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European Paediatric Translational Research Infrastructure

Automated Neonatal Seizure Recognition (ANSeR)

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EPTRI MD webinar - A magnifying glass in the world of medical device development

20th January 2022

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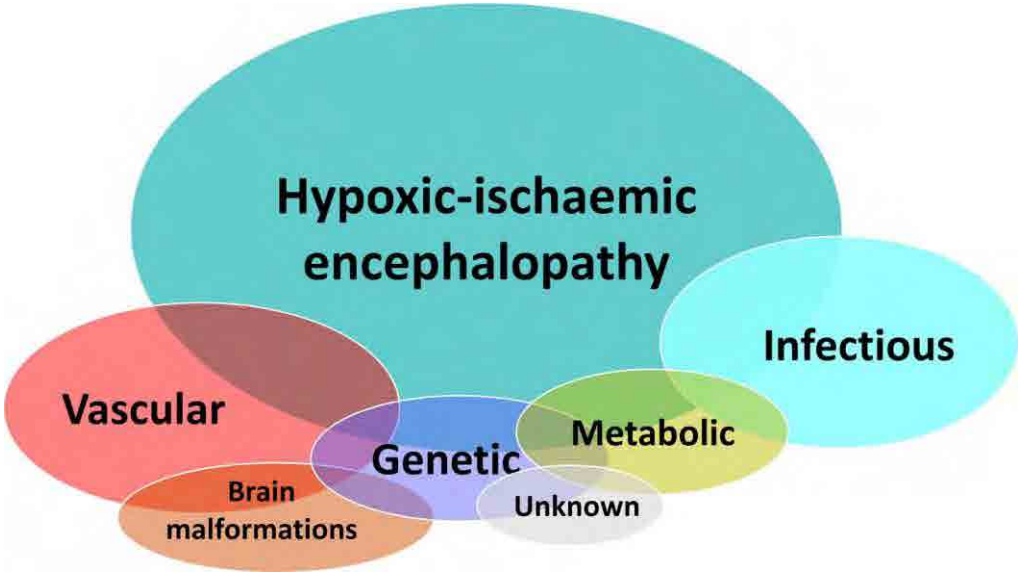
UCC University College Cork, Ireland Coláiste na hOllscoile Corcaigh

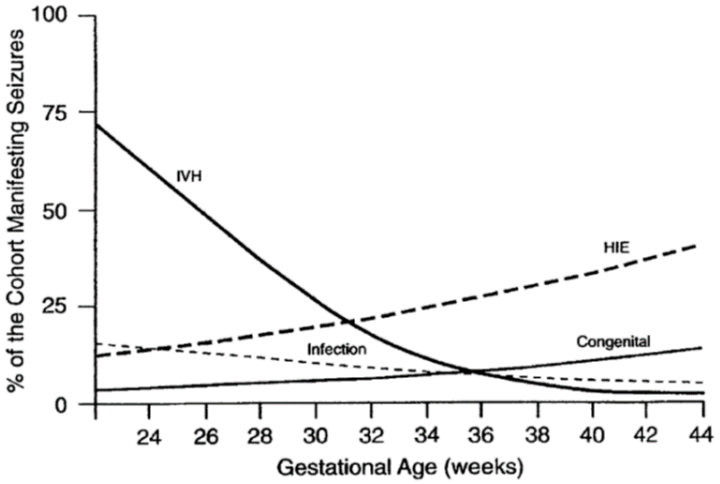
Overview

- Why a seizure detection algorithm is needed in the NICU
- ANSeR - the Algorithm for Neonatal Seizure Recognition
- Bench to cot-side in the NICU

Etiology of neonatal seizures



Pressler et al Epilepsia 2021: 62, 615-628



McCoy and Hahn 2013

Seizures & Outcome

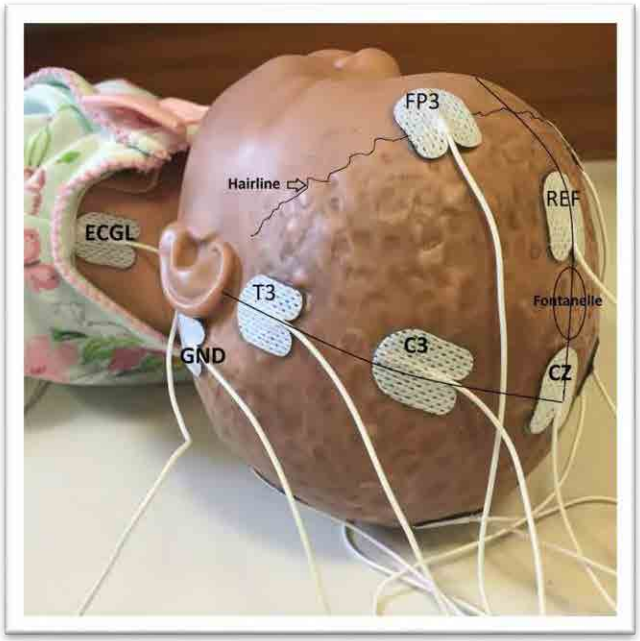
Seizures in HIE are independently associated with brain injury (Miller 2002)

