Update on chest compressions

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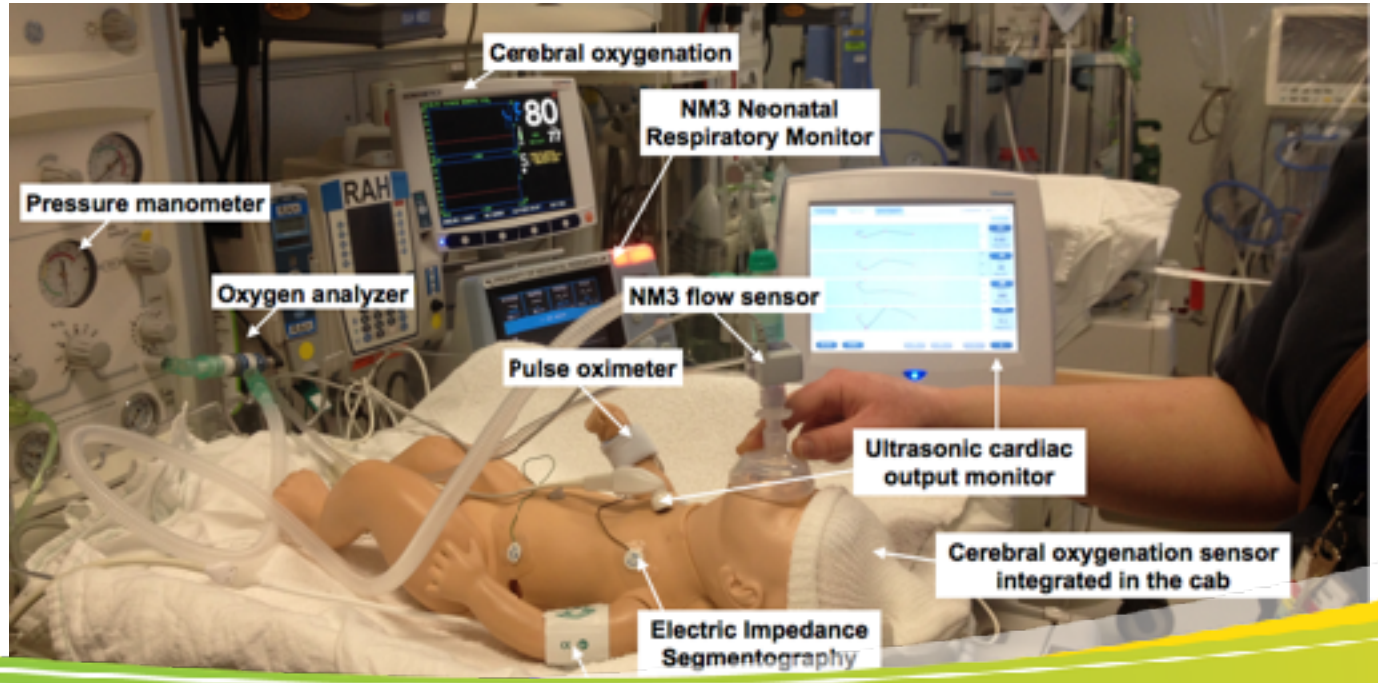

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Disclosure

GM Schmölzer is supported by:

- Heart and Stroke Foundation Alberta Professorship of Neonatal Resuscitation
- Heart and Stroke Foundation Canada - New Investigator Award

Funding

- Canadian Institute of Health Research
- Heart and Stroke Foundation Canada

- Member of ILCOR since 2015

Background

- Majority of newborns make the transition successfully
- 10% of newborns need respiratory support
  - Most critical step of neonatal resuscitation
- Need for CC or medications in the DR is rare
  - 0.1% of term and up to 15% of preterm infants
  - ~2.3 million infants need CC very year
- Resulting in ~1 million newborn deaths annually worldwide

Perlman et al. Circulation 2015

Background

- Infants who received chest compressions
  - High incidence of mortality (41%) and short-term neurologic morbidity (57% HIE and seizures)

- Prolonged CC+Epinephrine and no signs of life at 10 min[2]
  - 83% mortality
  - 93% of survivors suffering moderate-to-severe disability

[1]Wyckoff et al. Semin Fetal Neonatal Med 2013
[2]Soraisham et al. Resuscitation 2014

The poor prognosis associated with receiving CC alone or with medications in the DR raises questions as to whether improved CPR methods specifically tailored to the newborn could improve outcomes

The inability to predict which newborns need CPR, and the infrequent use of CPR in the DR have limited neonatologists' ability to perform rigorous clinical studies to determine the best method for delivering CC to newborn infants

