# The Threatening Silence of Nocturnal Seizures: A journey into applied research

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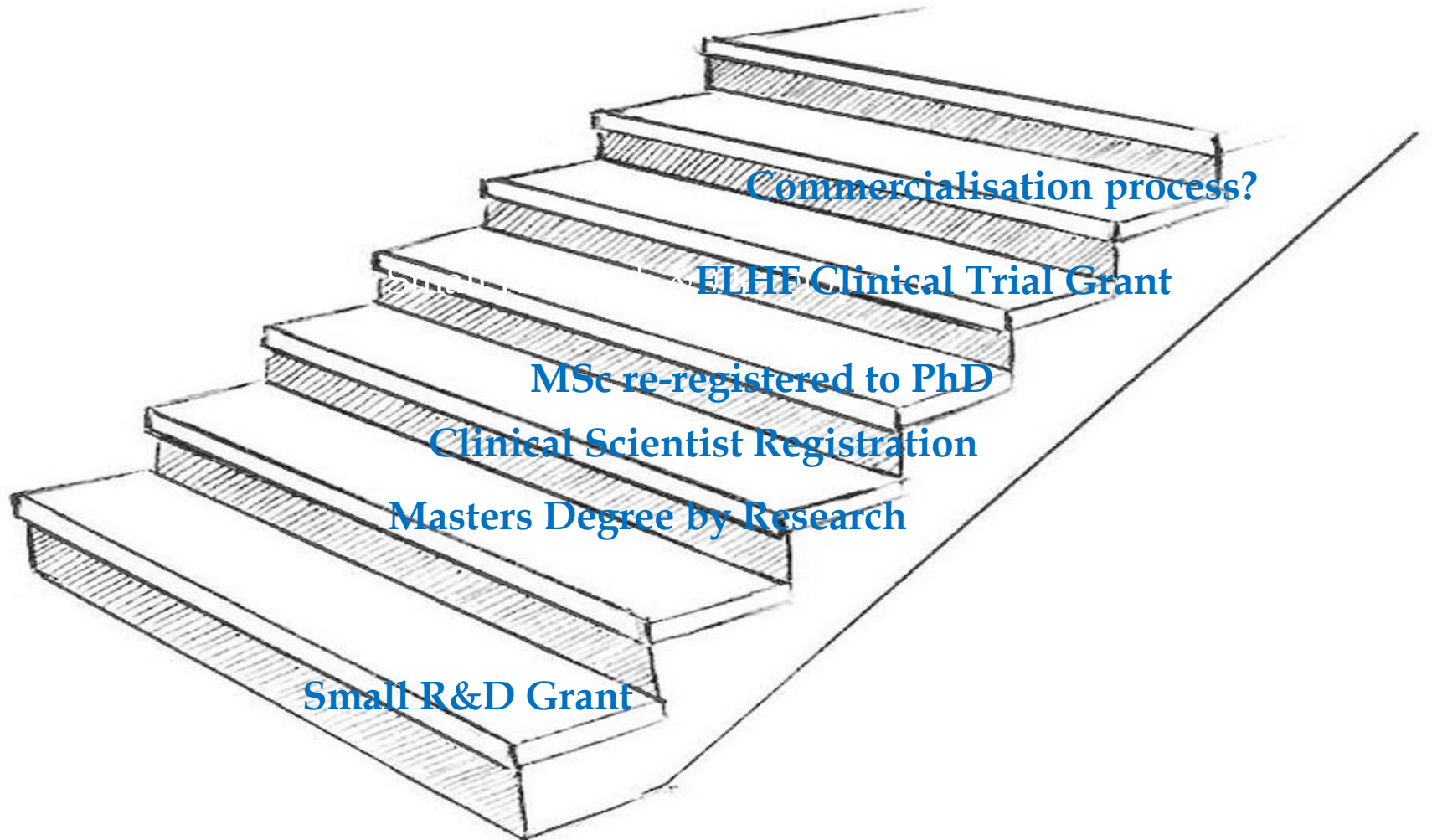& Royal Hospital for Sick Children.

# Why do we need reliable seizure detection?

- More than 500,000 people in the UK have epilepsy (60 million worldwide).