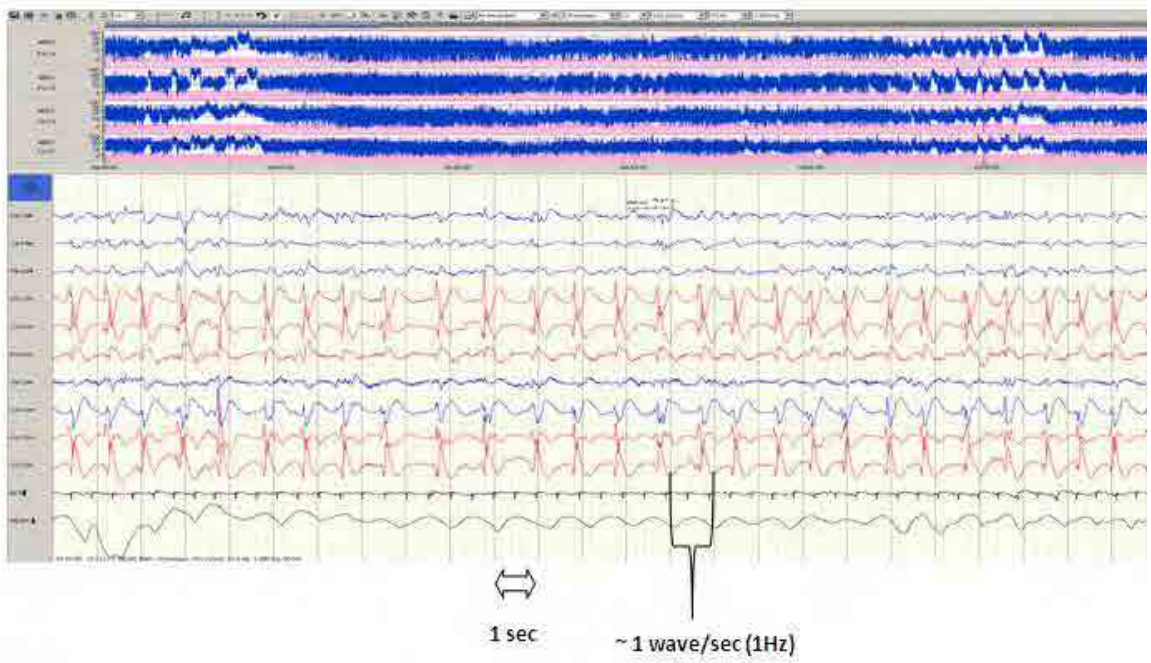
High seizure burden associated with abnormal outcome (Payne et al 2014, Srinivasakumar 2015, Glass et al 2016, Kharoshankaya et al 2016, Fitzgerald et al 2018)

Early diagnosis & treatment associated with better seizure control, less progression to status epilepticus and shorter hospital stay (Harris et al 2016, Bashir et al 2015, Wietstock et al 2016)

Neonatal Seizures

Neonatal EEG & Seizures





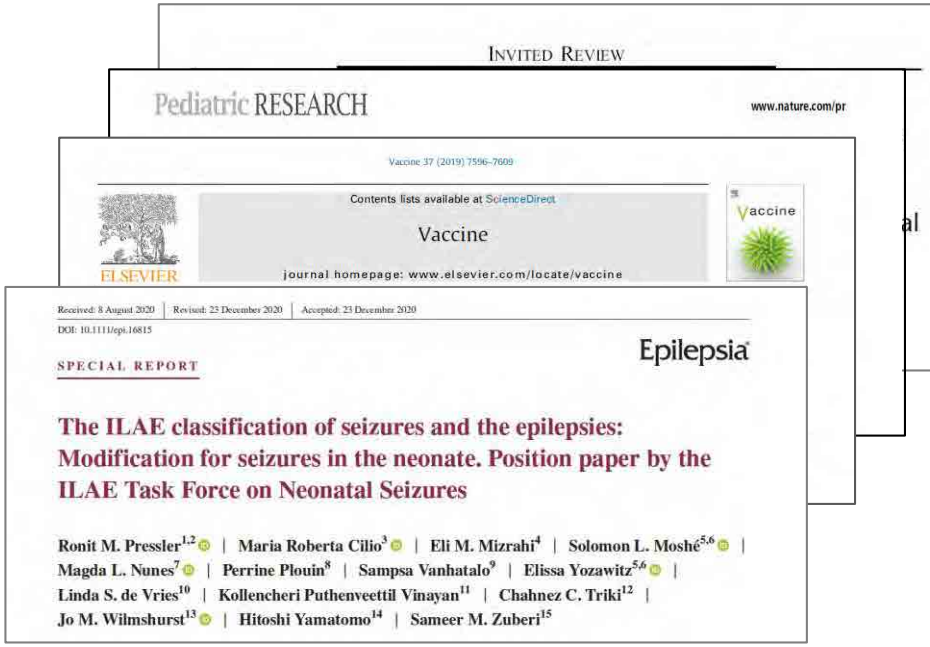
Uncoupling of Electroclinical seizures

- 'uncoupling' occurs in at least 50% of infants after treatment with antiseizure drugs
- Phenobarbitone and phenytoin result in equal rates of uncoupling

