The BabyLux project

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“Light-to-Cure”: Steps from Photonics to Improved Care of Neonates Born Preterm
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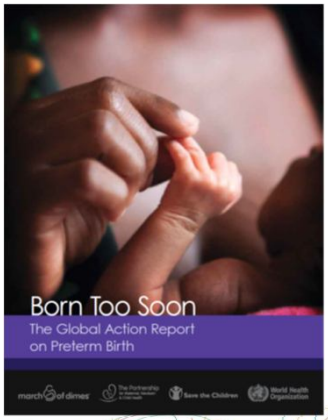
GA no. 620996 CIP ICT-PSP

Outline

- **Monitoring cerebral metabolism and oxygenation in preterm newborns: an unmet clinical need**
- **The BabyLux project: Photonics as a solution**
- **A new business models with industry partners**
- **The BabyLux project: main results and open issues**

Preterm birth – Key facts

- **Every year**, an estimated **15 million babies** are born preterm (before 37 completed weeks of gestation), and this number is rising.
- Across 184 countries, **the rate of preterm birth ranges from 5% to 18% of babies born**.
- **Preterm birth complications** are the leading cause of death among children under 5 years of age, **responsible for nearly 1 million deaths** in 2013.
- **Preterm birth** is associated with an **increased risk of brain damage** and **neurodevelopmental deficit**.



World Health Organization

- Born too soon: the global action report on preterm birth, WHO 2012
- Preterm birth, Fact sheet N°363, WHO 2014

Monitoring cerebral metabolism and oxygenation in preterm newborns

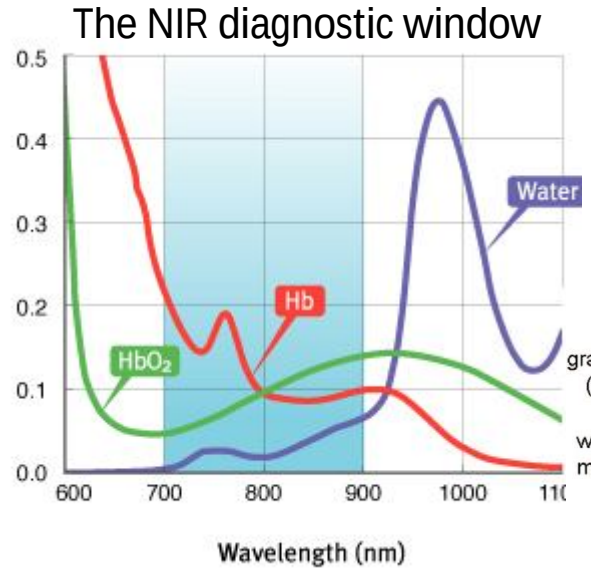
- The most vulnerable period for the developing brain is the first hours and days after birth due to **abnormal haemodynamic adaptation** during the transitional circulation combined with the impact of respiratory distress syndrome.
- Several techniques are used in the neonatal intensive care units to provide physiologically relevant information directly or indirectly related to cerebral blood flow and oxygenation:
  - respiratory volume control
  - transcutaneous pCO_2
  - Doppler ultrasound
  - cerebral oximetry

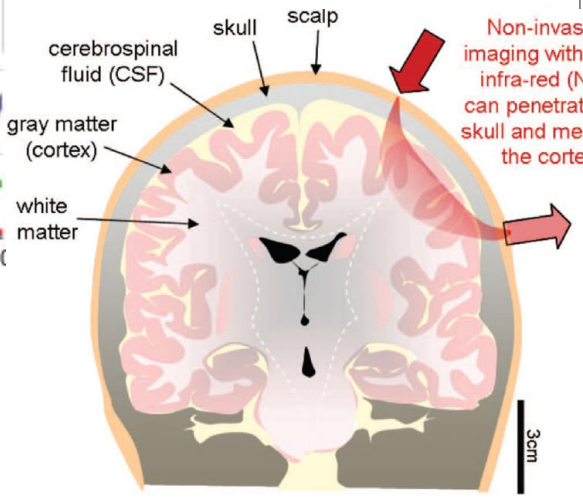
Courtesy of G.Greisen, Rigshospitalet and University of Copenhagen (DK)

