Physikalisch-Technische Bundesanstalt
Braunschweig and Berlin
National Metrology Institute

# *Performance assessment and development of ISO/IEC standards in diffuse optics*

***Heidrun Wabnitz***

*Physikalisch-Technische Bundesanstalt (PTB), Berlin, Germany*

*Dept. Biomedical Optics*

*heidrun.wabnitz@ptb.de*

# *Outline*

Introduction

- fNIRS and cerebral tissue oximetry
- ISO/IEC standards in diffuse optics
- Research in diffuse optics – culture of performance assessment

Performance protocols and phantoms

- MEDPHOT
- BIP
- nEUROPt

Performance tests and phantoms in the ISO/IEC standards

- fNIRS
- Tissue oximetry

Other activities

# *Introduction: fNIRS and tissue oximetry*

**fNIRS** (functional Near-InfraRed Spectroscopy)

Hemodynamic response to (neuronal) brain activation

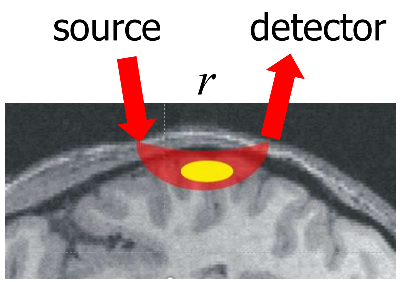
*Measurands:*

Hb concentration <u>changes</u> in the brain

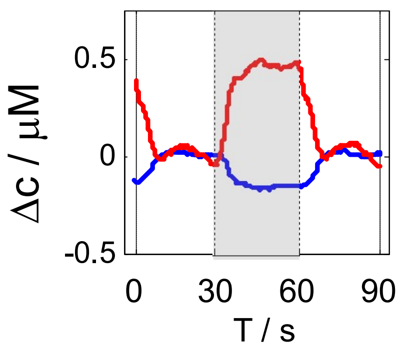
$\Delta c_{O2Hb}$ , $\Delta c_{HHb}$

← absorption <u>changes</u> $\Delta\mu_a(\lambda, T)$

← attenuation <u>changes</u> $\Delta A(\lambda, T)$ ( method)




$r$ ~ 3 cm




**Cerebral tissue oximetry**

Cerebral oxygenation monitoring (heart surgery, neonates,…)

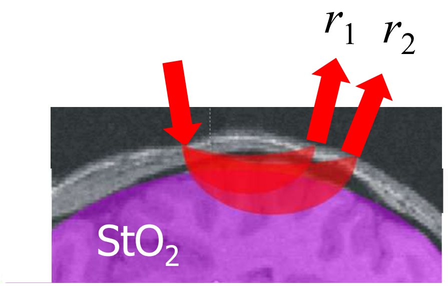
*Measurand:*

$StO_2$ = oxygen saturation of Hb of blood in (cerebral) tissue

$StO_2 = c_{O2Hb} / (c_{O2Hb} + c_{HHb})$

← (absolute) absorption coefficients $\mu_a(\lambda)$

← attenuation difference (intensity ratio) $A(r_1)$ - $A(r_2)$




e.g. 70%
(mixture of arterial, venous, capillary blood)

- 2 or more source-detector separations to suppress influence of superficial tissues
- most commercial devices (CW) rely on empirical calibration rather than model-based approaches