Weiner et al Ped Neurol 1991; Boylan et al Arch Dis Child 2002; Scher et al Ped Neurol 2003

Diagnosis of neonatal seizures

EEG is the gold standard for diagnosis



INVITED REVIEW

Pediatric RESEARCH

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SPECIAL REPORT

Epilepsia

The ILAE classification of seizures and the epilepsies: Modification for seizures in the neonate. Position paper by the ILAE Task Force on Neonatal Seizures

Ronit M. Pressler[1,2] | Maria Roberta Cilio[3] | Eli M. Mizrahi[4] | Solomon L. Moshé[5,6] | Magda L. Nunes[7] | Perrine Plouin[8] | Sampsa Vanhatalo[9] | Elissa Yozawitz[5,6] | Linda S. de Vries[10] | Kollencheri Puthenveettil Vinayan[11] | Chahnez C. Triki[12] | Jo M. Wilmshurst[13] | Hitoshi Yamatomo[14] | Sameer M. Zuberi[15]

Tsuchida et al 2013; Soul et al 2019; Pellegrin et al 2019; Pressler et al 2021

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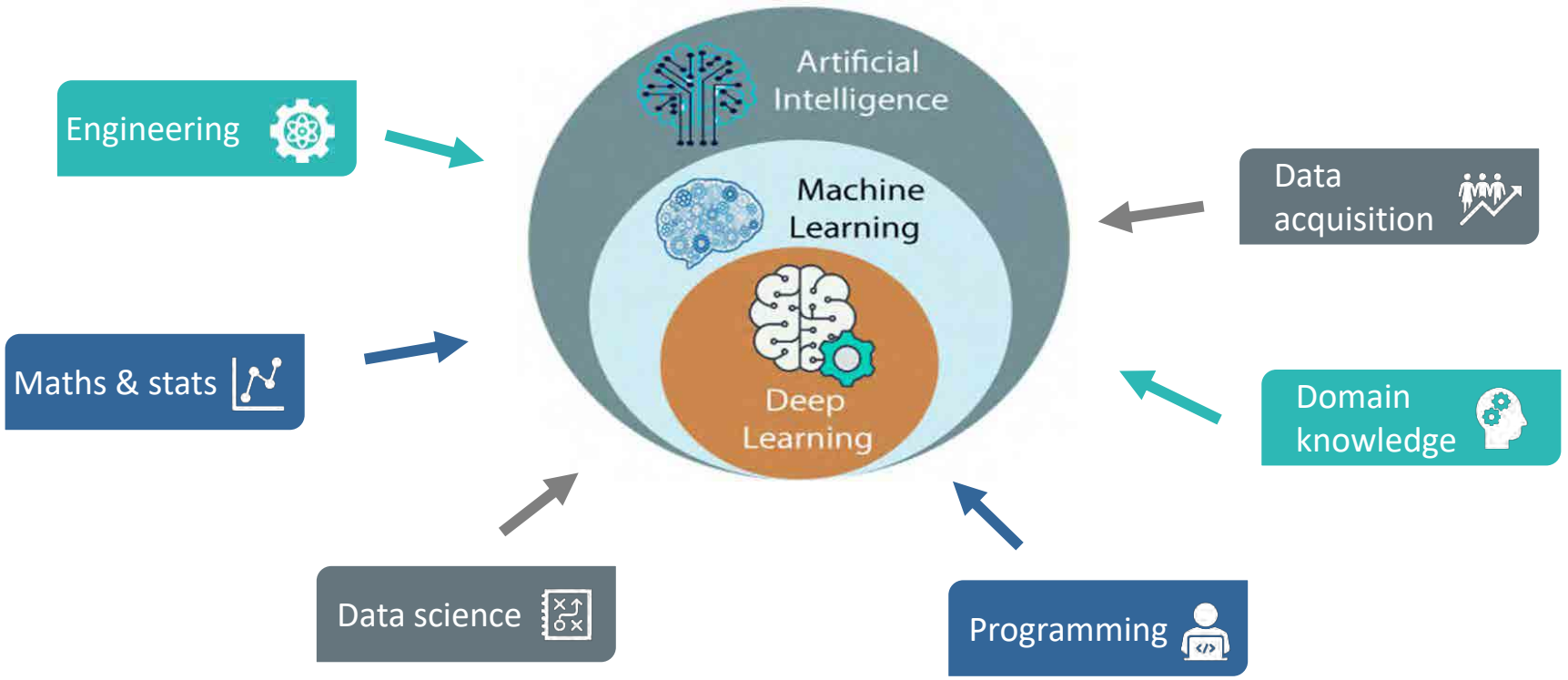
174 97
50
149 99
54

