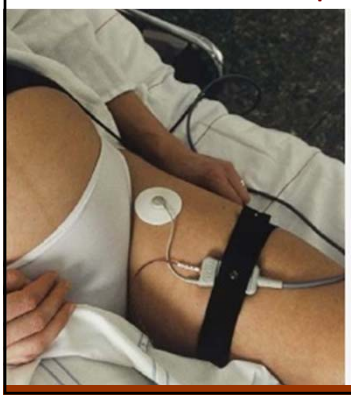
ST rise – a fetus responding to hypoxia



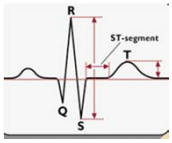
Biphasic ST – a fetus not fully capable of responding with ST rise, or has not had time to respond

Fetal monitoring with STAN

STAN Components



The T/QRS ratio



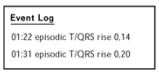
T
------ = 5/50 = 0.10
QRS

Episodic T/QRS rise

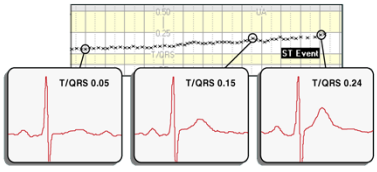
Episodic rises occur with short periods of hypoxia

T/QRS ratio increases and then returns to normal

- epinephrin surge
- anaerobic myocardial metabolism

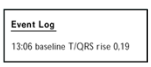


Baseline T/QRS rise



Baseline rise - lasts >10 minutes

- ongoing anaerobic myocardial metabolism
- persistent stress, no opportunity for recovery



ST Analysis and STAN Events

- Each 30 beat T/QRS ratio average is plotted on a scale with normal upper and lower limits
- Using the average ECG waveform 2 specific evaluations are done

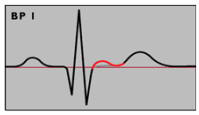
1. T/QRS ratio
   - episodic increases
   - persistant increase
2. Biphasic ST

Abnormalities in T/QRS ratio or ST segment changes are reported as STAN events

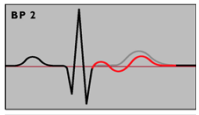
Biphasic ST segments

Biphasic ST

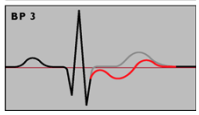
Grade 1 - NS



Grade 2 – STAN event



Grade 3 – STAN event



Caused by an inability of the myocardium to respond:

- Prematurity
- Infections
- Increase in overall demand (maternal fever)
- Myocardial dystrophy
- Chronic hypoxia
- Initial phase of acute hypoxia

STAN Interpretation

- FHR data
  - Baseline, accelerations, decelerations, variability
  - Categorization (3-Tier system)
- ST analysis
  - Presence or absence of ST Events
    - Baseline, episodic, 2-biphasic (type 2,3)

↓

- STAN category + ST information

FHR Zones for STAN

Table 3. Fetal Heart Rate Zones

FHR Classification	Baseline Heart Rate	Variability	Decelerations
Green Zone	110 – 160 bpm	Moderate variability (6 – 25 bpm) Accelerations present	Early decelerations *Variable decelerations with a duration of < 60 seconds and depth < 60 beats*
Yellow Zone	Bradycardia < 110 bpm Tachycardia > 160 bpm >150 bpm with minimal variability	Minimal variability (≤ 5bpm) for > 40 min Marked variability (>25 bpm) for > 40 min	Variable decelerations with a duration of ≥ 60 seconds or depth ≥ 60 beats Recurrent late decelerations Prolonged deceleration for > 2 minutes regardless of variability and reactivity
Red Zone	Absent variability *regardless of other FHR patterns** Sinusoidal pattern		

* Variable deceleration in the Green Zone and absent variability without other FHR patterns in the Red Zone are in Category II NICHD classification[20]

The intended use of this FHR classification system is to suggest clinical conditions in which adjunctive use of ST waveform changes may aid the interpretation of specific FHR patterns.

FHR Classification	Baseline Heart Rate	Variability	Decelerations
Green Zone	• 110-160 bpm	• Moderate variability (6-25 bpm) • Accelerations present	• Early decelerations • ***Variable decelerations with a duration of <60 sec and depth <60 beats***
Yellow Zone	• Bradycardia <110 bpm • Tachycardia >160 bpm • >150 bpm with minimal variability	• Minimal variability (≤5 bpm) for >40 min • Marked variability (>25 bpm) for >40 min	• Variable decelerations with a duration of ≥60 sec or depth ≥60 beats • Recurrent late decelerations • Prolonged deceleration for >2 min regardless of variability or reactivity
Red Zone	• Absent variability ***regardless of other FHR patterns*** • Sinusoidal pattern		