Cerebral oximetry: basics

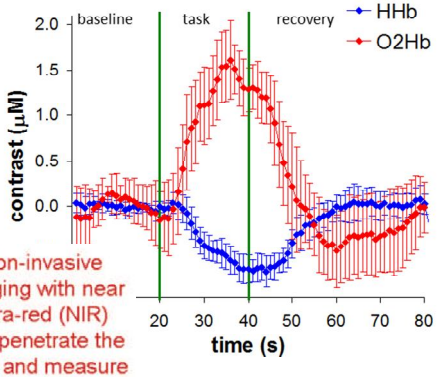
- Near infrared light can penetrate the scalp and the skull and measure the cortex thanks to the interplay of light absorption and light scattering

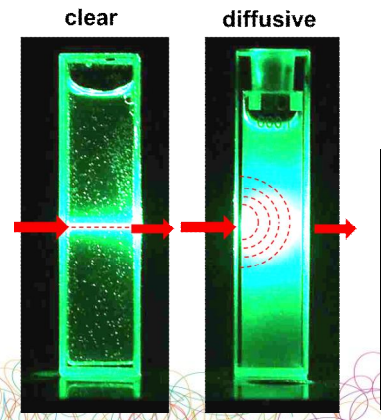
Georges de La Tour (1593 – 1652)
St Joseph, 1642, Louvre, Paris

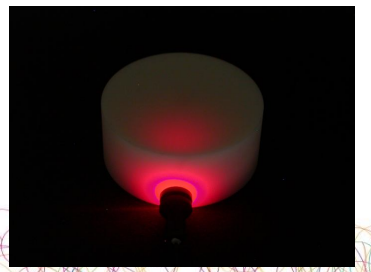




Non-invasive imaging with near infra-red (NIR) can penetrate the skull and measure the cortex



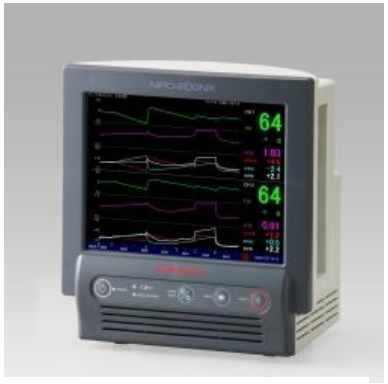




Cerebral oximetry: instruments

Commercial cerebral oximeters do exist …

- INVOS – Covidien/Medtronic (Ireland)



- NIRO – Hamamatsu (Japan)

- ForeSight – Cas Medical Systems (USA)

… however they share several problems

- quantification, reproducibility, no direct information on blood flow, …

→ A non-invasive, continuous, cot-side monitor of brain perfusion and oxygenation is **an unmet need** in clinical care