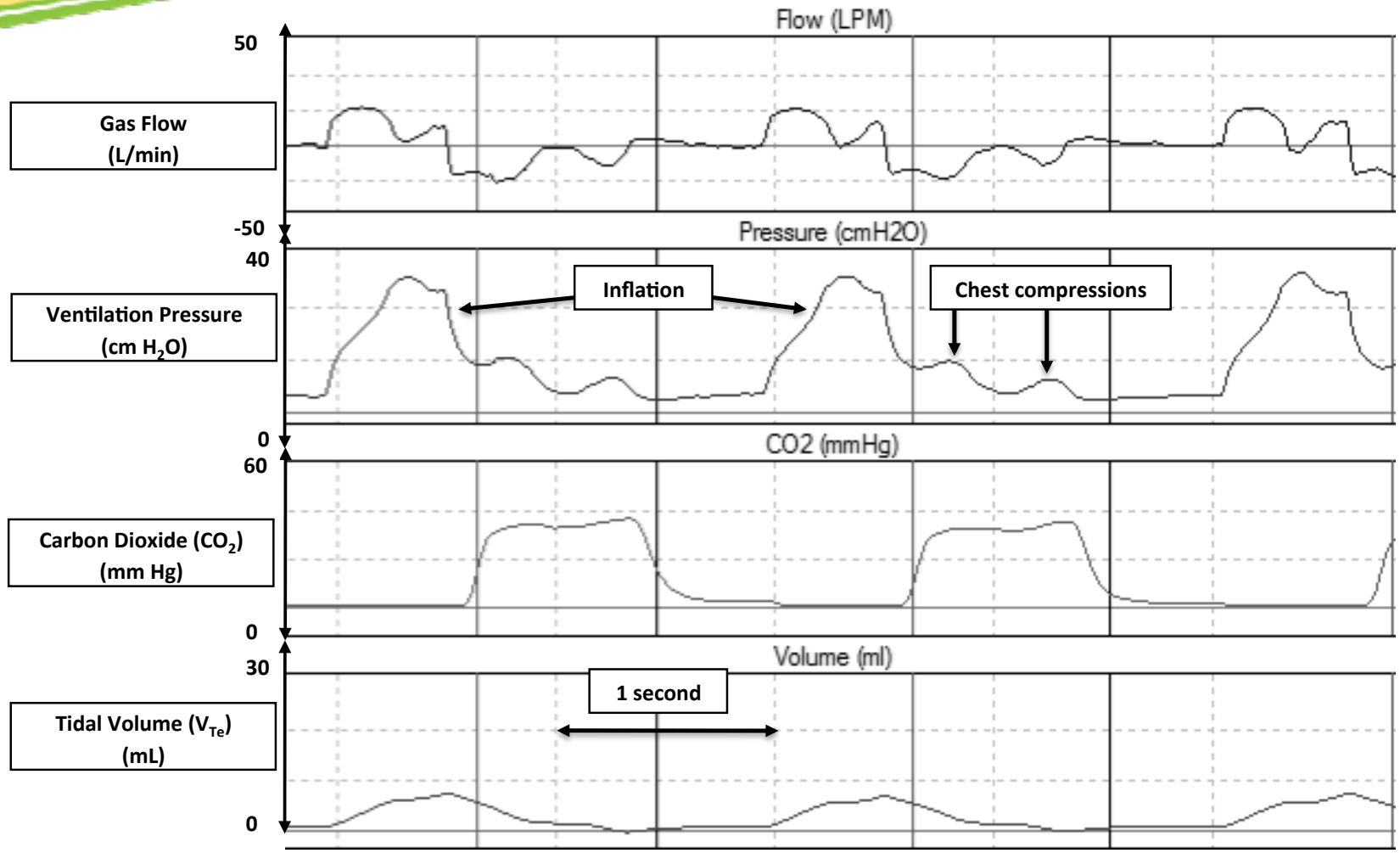
Part 7: Neonatal Resuscitation

2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations

Jeffrey M. Perlman, Co-Chair*; Jonathan Wyllie, Co-Chair*; John Kattwinkel; Myra H. Wyckoff; Khalid Aziz; Ruth Guinsburg; Han-Suk Kim; Helen G. Liley; Lindsay Mildenhall; Wendy M. Simon; Edgardo Szyld; Masanori Tamura; Sithembiso Velaphi; on behalf of the Neonatal Resuscitation Chapter Collaborators

- 90 CC and 30 manual inflations (3:1 C:V) per minute
- C:V should be synchronized to reduce the potential of interference with V_T delivery, hence impairment of oxygen delivery
- Most effective C:V ratio in newborns remains controversial

Perlman et al. Circulation 2015



Schmölzer et al. Circulation 2013

Knowledge Gaps

- Specific research is required, such as clinical and appropriate animal model studies.
- We need neonatal human data.
- How many compressions in a row are required to achieve forward blood flow and adequate coronary perfusion pressure during newborn asphyxial arrest?
- How many interposed ventilations are needed to achieve and maintain normocapnia during cardiac compressions due to newborn asphyxial arrest?
- Asynchronous technique deserves more investigation.
- Is ventilation adequate with SI cardiac compressions?
- How should we limit interruptions in compressions to assess efficacy?

Perlman et al. Circulation 2015

Why 3:1 C:V?

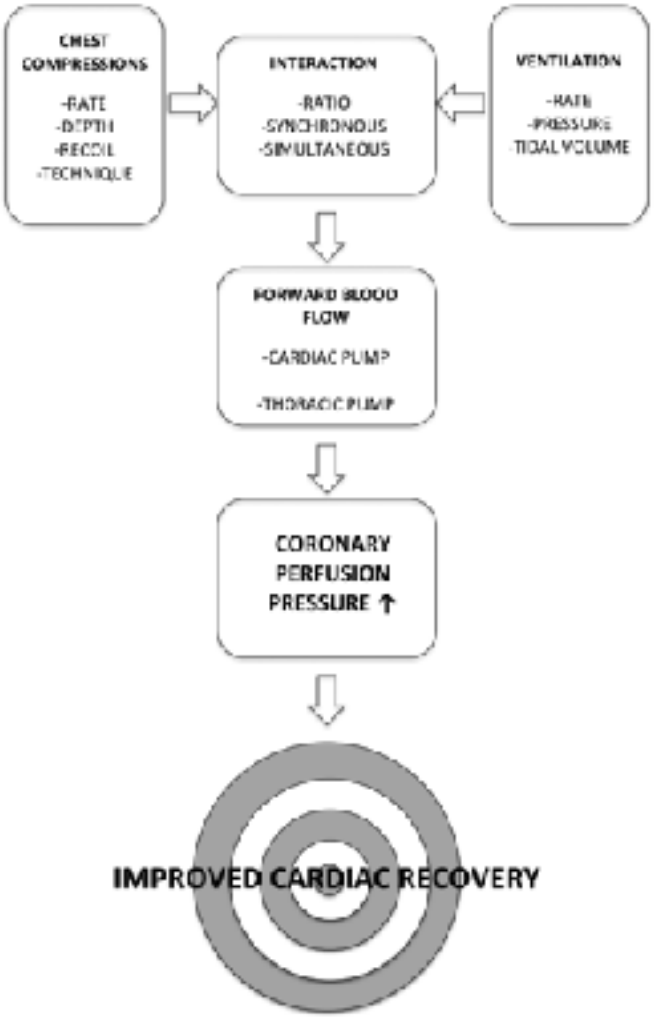
- Rationale:
  - Higher physiological heart rate of 120-160/min
  - Higher breathing rates of 40-60/min
  - Profound bradycardia or cardiac arrest caused by hypoxia and hypocarbia
- Providing ventilation more likely to beneficial in neonatal CPR
- Optimal C:V ratio - optimize coronary and cerebral perfusion while providing adequate ventilation unknown