- 1000 epilepsy related deaths occur in the UK each year. The National Sentinel Clinical Audit of Epilepsy-Related Death Report 2002

- Langan Y, Nashef L, Sander WAS. 'Sudden Unexplained Death in Epilepsy: A series of witnessed deaths.' Journal of Neurology, Neurosurgery and Psychiatry. 2000. Vol 68. Issue 2; 211-214.

# My Research Question

- Can we use physiological parameters of heart rate change and oxygen desaturation reliably in a seizure detection alarm system?

- I invented an algorithm. A real time moving window calculating heart rate change. Could it successfully differentiate between epileptic seizures and normal activities and only trigger an alarm during seizures?
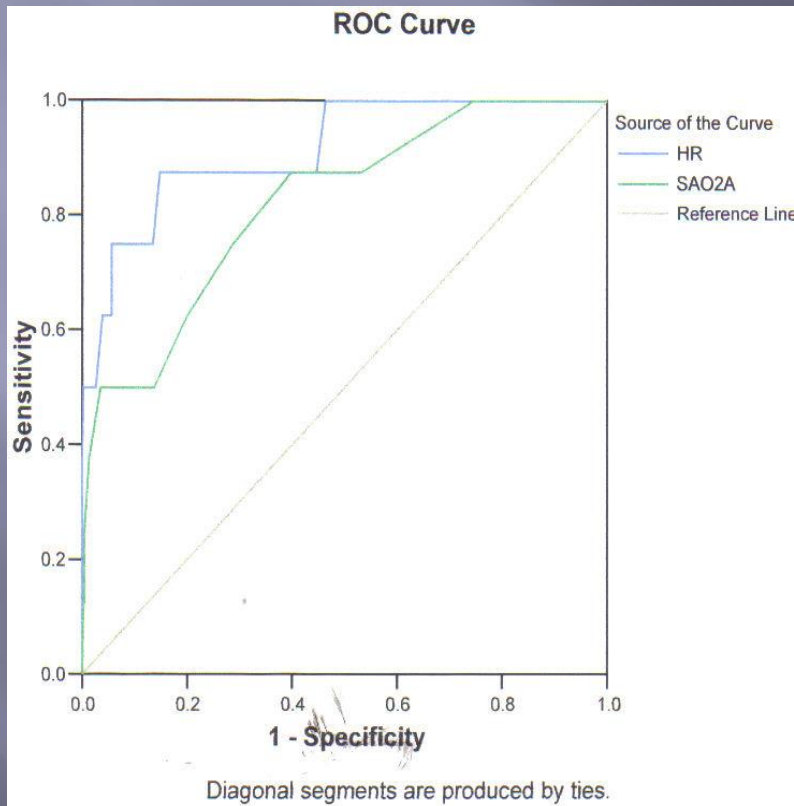
# The Journey

Commercialisation process?

ELHF Clinical Trial Grant

MSc re-registered to PhD

Clinical Scientist Registration

Masters Degree by Research

Small R&D Grant

# MSc/PhD Study

- 527 seizures were analysed from 50 patients from EEG Videotelemetry data.

- Changes in heart rate were calculated (manually) using my algorithm from ECG lead II and pulse oximetry.

- Absences (36), complex focal (102), frontal lobe (229), GTCS (11), myoclonus (28), temporal lobe (31) and tonic (90) were divided into clinically significant (181) and clinically insignificant seizures (466) and compared to changes in heart rate and oxygen saturation during normal physiological events (496).

# MSc/PhD Study Data (independently verified by PA Consulting Group).



**ROC Curve**

Source of the Curve
— HR
— SAO2A
— Reference Line

Diagonal segments are produced by ties.

**Clinically Significant Sz**
HR Trigger level 25.5%
Sensitivity 79%
Specificity 75%

**GTCS**
HR Trigger level 32.5%
Sensitivity 88%
Specificity 85%

**Combined HR & SpO2 one/other/both**
Sensitivity 91%
Specificity 75%

# Collaborators for ELHF Clinical Trial

- Edinburgh & Lothian Health Foundation awarded £250,000 to the project.
- BioQuarter
- PA Consulting Group
- NHS Lothian
- University of Edinburgh
- Investigation project team.
- Marks & Clerk Solicitors
- Western General Hospital
- Royal Hospital for Sick Children
- Ethics/ACCORD/R&D
- MHRA (Medicines and Healthcare Products Regulatory Agency)
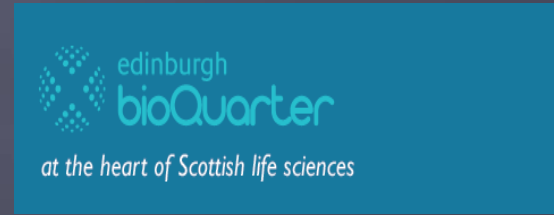
# The Clinical Trial