The BabyLux project

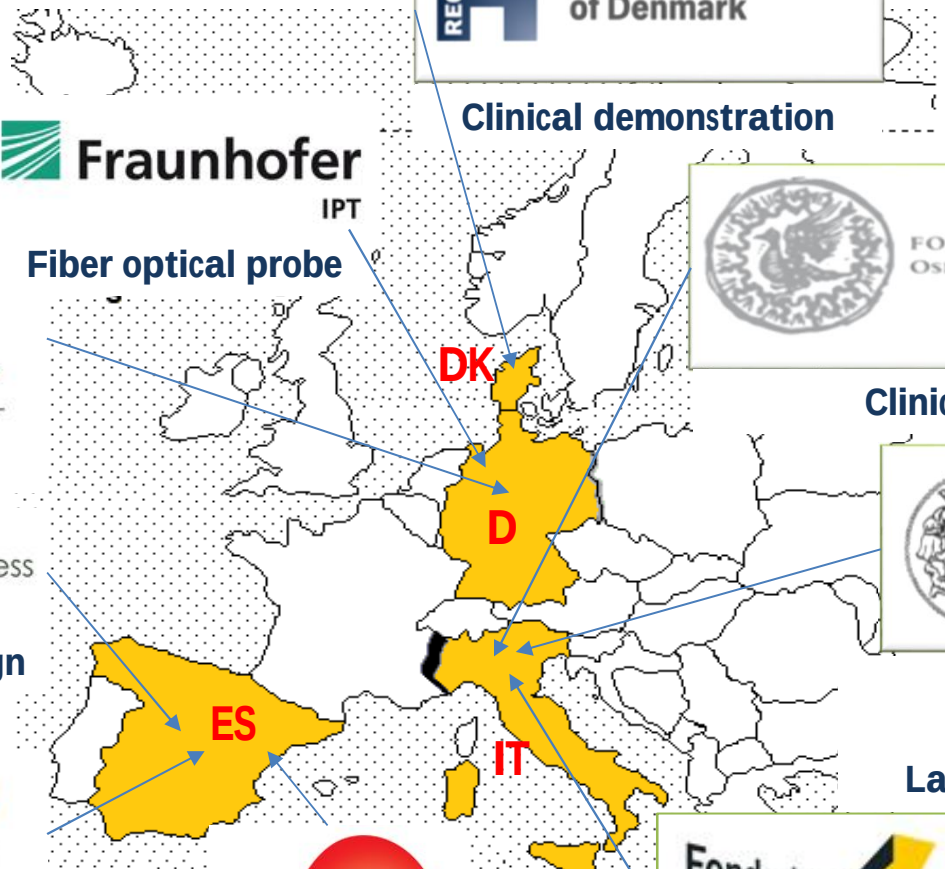
An optical neuro-monitor of cerebral oxygen metabolism and blood flow for neonatology

- The BabyLux project aims to provide a precise, **non-invasive** and robust integrated system to continuously **monitor cerebral oxygen metabolism and blood flow** in extremely **preterm newborns**.

- It will enable **neonatologists** to **prevent** the **neurological damage** due to lack of oxygenation in the brain that not infrequently is accompanied at premature birth.

- Started on 1st January 2014, 40 months 9 partners

The BabyLux Consortium



The Capital Region of Denmark

Clinical demonstration

Fraunhofer IPT

Fiber optical probe

PicoQuant

Laser technologies

Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico

Sistema Sanitario Regione Lombardia

Clinical demonstration

loop | new business models

Medical device design

Politecnico di Milano

Project management
TRS technology
Laboratory demonstration

ICFO The Institute of Photonic Sciences

DCS technology

HemoPhotonics

SW/FW Control
Further exploitation

Fondazione Politecnico di Milano

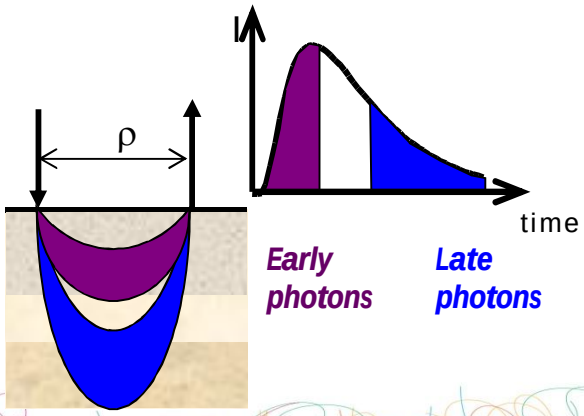
Administration management,
Dissemination, Exploitation