# *ISO/IEC standards in diffuse optics*

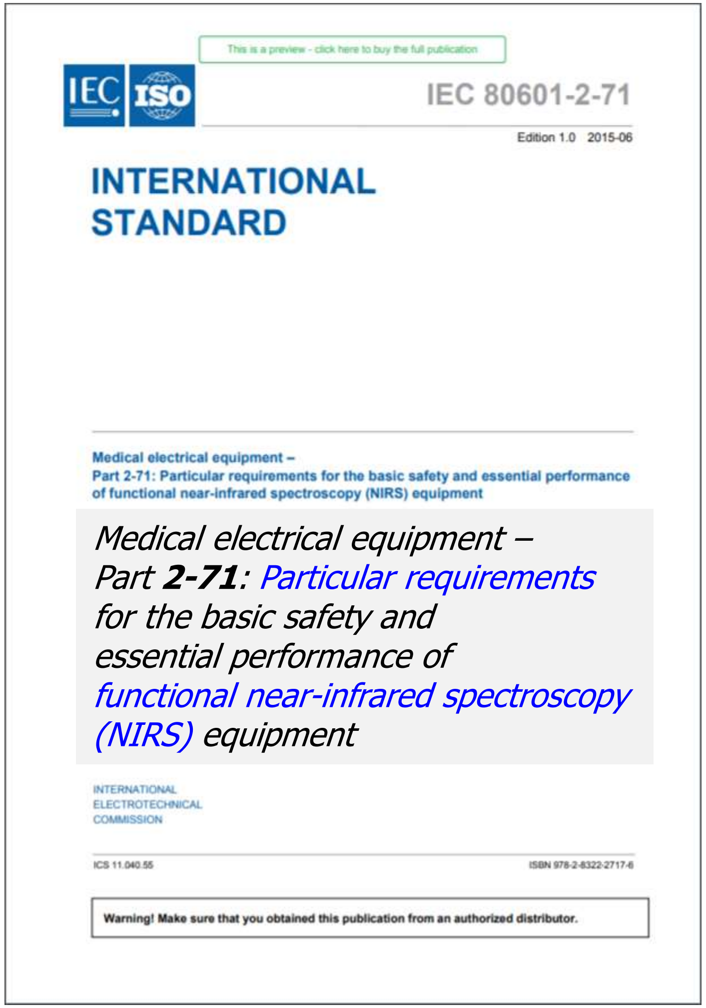
**General standard**

**IEC 60601-1** *- Medical electrical equipment - Part **1**: General requirements for basic safety and essential performance*

**Particular standards**
(requirements for specific products or measurements)

- ISO 80601-2-61:2017 (1st ed. 2011)
  *pulse oximeter equipment*
- IEC 80601-2-71:2016 (new)
  *functional near-infrared spectroscopy (NIRS) equipment*
- ISO 80601-2-85 (under development)
  *cerebral tissue oximeter equipment*

developed by
ISO TC121/SC3/JWG10 – IEC TC62/SC62D/JWG5
= **JWG "Oximeters"**


This is a preview - click here to buy the full publication

IEC ISO

IEC 80601-2-71

Edition 1.0 2015-06

INTERNATIONAL STANDARD

Medical electrical equipment –
Part 2-71: Particular requirements for the basic safety and essential performance of functional near-infrared spectroscopy (NIRS) equipment

*Medical electrical equipment –*
*Part **2-71**: Particular requirements for the basic safety and essential performance of functional near-infrared spectroscopy (NIRS) equipment*

INTERNATIONAL ELECTROTECHNICAL COMMISSION

ICS 11.040.55

ISBN 978-2-8322-2717-6

Warning! Make sure that you obtained this publication from an authorized distributor.

# ISO/IEC standards in diffuse optics

**General standard**

**IEC 60601-1** - *Medical electrical equipment - Part **1**: General requirements for basic safety and essential performance*

**Particular standards**
(requirements for specific products or measurements)

- ISO 80601-2-61:2017 (1st ed. 2011)
  *pulse oximeter equipment*
- IEC 80601-2-71:2016 (new)
  *functional near-infrared spectroscopy (NIRS) equipment*
- ISO 80601-2-85 (under development)
  *cerebral tissue oximeter equipment*

developed by
ISO TC121/SC3/JWG10 – IEC TC62/SC62D/JWG5
= **JWG "Oximeters"**

Standards of the 60601 family are "safety standards"
(not "performance standards")

**3.27**
*** ESSENTIAL PERFORMANCE**

performance of a clinical function, other than that related to BASIC SAFETY, where loss or degradation beyond the limits specified by the MANUFACTURER results in an unacceptable RISK

~ "functional safety"!