The above classification of FHR developed for the STAN S31 has been updated to conform with terminology and nomenclature of the 2008 NICHD Workshop Report on EFM. Differences between the STAN classification and the NICHD classification

STAN Zones vs. 3-Tier NICHD

- Green — Category I
- Yellow — Category II
- Red — Category III
  - Variable deceleration in the Green Zone (< 60/60)
  - Absent variability without other FHR patterns in the red Zone

STAN Guidelines (Management)

Table 4. Guidelines given Fetal Heart Rate Zone and ST event status

	No ST Event	ST Event Episodic, Baseline or 2 Biphasic** log messages
Green Zone	Expectant management Continued observation	Expectant management Continued observation
Yellow Zone	Expectant management, closer observation If >60 min (or earlier if FHR shows rapid deterioration of fetal condition), direct physician assessment of fetal state	Direct physician assessment Intrauterine resuscitation as appropriate If no improvement in fetal condition, expeditious delivery In second stage with active pushing, expeditious delivery
Red Zone	Expeditious delivery regardless of any ST changes	Expeditious delivery regardless of any ST changes

**The time span between the biphasic messages should be related to the FHR pattern and the clinical situation

STAN Interpretation Steps

- STAN fetal scalp electrode
- Achieve ST analysis baseline
- Adequate ST signal
- STAN zone
  - Green, Yellow, Red
- STAN events
  - YES vs. NO
- Follow STAN guidelines

STAN Interpretation Caveats

- NEED baseline (ZONE= green or yellow with moderate FHR variability)
- Loss of ST signal > 4 minutes
- Maternal fever and related infection

Revert to EFM data

Green Zone
with/without ST events

- If you see GREEN, routine care
- Management similar to Category NICHD I
- Will have occasional ST events in GREEN

STAN Guidelines (Management)

Table 4. Guidelines given Fetal Heart Rate Zone and ST event status

	No ST Event	ST Event Episodic, Baseline or 2 Biphasic** log messages
Green Zone	Expectant management Continued observation	Expectant management Continued observation
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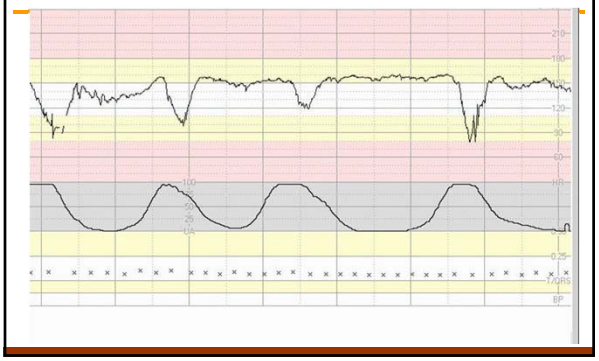
Red Zone	Expeditious delivery regardless of any ST changes	Expeditious delivery regardless of any ST changes

**The time span between the biphasic messages should be related to the FHR pattern and the clinical situation

Red Zone
with/without ST events

- If you see RED, proceed to delivery
- Management similar to Category NICHD III

Yellow Zone



Yellow Zone

1. Evaluation, close observation
2. Direct physician assessment if > 60 min or rapid decompensation

- Operative delivery if rapidly decompensation FHR
- Not “time enough” to develop ST events

Yellow Zone + ST events

Yellow Zone + ST Events

- Direct physician assessment
- Intrauterine resuscitation (as appropriate)
- If no improvement, expeditious delivery
- In 2nd stage with active pushing, expeditious delivery

Yellow Zone + ST Events

Devil in details

- How long to wait?
  - 1st stage labor
  - 2nd stage labor
- What is "no improvement"?

Yellow Zone + ST Events

Customize to US trial

- How long to wait?
  - 1st stage labor ≈ 60 minutes for decision
  - 2nd stage labor = immediate unless delivery expected 5-10 minutes
- What is "no improvement"?
  - Lack of return to GREEN zone (must last 10 min)

STAN Challenges

- 3 unanswered and unknown questions
  - STAN is a technology BUT intrapartum management is driven by human behavior
  - Yellow zone (or Category II) is most important

1. Will US providers intervene in Yellow Zone but absent ST?
   - *"Overcall" rapidly deteriorating*

2. Will US providers wait for resuscitation after Yellow zone plus ST events?
   - Jump to cesarean delivery

3. Will US providers expedite OVD in 2nd stage ?
   - *Do they know how and are not too afraid …*

STAN Challenges

- Do providers agree on ZONE?
  - Green vs. Yellow
  - *E.g. FHR variability or depth/degree variable deceleration*
- Do providers agree change ZONE (return to Green)?
- Do providers agree "rapidly deteriorating"?
  - Exception to awaiting ST events for operative intervention