Mode of Action

- CC serve to mechanically pump the blood until ROSC
- Cardiac pump theory - CC directly ejects blood from the heart into the circulation with each compression
- Thoracic pump theory - CC creates changes in intrathoracic pressure gradient to achieve blood flow
- Optimized CC generates 30% of normal organ perfusion
- Coronary perfusion pressure difference of aortic blood pressure and right atrial pressure

Factors influencing the overall efficacy of CC

- Balancing CC and ventilation
  - CC to ventilation ratio
  - Synchronization of CC with ventilation
  - Alternative ways of combining CCs with ventilation
- Adequate CC rate
- CC depth
- Full chest recoil between CC
- Correct technique
- Epinephrine


CHEST COMPRESSIONS
-RATE
-DEPTH
-RECOIL
-TECHNIQUE
INTERACTION
-RATIO
-SYNCHRONOUS
-SIMULTANEOUS
VENTILATION
-RATE
-PRESSURE
-TIDAL VOLUME
FORWARD BLOOD FLOW
-CARDIAC PUMP
-THORACIC PUMP
CORONARY PERFUSION PRESSURE ↑
IMPROVED CARDIAC RECOVERY

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Mannikin studies

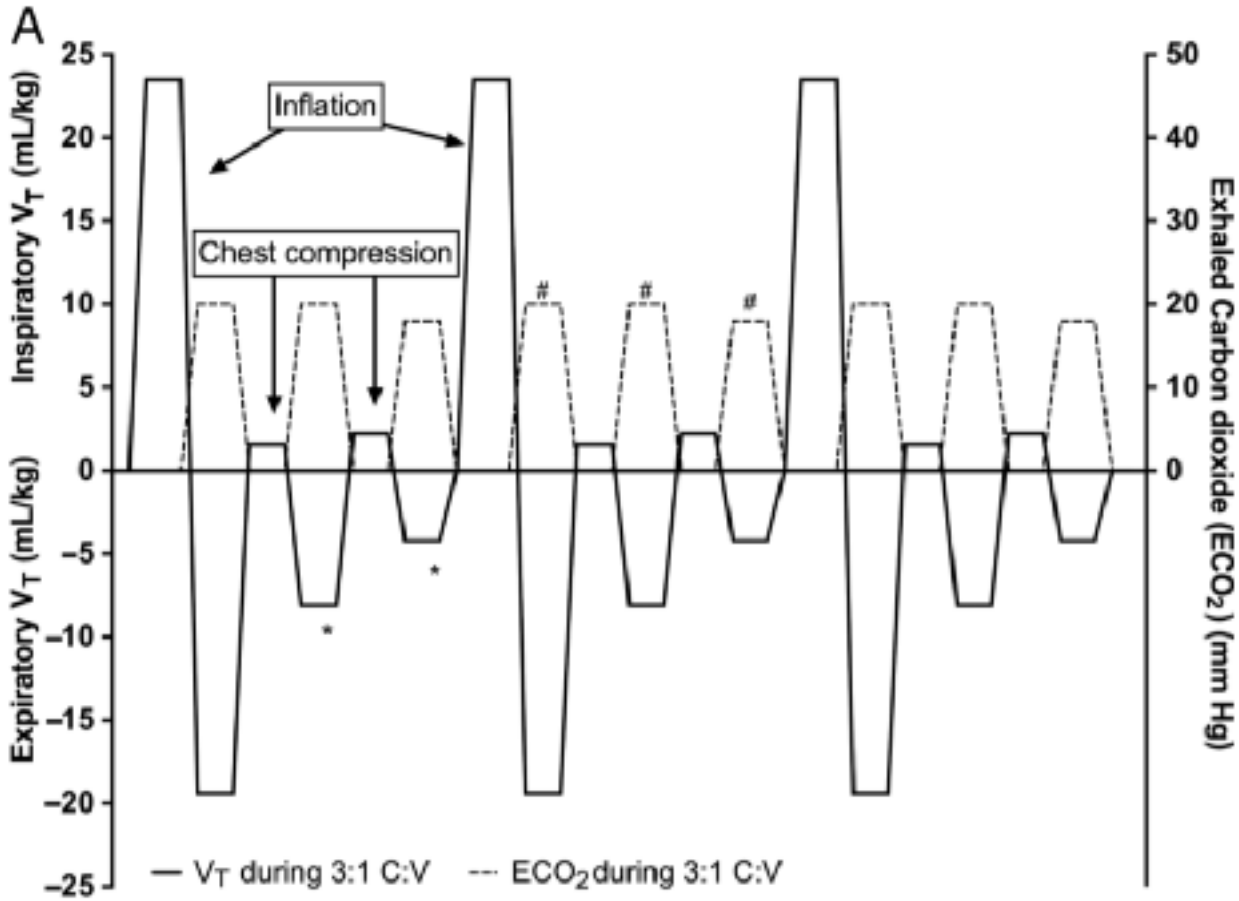
- 3:1 had significantly higher MV 191 mL/kg/min compared to 140 (9:3 C:V) and 77 (15:2 C:V) mL/kg/min
- CCaV using 90 CC and 30 non-synchronized inflations had even higher MV 221 mL/kg/min
- Similar V_T delivery between 3:1 C:V and CCaV
  - 6.4 and 5.6 mL/kg