# *Research in diffuse optics*

**Culture of performance assessment in various EU projects**
**(WPs related to performance assessment and standardization)**

- clinical problem → physical problem (model)
- protocols (guidelines, tests, measurands)
- implementation (phantoms, measurement conditions)
- multi-laboratory comparison of instrumentation
- potential contribution to standardization

**MEDPHOT** 2000-2004 "MEDPHOT protocol"

**nEUROPt** 2008-2012 "BIP protocol"
"nEUROPt protocol"

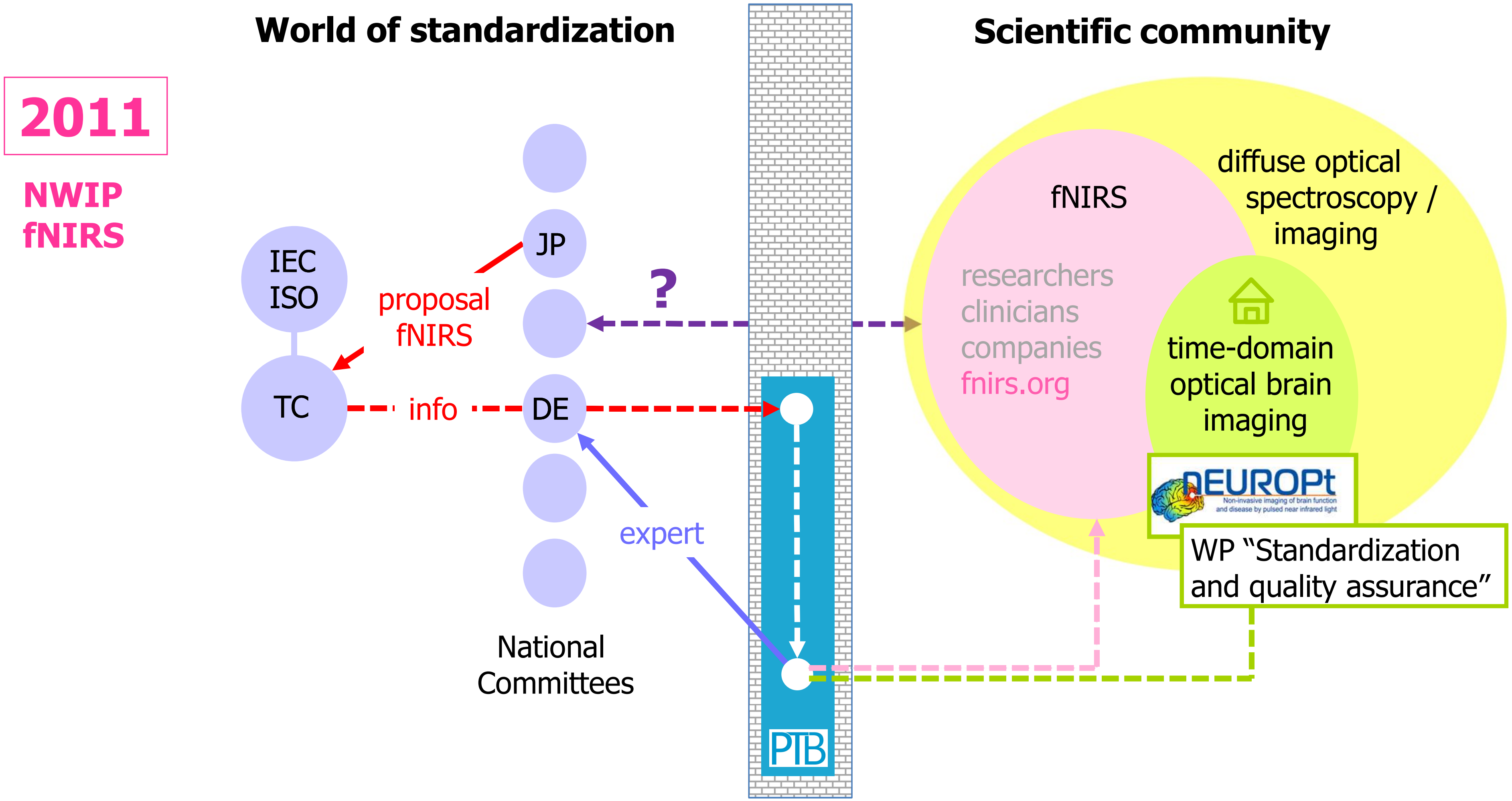
⋮ several other EU projects

**BitMap** (MSCA-ITN) 2016-2019

application of selected tests of these protocols

- measurements (~30 instruments, 9 institutions – EU and beyond)
- open data
- advanced analysis of all data with various models