NICHD MFMU Network Trial

A Randomized Trial of Fetal ECG ST Segment and T Wave Analysis as an Adjunct to Electronic Fetal Heart Rate Monitoring (STAN)

STAN RCT

- Leaders of RCT
  - George Saade and Mike Belfort
- Neoventa
  - Provided monitors, training/education, some financial support for trial
- MFMU Network sites for RCT (14 centers)

STAN RCT

- Memory of FOX (pulse oximetry) trial
- STAN
  - New concepts, technology, and guidelines
  - Application to US physicians
  - Need large trial to assess neonatal outcomes
- Optimize
  - Training and education
  - Adherence to management protocol

Primary Hypothesis

- In laboring women at 36 weeks of gestation or more, the use of STAN as an adjunct to conventional electronic fetal heart rate monitoring, decreases perinatal hypoxic/ischemic morbidity.

Primary Research Question

- Does fetal STAN, as an adjunct to conventional electronic fetal heart rate monitoring in pregnancies at 36 weeks or more, decrease the risk of fetal compromise, a composite adverse neonatal outcome defined as one or more of the following outcomes: Intrapartum fetal death, neonatal death, Apgar score ≤ 3 at 5 minutes, seizure(s), cord artery pH ≤ 7.05 and base deficit ≥ 12 mmol/L, intubation for ventilation at delivery or presence of neonatal encephalopathy.

Eligibility

- Singleton gestation
- GA > 36 wks
- Cervical dilation 2 cm – 7 cm
- Rupture of membranes

Exclusion

- Multiple gestation
- Need or plan for cesarean delivery
- Prior cesarean delivery or uterine surgery
- Chorioamnionitis or fever/infection
- Absent FHR variability or sinusoidal pattern
- Category II FHR with minimal variability within 20 minutes prior to randomization
- ST event while doing baseline assessment (affect blinding)

Protocol

- Consent
- Confirm eligibility
- STAN fetal electrode
- Baseline ST signal
- Then randomize
  - OPEN (ST analysis + EFM + STAN guidelines)
  - MASKED (EFM alone)
- Fetal scalp sampling not part of protocol

Training/Certification

- Research staff
- Clinical nurses
- Treating physicians
  - Certification (anyone who touches patient)
  - Credentialing (management decisions)
  - Authorized (final decision –maker)
  - Proctor

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Pilot Study

- Each hospital participating
  - N = 50 subjects
- All OPEN cases
- Cases reviewed by STAN subcommittee
- Start RCT

Primary outcome

- The primary outcome is a composite of one or more of the following:
  - Intrapartum fetal death
  - Neonatal death
  - Apgar score ≤ 3 at 5 minutes
  - Neonatal seizure
  - Cord artery pH ≤ 7.05 and base deficit ≥ 12 mmol/L.
  - Intubation for ventilation at delivery
  - Presence of neonatal encephalopathy

Secondary outcomes

- Cesarean delivery
- Indication for cesarean delivery
- Forceps or vacuum delivery
- Chorioamnionitis
- Multiple other outcomes

Sample size estimates
(Primary outcome)

Table 6. Sample Sizes per Group for Different Primary Outcome Rates, Power and Effect Sizes

		Primary Outcome Rate in Masked Group		
% Reduction	% Power	1.5%	1.75%	2.0%
33	80	7900	6800	5900
	85	9000	7700	6800
	90	11000	9000	7900
40	80	5300	4500	4000
	85	6000	5200	4500
	90	7000	6000	5300

Cesarean delivery

- If the cesarean delivery rate is 25%, a sample size of 11,000 yields more than 85% power to detect a 10% reduction to 22.5% in the open STAN arm, assuming type I error of 5% 2-sided.
  - Even if the rate is lower, say 20%, there is still ample power to detect a 12.5% reduction.
- If the cesarean delivery rate for non-reassuring fetal status is as low as 5%, there is 88% power to detect a 25% reduction in cesarean delivery for this indication.

Status of RCT

- Started in 2010
- Continued training/education
- Audit & feedback
  - Compliance with STAN guidelines
- Randomized > 10,000+ subjects
- > 95% umbilical cord blood gases (A&V)

Potential Study Outcomes

Adverse perinatal outcome	Cesarean delivery
No difference	No difference
No difference	Increase
No difference	Decrease
Increase	No difference
Increase	Increase
Increase	Decrease
Decrease	No difference
Decrease	Increase
Decrease	Decrease

Summary

- ST analysis and STAN monitoring
  - Developed in Sweden
  - Used mainly in Europe
  - FDA approved for use in US
- Multiple RCT's performed but none in US
- MFMU RCT will be largest RCT fetal monitoring in US
  - Powered for neonatal outcomes and CD