Automated Neonatal Seizure Detection

- Human computer is difficult to replicate
- Neonatal seizures demonstrate inter and intra individual variability
  - They evolve both temporally and spatially
  - Can be relatively low amplitude
  - Influenced by background EEG activity
  - Artefacts are common and impact detection

Artificial Intelligence



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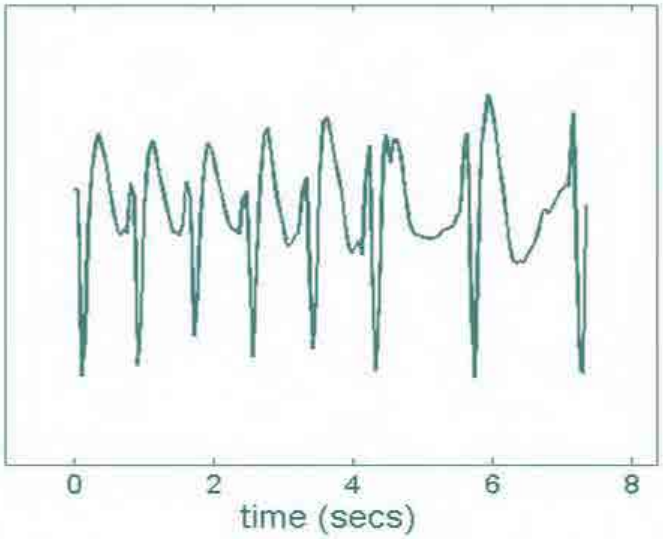
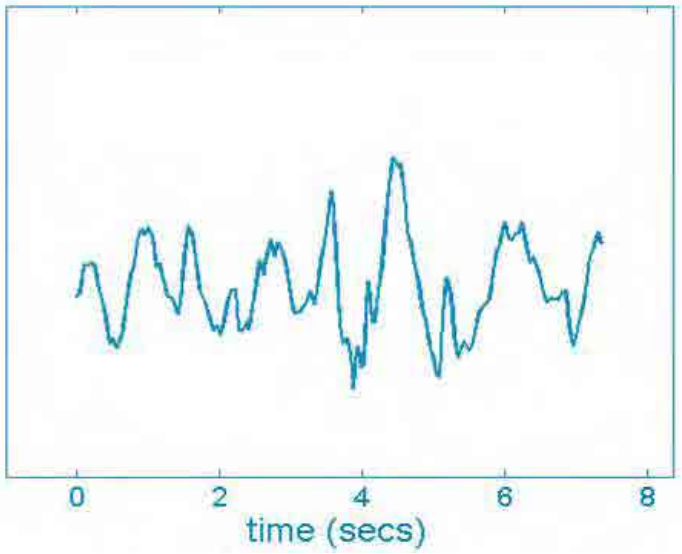
Automated seizure detection algorithm

Training an algorithm to correctly identify **seizure** and **nonseizure** epochs of EEG