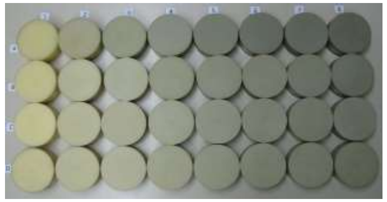
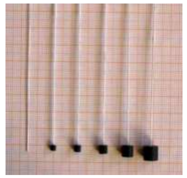
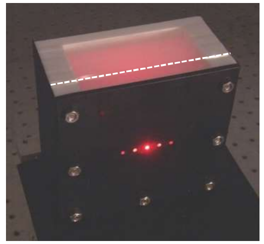
# *Science and standardization?*



Performance protocols and phantoms (EU projects)

- MEDPHOT
- BIP
- nEUROPt

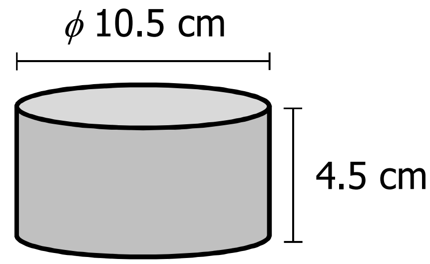
# *Performance protocols*

| **Guidelines** | **Model** | **Tests** | **Phantoms** |
|---|---|---|---|
| "Basic instrumental performance" protocol<br>*H. Wabnitz et al. JBO 2014, part 1* | ~ no sample | in particular: responsivity of detection system |  |
| "MEDPHOT" protocol<br>*A. Pifferi et al. Appl. Opt. 2005* | $\mu_s'$, $\mu_a$<br>homogeneous | accuracy, linearity, noise, stability, reproducibility |  |
| "nEUROPt" protocol<br>*H. Wabnitz et al. JBO 2014, part 2* | $\Delta\mu_a$<br>model of brain activation (fNIRS) | sensitivity<br>spatial resolution<br>accuracy |   |

# *MEDPHOT protocol and solid phantom kit*

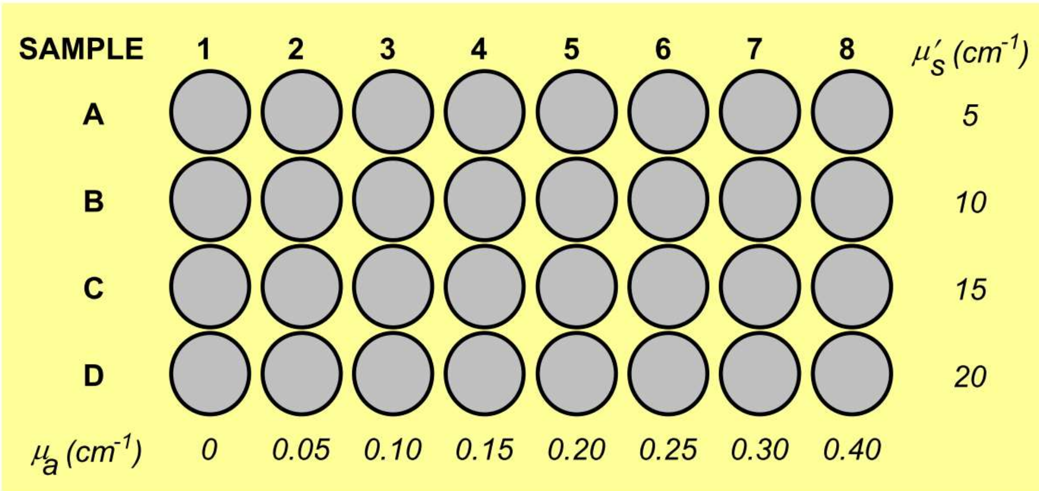
Determination of $\mu_a$ , $\mu_s'$ of a homogeneous turbid medium

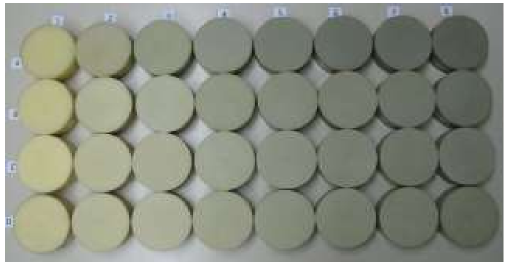
**Tests:** accuracy, linearity, noise, stability, reproducibility