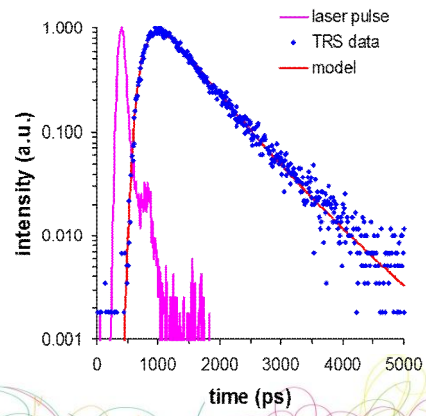
Photonics as key-enabling technology:
TRS & DCS for next generation cerebral oximetry

- The project integrates two **advanced photonic techniques**
  - time resolved near-infrared spectroscopy, **TRS**
  - diffuse correlation spectroscopy, **DCS**

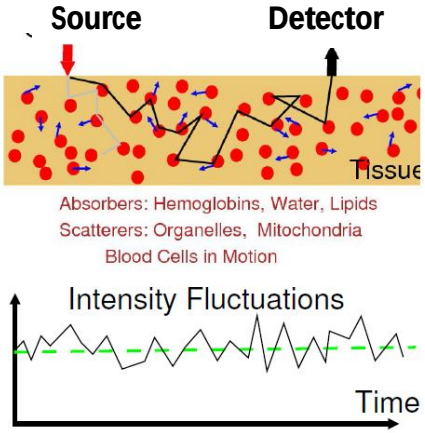
TRS uses intensity changes of scattered light related to regional blood volume and oxygenation changes in brain cortex

- depth information encoded in photon time-of-flight
- absolute oxygenation values

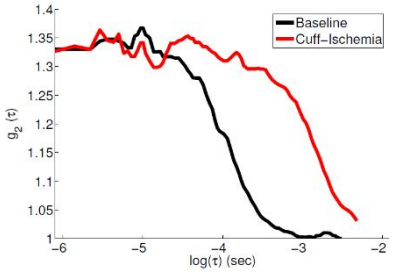




DCS uses intensity fluctuations of scattered light due to motion of red blood cells to probe blood flow



Intensity autocorrelation



Torricelli et al. NeuroImage 85:28 (2014)

Durduran and Yodh, Neuroimage 85:51 (2014)

A new business models with industry partners

- Take up **complete R&D** works
- Extend already **tested prototypes** to the level of **demonstrator**
- **Bridge the gap** between research products and commercialization.

TRL 1	TRL 2	TRL 3	TRL 4	TRL 5	TRL 6	TRL 7	TRL 8	TRL 9
Basic principles observed	Technology concept formulated	Experimental proof of concept	Technology validation in lab	Technology validation in relevant environment	Demonstration in relevant environment	Demonstration in operational environment	System completed and qualified	Successful mission operations