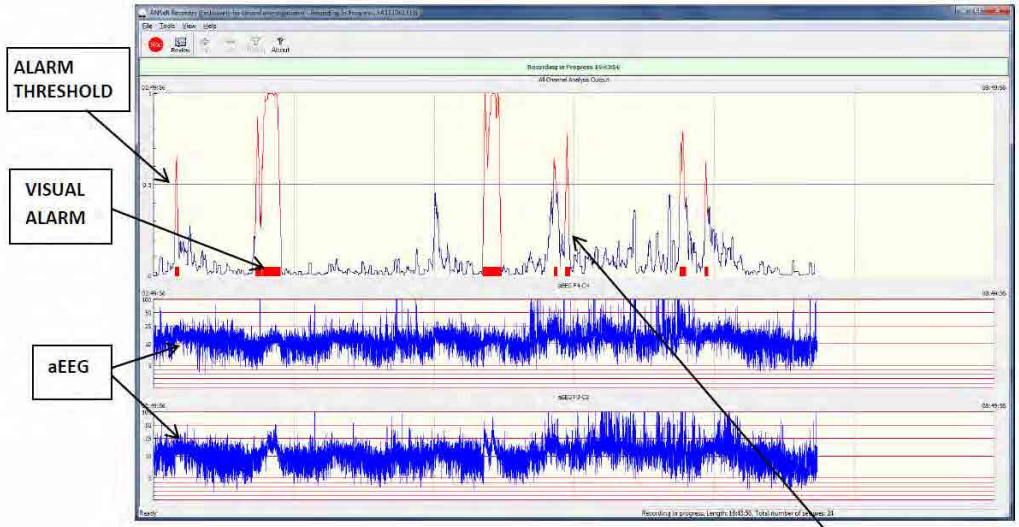


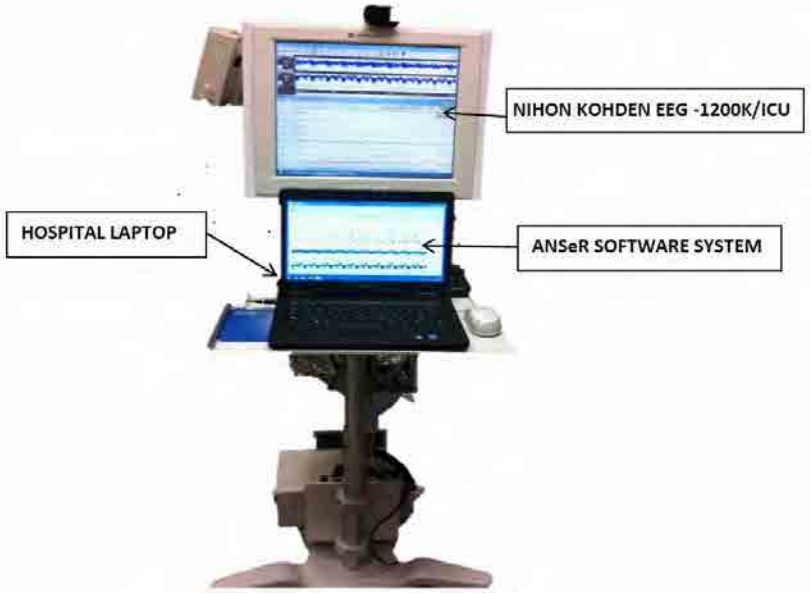
Automated Neonatal Seizure Detection

Study	Seizure detection rate (%)	false alarms per hour	sensitivity (%)	specificity (%)
Cherian et al 2011	-	0.28	66 - 87	-
Temko et al 2011	89	1.0	90	90
Mitra et al 2009	80	0.86	-	-
Deburchgraeve et al 2008	88	0.7	-	-
Navakatikyan et al 2006	90	2.0	83	87
Aarabi et al 2006	-	1.6	74	86
Gotman et al 1997	71	2.0	-	-
Liu et al 1992	-	-	66	90

Real time automated neonatal seizure detection

NIHON KOHDEN





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ANSeR Clinical Investigation

A multi-centre, randomised, controlled, clinical investigation of a standalone decision support **Algorithm for Neonatal Seizure Recognition (ANSeR)**

Primary Objective

Diagnostic accuracy in detecting (a) neonates with seizure and (b) seizure events

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ANSeR - Recruitment Sites

1. Cork University Maternity Hospital, Cork, Ireland
2. University College London Hospital, London, UK
3. Utrecht Medical Centre, Wilhelmina Children's Hospital, Utrecht, Netherlands
4. Karolinska Institutet and University Hospital, Huddinge, Stockholm, Sweden
5. The Royal London Hospital, London, UK
6. Rotunda Maternity Hospital, Dublin, Ireland
7. Homerton University Hospital, London, UK
8. Great Ormond Street Hospital, London, UK