(epoxy, $TiO_2$, toner)

constructed at LLC
by LLC & POLIMI



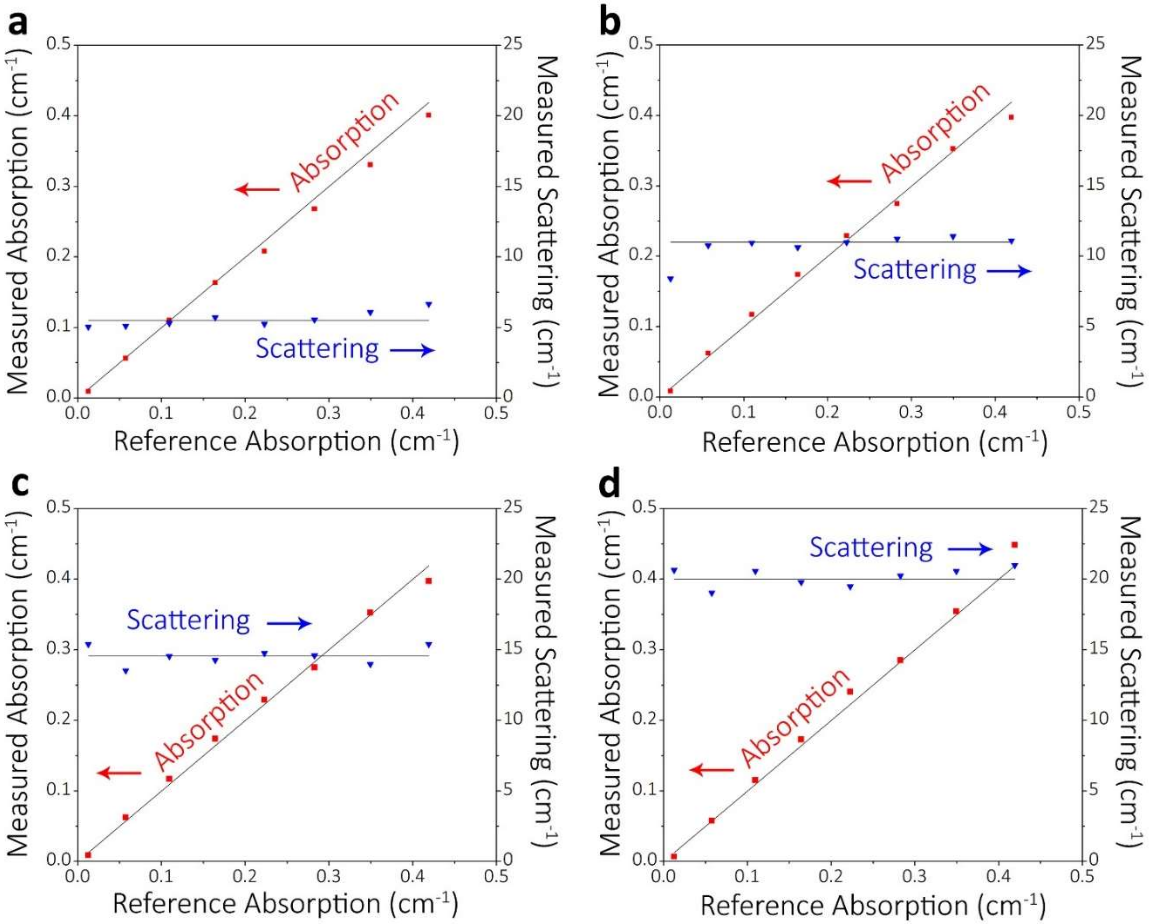



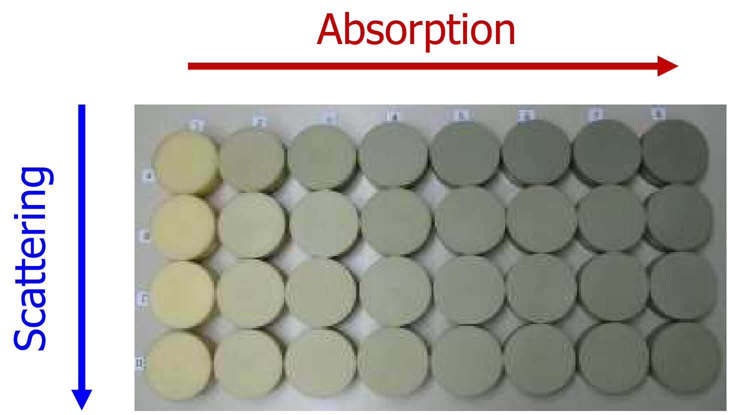
*A. Pifferi et al.*
*“Performance assessment of photon migration instruments: the MEDPHOT protocol“*
*Appl. Opt. 44 (2005), 2104-2114*