Solevåg et al. Scand J Trauma Resusc Emerg Med. 2012

Animal studies - different C:V ratios

- Combining CC with ventilations improves ROSC and neurological outcome at 24 hours compared to ventilations or CC alone[1]
- 3:1 C:V vs. 9:3 C:V[2]
  - ROSC 150sec (3:1 C:V) and 148 sec (9:3 C:V)
  - No differences in diastolic blood pressure during CC
- 3:1 C:V vs. 15:2 C:V[3]
  - ROSC 150sec (3:1 C:V) and 195 sec (15:2 C:V)
- Higher C:V ratios did not improve outcomes

[1]Berg et al. Circulation 1993
[2]Solevåg et al. Resuscitation 2010
[3]Solevåg et al. ADC FN 2011



Li et al. ADC FN 2016

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Synchronization of CC with ventilation

- Synchronized CPR improves V_T delivery
  - hence impairment of oxygen delivery
- Manikin study
  - 3:1 C:V CPR with CCaV and reported a similar V_T with significantly higher MV during CCaV.

Animal studies - 3:1 C:V vs. CCaV

- Similar MV 387 vs. 275 mL/kg/min
- Similar ROSC (143 and 114 sec)
- Survival (3/8 and 6/8)
- Similar V_T delivery 14.7 vs. 11.0 mL/kg
  - 3:1 C:V a V_T loss of 4.5 mL/kg for each 3:1 C:V cycle
  - CCaV a V_T loss of 9.1 mL/kg for each cycle
- V_T delivery affected by compression:
  - 25% and 29% of manual inflations during CC
- CCaV was no advantage

Schmölzer et al. Resuscitation 2014

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Adequate CC rate

- 3:1 C:V ratio with 90 CC and 30 breaths = 120 events/min
- Optimal CC rate during neonatal CPR remains unclear
- Normal HR in newborns are 120–160 bpm

- Would an increase in CC frequency boost artificial cardiac output?

Adequate CC rate

- Mathematical model suggests higher CC rates to optimize systemic perfusion[1]
- CC rate depends upon body size and weight
  - 180/min for term and even higher for preterm infants
- Simulation study (90 vs. 120CC/min) faster fatigue with higher CC[2]
  - Most preferred number of CC
- Force measurements showed fatigue with higher CC rates[3]
- 90/min will be the least fatiguing CC rate

[1]Babbs et al. Resuscitation 2009
[2]Li et al. J Perinatology 2015
[3]Solevåg et al. Maternal Fetal Neonatal Med 2015

CC+SI - Animal studies

- Animal RCT CC+SI with CC 90/min vs. 120/min
  - Similar time of ROSC, survival rates
  - During CC+SI 90/min higher:
    - Carotid blood flow
    - Mean arterial pressure
    - % change in ejection fraction
    - Cardiac output

Li et al. PlosOne 2016

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Optimal CC depth

- CC depth should be approximately 33% of AP chest diameter
  - In adults only 20% of AP diameter
- There is a positive correlation between adequate CC depth and improved outcomes
- Unfortunately, even experienced resuscitators do not achieve the required CC depth

Optimal CC depth

- Adequate CC depth is important to optimize cardiac output
- Overcompressing might cause rib fractures, cardiac contusion and other thoracic injuries

Optimal CC depth

- Manikin studies compared the CC depth using C:V ratios of 3:1, 5:1 and 15:2 during 2-min simulated CPR.
- Participants had higher and more consistent CC depth during 3:1 C:V CPR, however the CC rate was lower compared with a 15:2 C:V ratio.
- In addition, the 2-min depth decay during CC was significantly higher during 5:1 and 15:2 compared with a 3:1 C:V ratio.

Optimal CC depth

- The optimal CC depth has not been rigorously evaluated in neonates
- Better left ventricular EF using a 1/3 AP CC depth compared with a 1/4 AP CC depth
- 1/2 AP CC depth produced significantly higher SPB but similar DBP compared with a 1/3 AP CC depth

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Effect of leaning / Full chest recoil between CC

- Leaning or incomplete recoil is the incomplete release of the downward force on the chest wall after a CC
- Reduces the negative intrathoracic pressure during decompression, thereby impeding blood flow and reducing CC effectiveness
- Leaning decreases coronary and cerebral perfusion pressures lasting for a significant period of time after the cessation of leaning

Effect of leaning / Full chest recoil between CC

- CC leaning is very common and exhibited a wide distribution, with most leaning within a subset of resuscitations.
- Leaning decreased with time during continuous CC, suggesting that either leaning is not caused by rescuer fatigue, or that it may be mitigated by automated feedback during CPR.
- It has not been systematically analyzed during neonatal CPR