Prototype / Product
No CE marked
For research purposes only

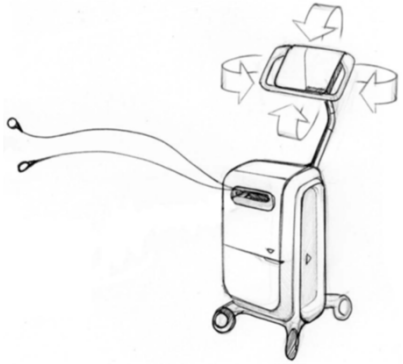
BABYLUX

Product
CE marked
For clinical use

The BabyLux project workplan

Phase 1

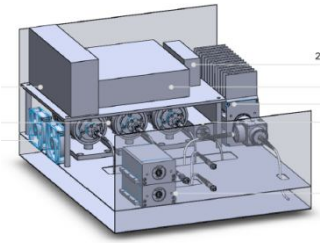
components



concepts

Phase 2

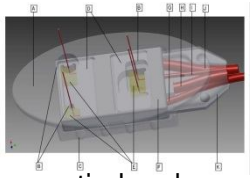
TRS module



internal layout

DCS module

external layout



optical probe

Phase 3

Clinics

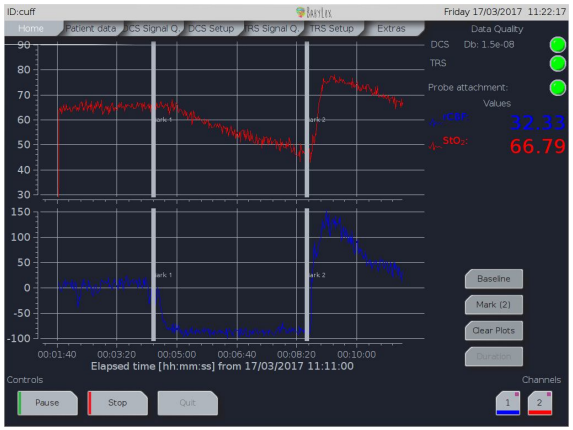
Problem definition

Service integration, localisation and demonstration in laboratory settings

Operational phase in real-life settings

The BabyLux project: main results → technology

- We have designed and built an **innovative medical device for clinical research** combining two advanced biophotonic technologies (TRS and DCS), extending already tested prototypes to the level of **demonstrator**.
- **Two devices** were installed in the neonatology units in Copenhagen and Milan and **used by clinical doctors** for at least 6 months, with **minimal support from developers**, mainly limited to data analysis.



The BabyLux project: main results → clinical research

- **More than 60 neonates** were enrolled in the validation study.
- We obtained simultaneous, continuous measurements of **tissue oxygenation and blood flow index** from the heads of term and preterm infants with:

  a) acceptable short time variability;

  b) qualitatively reasonable dynamic responses.
- Moving the optode from one site on the head to another resulted in:

  a) **less than 5% variability in tissue oxygenation** (better than existing commercial devices currently used in the neonatology units).

  b) **15-25% variability in blood flow index** (comparable to trancranial Doppler ultrasound measures of macrovasculature, Xenon clearance and other modalities).
- The device proved to be **safe** in terms of acute adverse reactions as we never observed skin marks after measurements.

→ see next presentation by G.Greisen RegionH

The BabyLux project: main results → exploitation & dissemination

- Major steps towards industrialization and production were taken, **bridging the gap between research products and commercialization**.
- Exploitation plans were drawn up

  → see next presentation by U.Weigel Hemophotonics SL

- Several **dissemination, communication and outreach activities** leaded by Fondazione Politecnico di Milano

  → Website www.babylux-project.eu

  → Press releases & newsletters

  → Social media (YouTube, Twitter, Facebook, Linkedin, ..)

  → National and European broadcasting (e.g. EuroNewsTV)

  → General public events (e.g. European Researchers' Night)

Beyond the project lifetime

Phase 4

Clinics

Extended clinical trials (intended used)

Phase 5

CE

FC

RoHS

Pre-Market Certifications

Phase 6

Medical device market

The BabyLux project: open issues

- **Hardware and software improvements** (optimize calibration procedure on phantom, reduce warmup time, optimize adjustment after probe placement, reduce number of wavelengths, upgrade capacitive sensors, revise laser eye-safety measure of protection for unattended use, …).
- Design and test a **handheld probe** for occasional use and/or an **improved probe** (lighter, softer, smaller) for continuous use.
- Improve **user-friendliness** aiming at routine use by clinical staff with minimal or null training.
- **Advance data analysis** procedure (real-time and off-line), aiming at enhancing robustness and quantification.
- Measure more babies in current studies.
- Design and implement **new studies and clinical trials** to foster the use of the device in **clinical care**.
- Advance industrial design and production.
- Obtain **CE certification**.

→ see Round Table discussion

Conclusion / Roadmap to future

- Clinical end users identify an unmet need
- Researchers provide a validated photonic solution
- Industry supplies advanced ICT components
- A medical device manufacturer exploits the solution
- Funding agencies support all actors simultaneously

Acknowledgments

- European Commission – DG CNECT - A01
- BabyLux partners
- Parents of neonates enrolled in the studies