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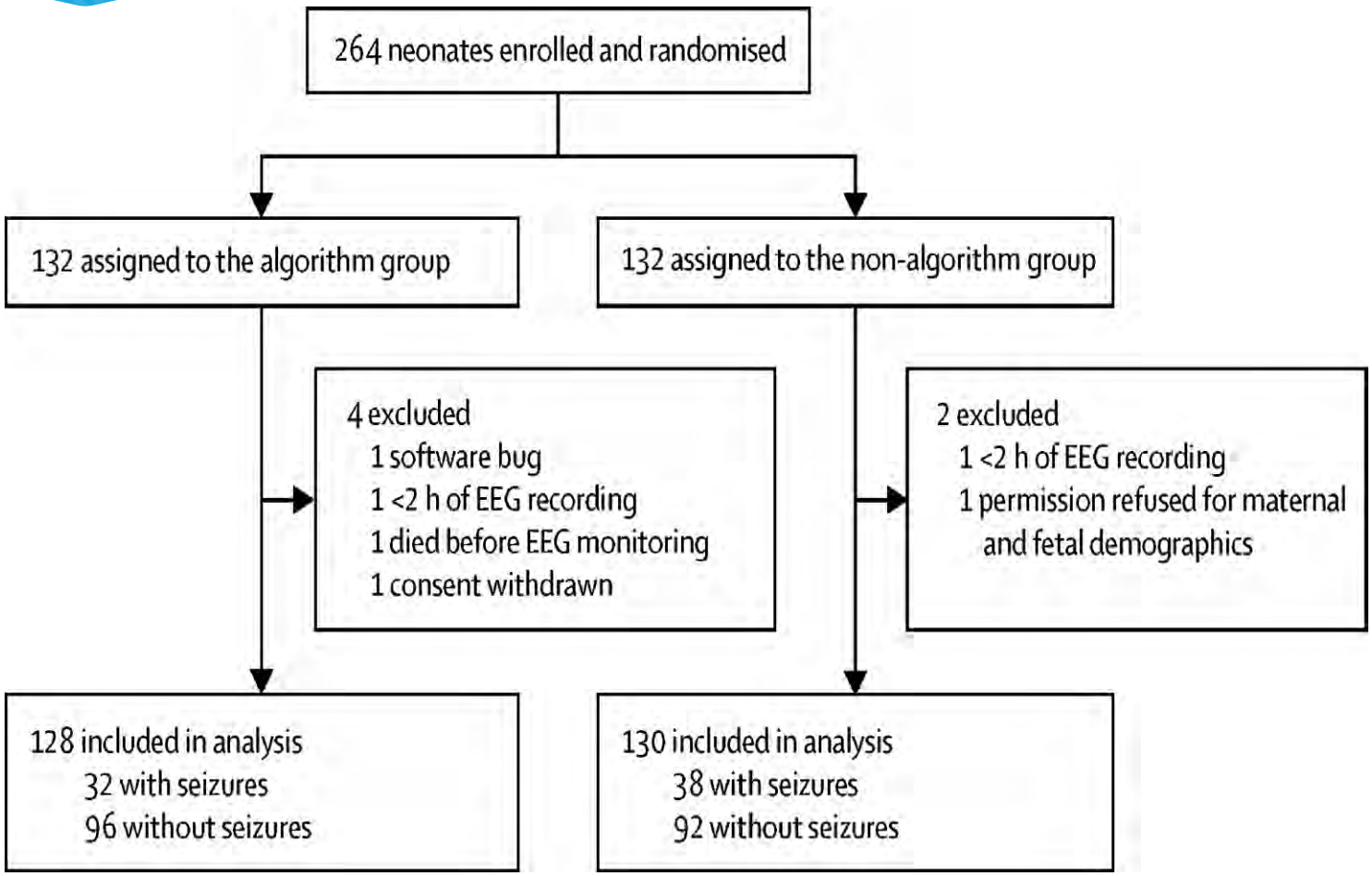
264 neonates enrolled and randomised
132 assigned to the algorithm group
132 assigned to the non-algorithm group
4 excluded
1 software bug
1 <2 h of EEG recording
1 died before EEG monitoring
1 consent withdrawn
2 excluded
1 <2 h of EEG recording
1 permission refused for maternal and fetal demographics
128 included in analysis
32 with seizures
96 without seizures
130 included in analysis
38 with seizures
92 without seizures

EEG Analysis: Expert Raters

- 13,548 hours of data from 258 infants
- 2 Experts independently reviewed all EEGs
- All seizures annotated – true seizure burden