- Project was originally 2 years but took 2 years just to set up all required documentation, pilot study data verification, prototype building and risk assessments and permissions from Ethics,MHRA, ehealth and R&D with collaboration with ACCORD governing the project.

- Real time data collection collected prospectively over 36 months

- Statistical power of project calculated from pilot study 126 participants or 288 seizures.

- Two prototype devices built to collect data from Royal Hospital for Sick Children and Western General Hospital and connected to hospital servers to synchronise with the hospital servers.

- CE marked finger Nonin finger sensor connecting participant (aged >6 months) to a non CE marked device.

# The Prototype Device

# Schematic diagram of device
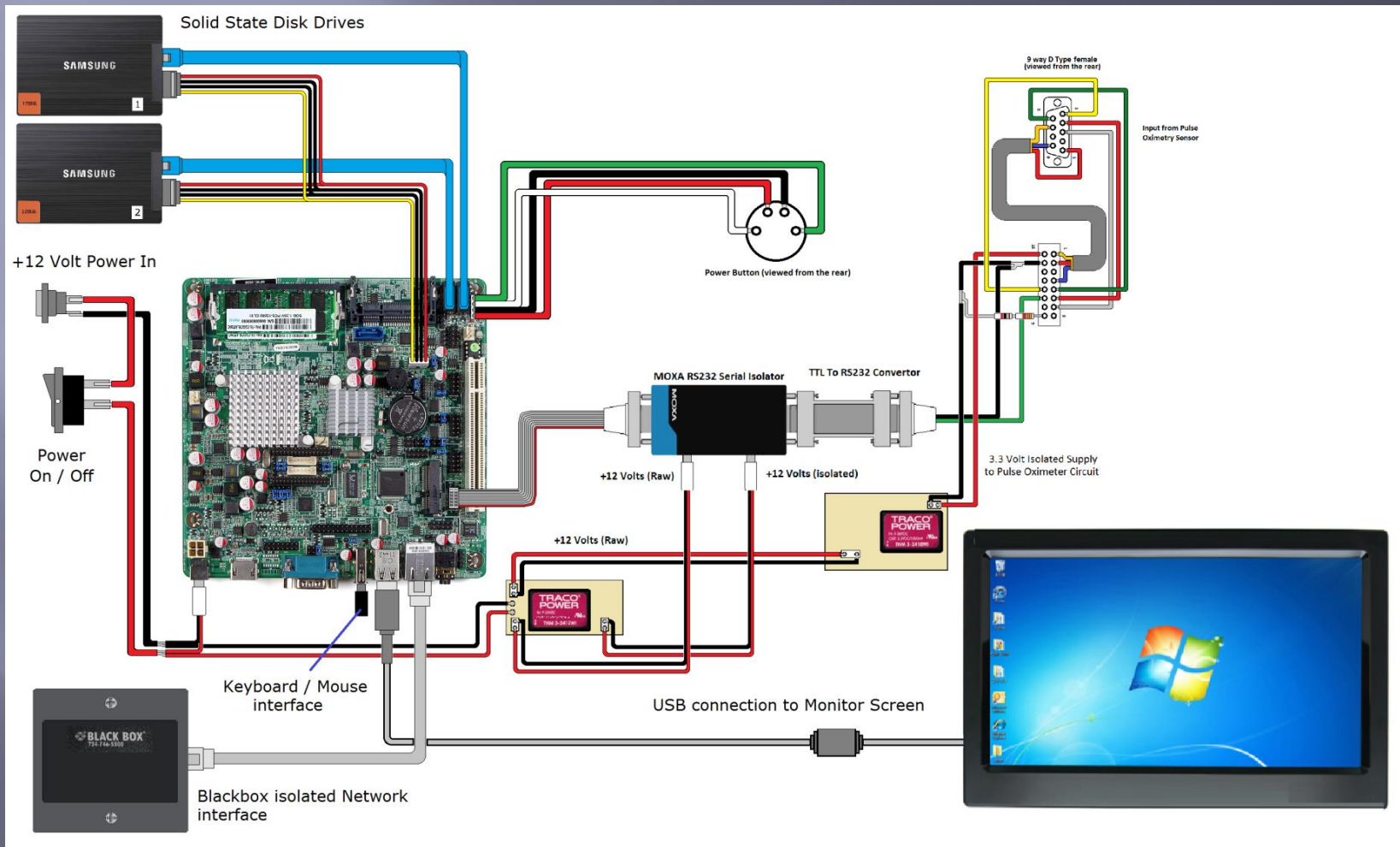
# Device Results

- 119 participants (mean age 23.44 years, min 0.66 to 62 years)
- 65 children and 54 adults
- 683 seizures: Absences (17), Myoclonus (33), Simple Focal (284), Temporal (70), Complex Focal (244), Complex Focal 2° Gen. (12), GTCS (12), Tonic (11).