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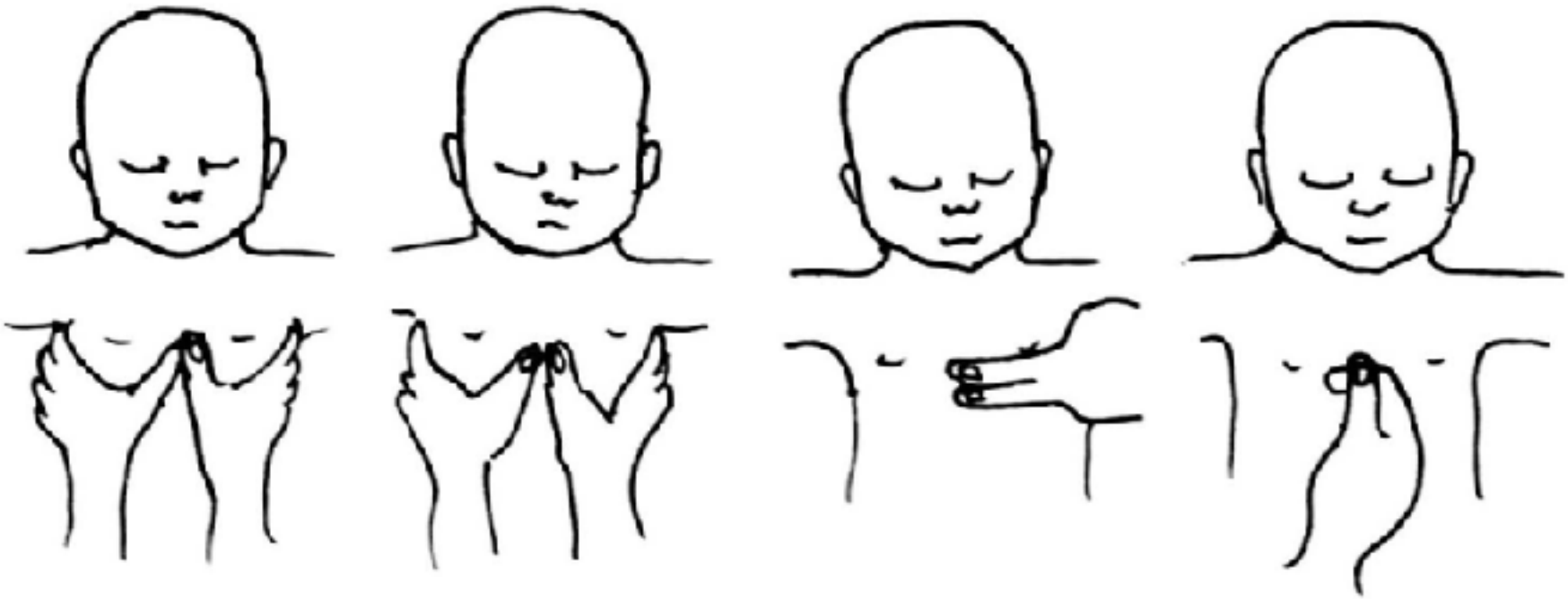

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Alternative methods

- Ventricular fibrillation model of adult cardiac arrest demonstrated that CC over ventilation increases neurologically intact survival in pigs[1]

- Simultaneous CC and ventilation at high airway pressure improves ROSC[2]

[1]Berg et al. Circulation
[2]Chandra et al. Lancet 1980

Chest Compression and Sustained Inflation

Circulation
JOURNAL OF THE AMERICAN HEART ASSOCIATION

American Heart Association

Cardiopulmonary Resuscitation With Chest Compressions During Sustained Inflations: A New Technique of Neonatal Resuscitation That Improves Recovery and Survival in a Neonatal Porcine Model

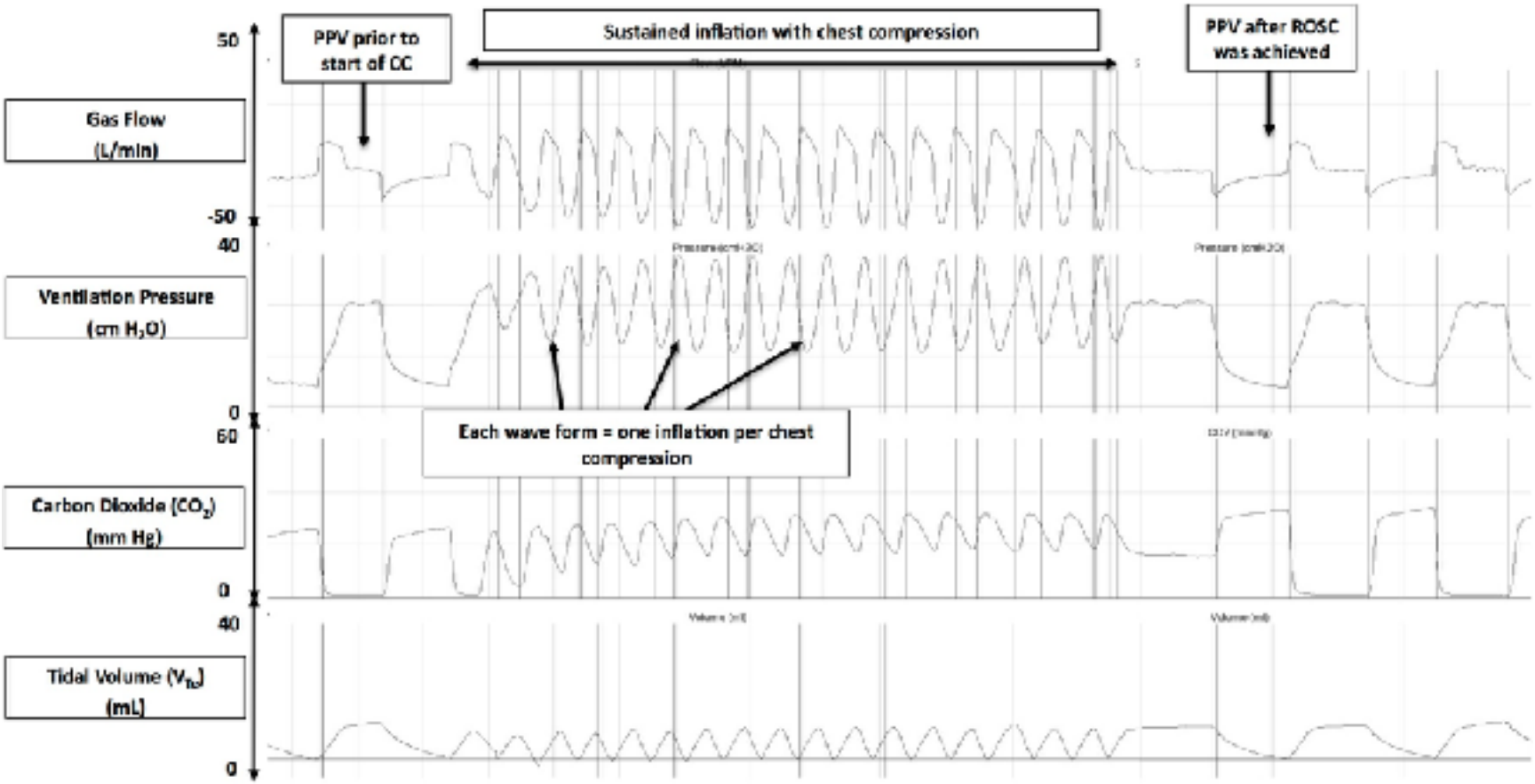
Georg M. Schmölzer, Megan O'Reilly, Joseph LaBossiere, Tze-Fun Lee, Shaun Cowan, Sharon Qin, David L. Bigam and Po-Yin Cheung