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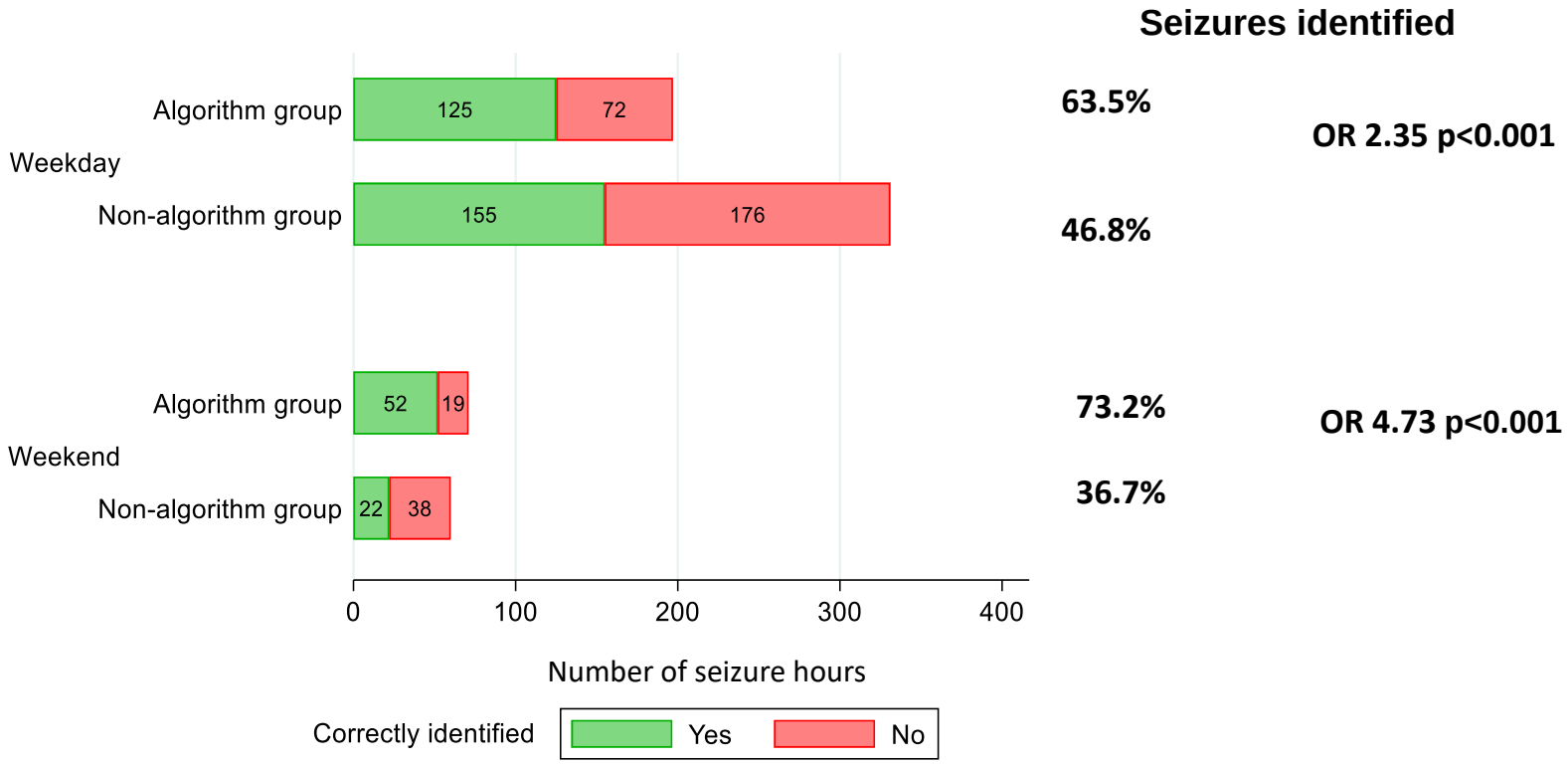
Identification of seizures in real time



Pavel et al. Lancet Child Adolesc Health. 2020 Oct;4(10):740-749

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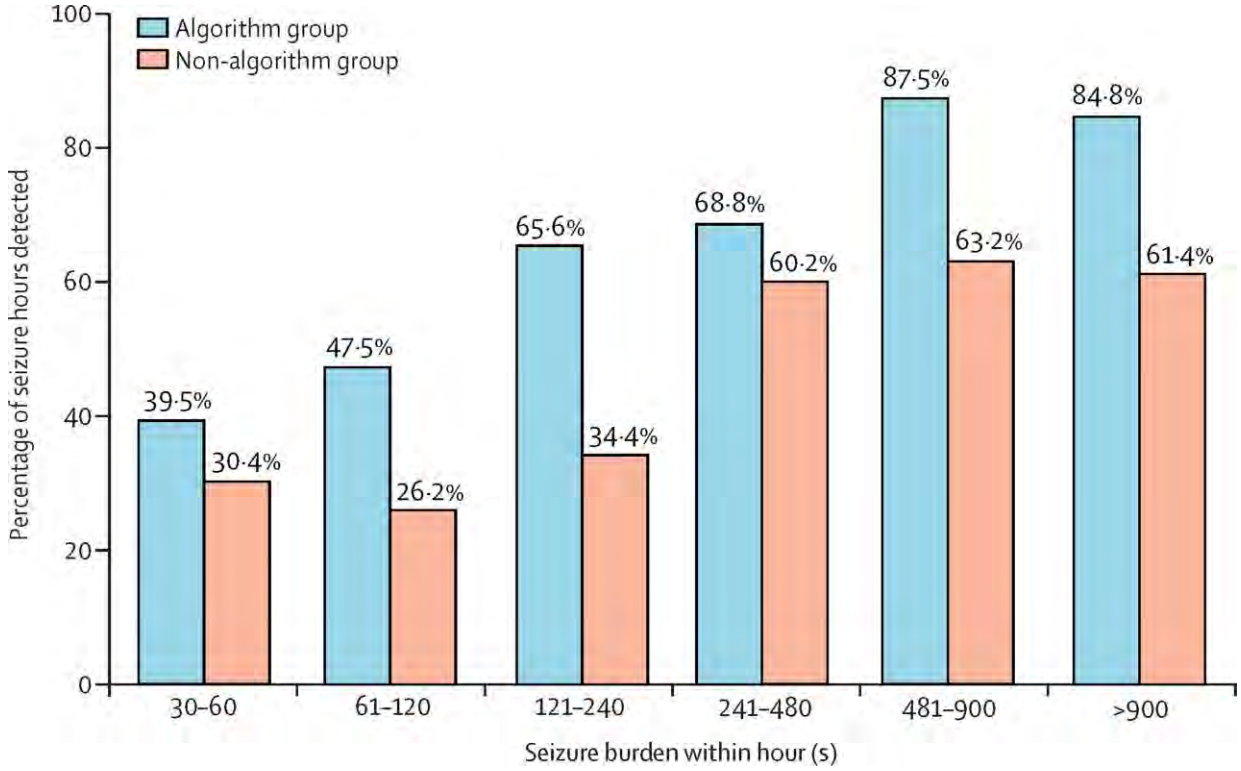
Identification of seizures by duration