- 2658 normal physiological events.
- Excellent agreement for Inter & Intra rater analysis.

# Results Device Project

- Using an optimum cut off point (Youden) Heart rate change 25%, SpO2 <85%, Sensitivity of 87%, specificity 93%
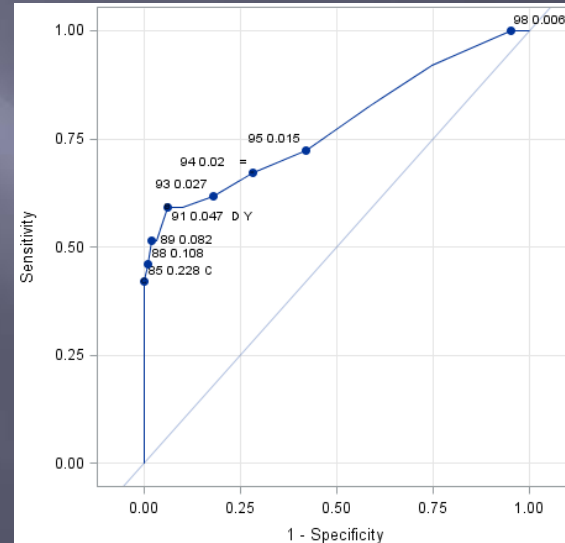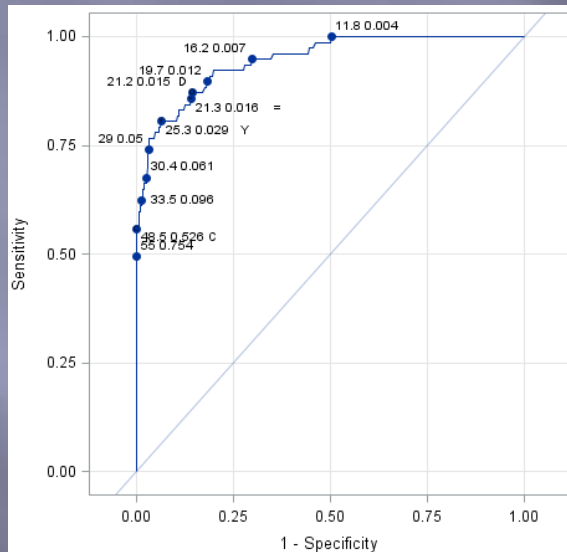




| | Heart Rate | | | |
|---|---|---|---|---|
| Criterion | Symbol | Cutpoint | Label | Value |
| Correct | C | 0.52633 | 48.5 0.526 C | 0.98919 |
| Dist To 0,1 | D | 0.01528 | 21.2 0.015 D | 0.19427 |
| Sens-Spec | = | 0.01552 | 21.3 0.016 = | 0.00114 |
| Youden | Y | 0.02862 | 25.3 0.029 Y | 0.74064 |

| Oxygen Saturation | | |
|---|---|---|
| Cutpoint | Label | Value |
| 0.22837 | 85 0.228 C | 0.98553 |
| 0.04720 | 91 0.047 D Y | 0.41249 |
| 0.01987 | 94 0.02 = | 0.04694 |
| 0.04720 | 91 0.047 D Y | 0.53070 |

| | Clinically significant | | | |
|---|---|---|---|---|
| | No | | Yes | |
| | N | % | N | % |
| Device alert | | | | |
| No | 3017 | 93 | 10 | 13 |
| Yes | 236 | 7 | 68 | 87 |
| All | 3253 | 100 | 78 | 100 |