[1]Berg et al. Circulation
[2]Schmölzer et al. Circulation 2013

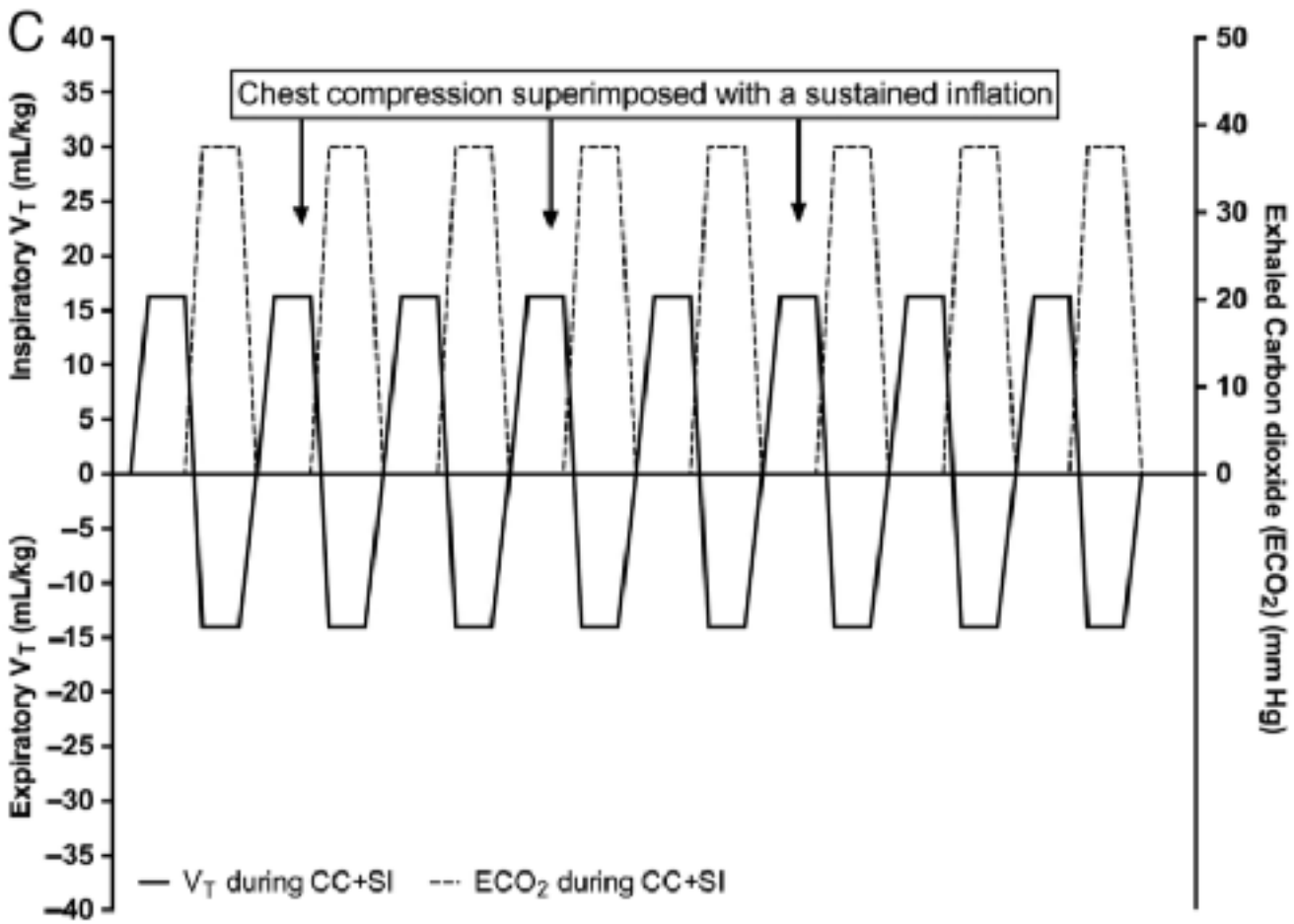
CC+SI - Animal studies

- Animal RCT CC+SI 120/min vs. 3:1 C:V
  - ROSC 38 (23–44)sec vs. 143 (84–303)sec (p=0.0008)
  - Survival 7/8 [87.5%] vs. 3/8 [37.5%] (p=0.038)
  - 100% oxygen 3/8 vs. 8/8 (p=0.0042).
  - Epinephrine 0/8 vs. 7/8 (p<0.0001)
  - Significantly improved MV and alveolar oxygen delivery
  - CC+SI allowed passive lung aeration
    - CC forced air out of the chest, and the passive chest recoil allowed air to be drawn back into the lungs

Schmölzer et al. Circulation 2013



Schmölzer et al. Circulation 2013



Li et al. ADC FN 2016

CC+SI - Animal studies

- Animal RCT SI+CC 90/min with 3:1 C:V ratio
  - ROSC 34 (28-156) sec vs. 210 (72-300) sec (p=0.05)
  - 3/8 versus 8/8 required 100% oxygen during CC (p=0.03)
  - 3/8 vs. 6/8 piglets received epinephrine
  - Improved respiratory and hemodynamic parameters in the SI+CC 90/min