Figure 2



Pavel et al. Lancet Child Adolesc Health. 2020 Oct;4(10):740-749

Bench to Cot-side

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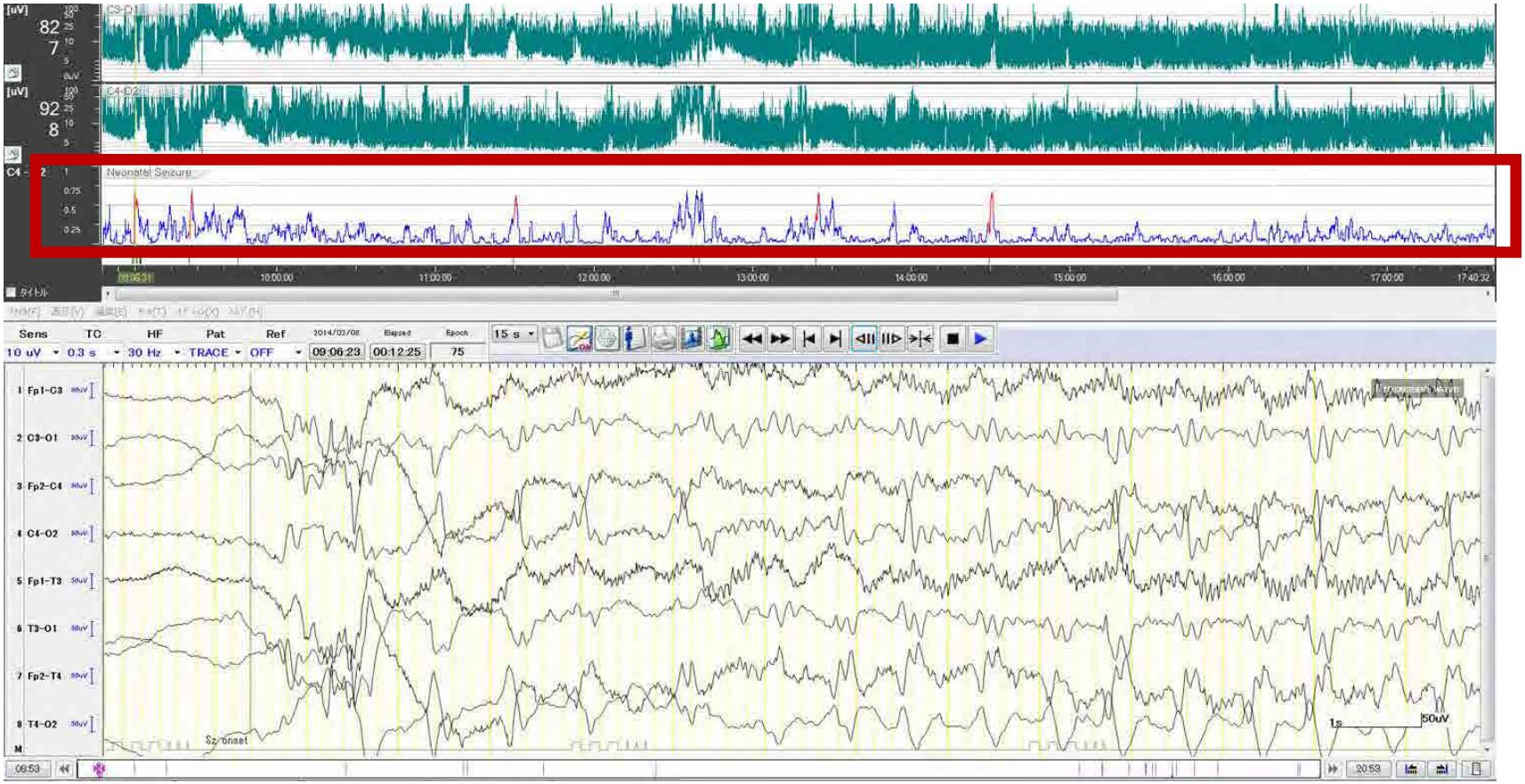

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Summary

- Real time automated neonatal seizure detection is possible in the NICU
- More seizures are detected using automated algorithm
- Anticipate much higher impact in non-expert centres
- Preterm seizure detection algorithms need to be developed

The ANSeR Team

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