# Assignation of Intellectual Property

- Assignation of intellectual property to NHS Lothian.
- Marks & Clerk Solicitors have filed a UK patent in May 2014.
- Inventor of the algorithm.
- If next stage funding is successful, device to be CE marked and marketed as it is &/or commercialised with the algorithm built into a wrist watch style device with Bluetooth technology and GPS.



The final device would also include safety-net trigger levels

# Summary & next steps

- Optimum cut off point (Youden) similar to that determined by Pilot Study.

- Perform false alarm rate (FAR) to submit research paper as a phase 3 project. This may indicate a revised cut off point for trigger level.

- Apply for grant to develop wrist watch style prototype device and multicentre clinical trial?

- It is envisaged that the wearable device would incorporate additional safety net trigger levels of dropping SpO2 at 85%, 70% & 60% with Bluetooth technology to a smart phone app and GPS.
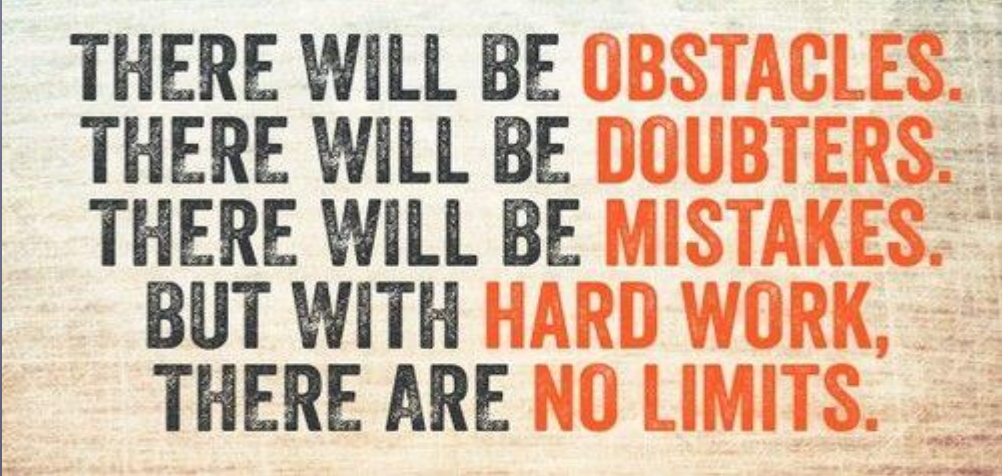
# The journey
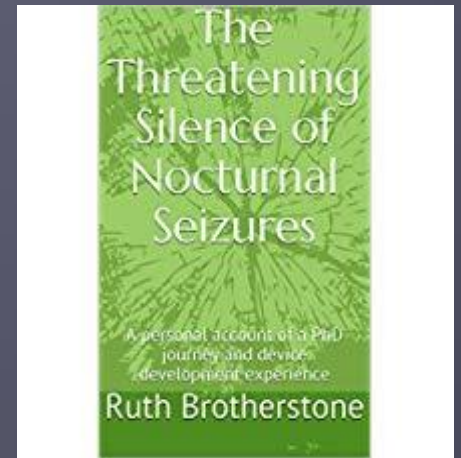
- I have recently published on Amazon Kindle describing my journey from Masters degree to PhD and this research. It is a story of how this has fitted into my clinical career and family. It is a very honest account of human factors and the challenges involved.
- The kindle ebook is entitled

'The Threatening Silence of Nocturnal Seizures'

# Final Remarks

- Support from your Supervisor is key.
- If you can't find the solution to a problem- keep looking.
- Believe in yourself and DON'T give up!
- Your research success is our future world. Good Luck!

THERE WILL BE **OBSTACLES.**
THERE WILL BE **DOUBTERS.**
THERE WILL BE **MISTAKES.**
BUT WITH **HARD WORK,**
THERE ARE **NO LIMITS.**