Li et al. Neonatology 2017

CC+SI - Human Pilot study

- Pilot trial in preterm infants <32 weeks gestation
  - ROSC
    - CC+SI group 31 (9) sec
    - 3:1 C:V group 138 (72) sec (p=0.011)
    - Overall 0/5 in the CC+SI group and 1/5 in the 3:1 C:V group received epinephrine

Schmölzer et al. ADC FN accepted

Table 1: Demographics of study infants

	CC+SI group (n=5)	3:1 C:V group (n=4)
Birth weight (g)	707 (208)	808 (192)
Gestational age (weeks)	24.6 (1.3)	25.6 (2.3)
Male (n)*	2 (40%)	3 (75%)
Antenatal steroids (n)	4 (80%)	4 (100%)
Apgar 1 minute#	2 (1-4)	2 (1-2)
Apgar 5 minutes#	4 (3-6)	3 (3-3)
Delayed Cord Clamping (n)*	2 (40%)	3 (75%)

Data are presented as mean (SD), unless indicated #median (IQR), *n (%)

Table 2: Secondary neonatal outcomes

	CC+SI group (n=5)	3:1 C:V group (n=4)	p-value
Surfactant	3 (60%)	4 (100%)	0.236
Use of Inotropes	4 (80%)	2 (50%)	0.058
Air leak	0/5	0/5	1.00
Neonatal death < 28 days	2/5	0/4	0.114
Death before discharge	2/5	0/4	0.114
Intraventricular hemorrhage all grades	1 (20%)	4 (100%)	0.058
Intraventricular hemorrhage grade ≥3	1 (20%)	2 (50%)	0.599
Patent ductus arteriosus	2 (40%)	4 (100%)	0.168
Necrotizing enterocolitis	3 (60%)	1 (25%)	0.197
Chronic lung disease in survivor	2/3	3/4	0.809
Retinopathy of prematurity in survivor	1 (20%)	3 (75%)	0.127
Days in hospital in survivor	107 (16)	109 (24)	0.741

Data are presented as n (%), unless indicated [a]median (IQR)

Sustained inflation and chest comp**r**ession **v**ersus 3:**1** chest compression to **v**entilation ratio during cardiopulmonary resuscitation of asphyxiated n**e**wborns –

a cluster randomized controlled trial

ClinicalTrials.Gov Trial NCT02858583

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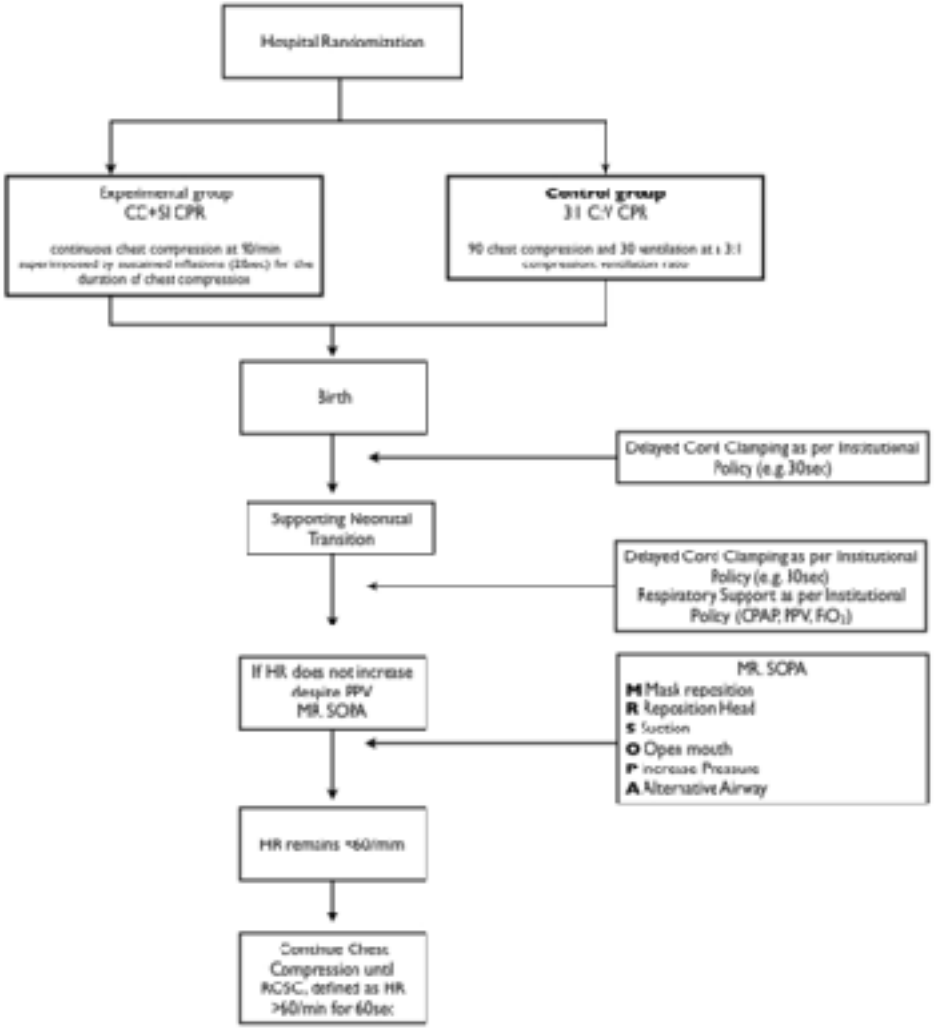
- Population:
  - Infants (preterm and term) requiring CC in the DR
- Primary Objective:
  - Chest Compression during sustained inflation (CC+SI) will improve short- and long-term outcomes in preterm and term newborns
- Primary Hypothesis:
  - By using CC+SI during CPR the time needed to achieve ROSC compared to the current 3:1 C:V will be reduced in asphyxiated newborns

- Inclusion Criteria:
  - Infants (preterm and term) requiring CC in the DR.

- Exclusion Criteria:
  - Congenital abnormality
  - Condition that might have an adverse effect on breathing or ventilation (e.g. CDH)
  - CHD requiring intervention in the neonatal period
  - Parents' refusal to give consent for data collection

- Sample Size:
  - This prospective multi-centre RCT is a two-arm parallel design of two alternative courses of treatment
  - 218 infants – 109 control / 109 intervention

- Primary outcome:
  - Time to achieve ROSC defined as a heart rate of >60/min for 60sec



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- DSMB
  - Myra Wyckoff, Neil Finer, and Maryna Yaskina
- Stopping rules
  - Safety interim analyses at 10%, 25% and 50%
  - Predefined stopping rules:
    - Increased mortality in the SI+CC group by 25%
    - Increase in rate of either morbidities including pneumothorax, IVH or both in the SI+CC group
- Opt-out Rule
  - CPR ongoing for 5 minutes, the clinical team must convert to the standard method of care using 3:1 C:V ratio

surv1ve

Participating Centers North America	Centre #	PI
University of Alberta, Edmonton, Canada	101	Georg Schmölzer
BC Children's Hospital, Vancouver, Canada	102	Deepak Manhas
CHU Sainte-Justine, Montreal, Canada	103	Ahmed Moussa
McMaster Children's Hospital, Ontario, Canada	104	Salhab el Helou
IWK Health Centre, Halifax, NS, Canada	105	Souvik Mitra
Mary Birch Hospital, San Diego, USA	106	Anup Katheria
Participating Centers Europe		
Medical University Graz, Austria	201	Gerhard Pichler
Akershus University Hospital, Norway	202	Anne Solevåg
Medical University Vienna, Austria	203	Michael Wagner and Monika Olischar
University Hospital Ulm, Germany	204	Helmut Hummler
Division of Neonatology, University & Polytechnic Hospital La Fe, Valencia, Spain	205	Max Vento
John Radcliffe Hospital, Oxford, United Kingdom	206	Charles-Christoph Roehr
University College Cork, Ireland	207	Eugene Dempsey
Landeskrankenhaus Feldkirch, Austria	208	Burkart Simma
Erasmus MC-Sophia Children's Hospital, Rotterdam, The Netherlands	209	Irvin Reiss
Ospedale dei Bambini Vittore Buzzi, Milano, Italy	210	Francesca Castoldi and Francesco Cavigioli
Poznan University of Medical Sciences, Poland	211	Jan Mazela

★ Ethics approval

☆ submitted to Ethics

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Update on chest compressions

http://www.research4babies.org

https://twitter.com/Research4Babies

YouTube: Centre - Studies of Asphyxia and Resuscitation

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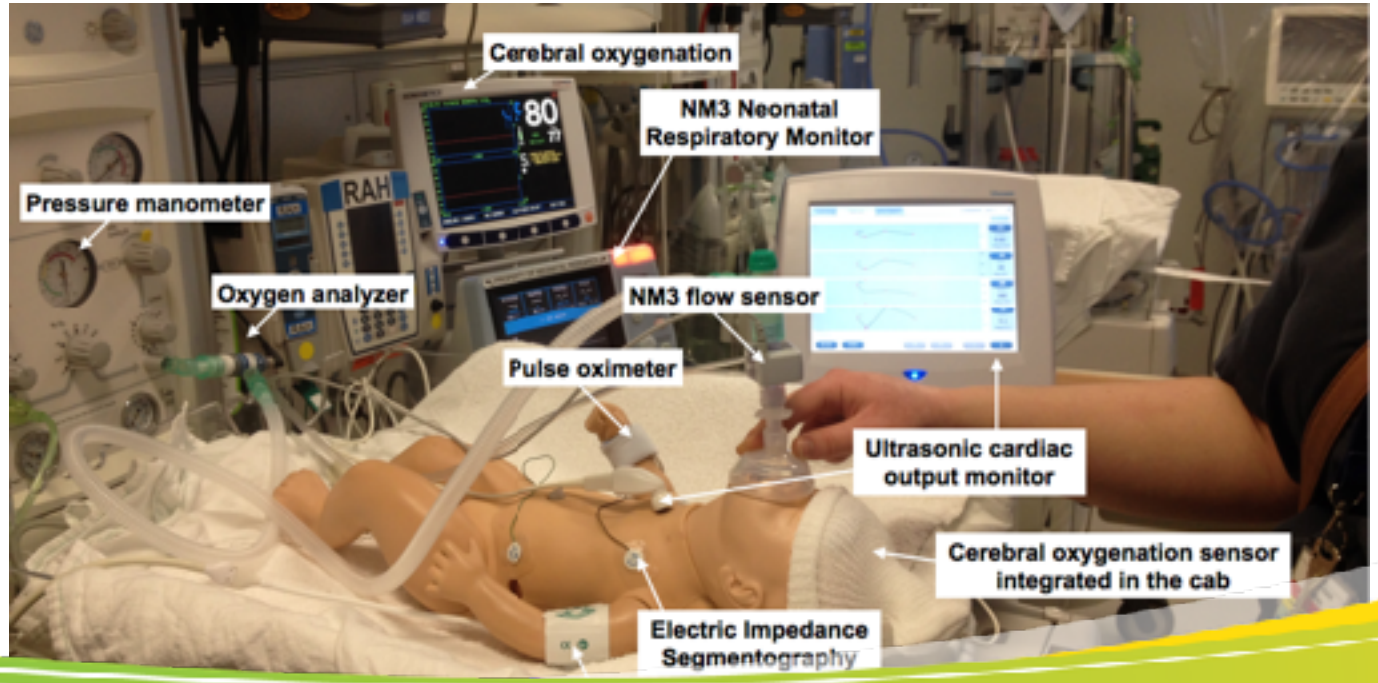

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