- well characterized during MEDPHOT measurement campaigns
- but: accuracy of characterization of $\mu_a$ , $\mu_s'$ ~10…20%

# MEDPHOT protocol - linearity

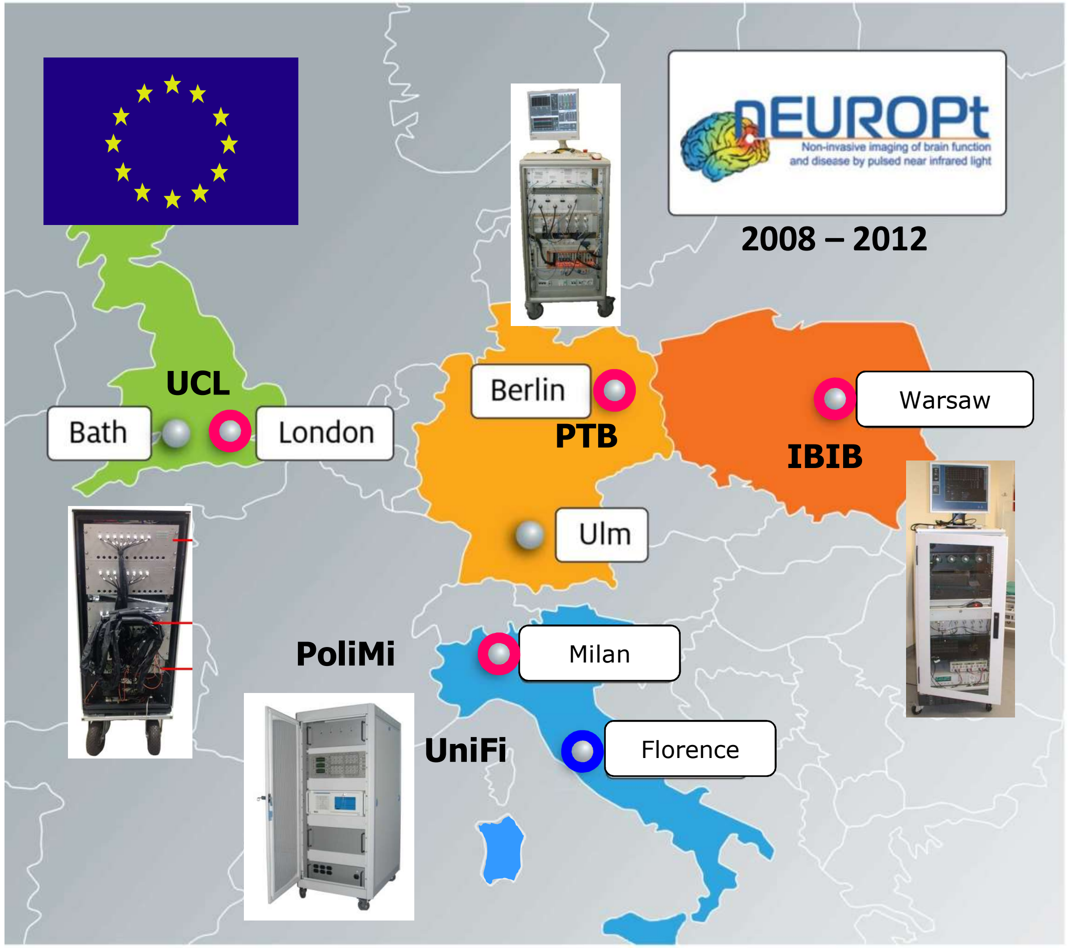
Example of linearity plots of a diffuse spectroscopy instrument



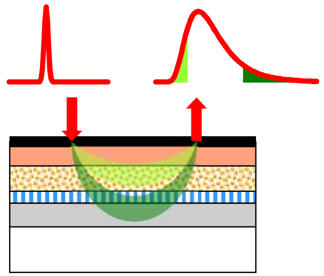




*A. Pifferi et al. Appl. Opt. 2005*
*A. Dalla Mora et al. Opt. Expr. 2015*

# *Performance assessment (nEUROPt project)*



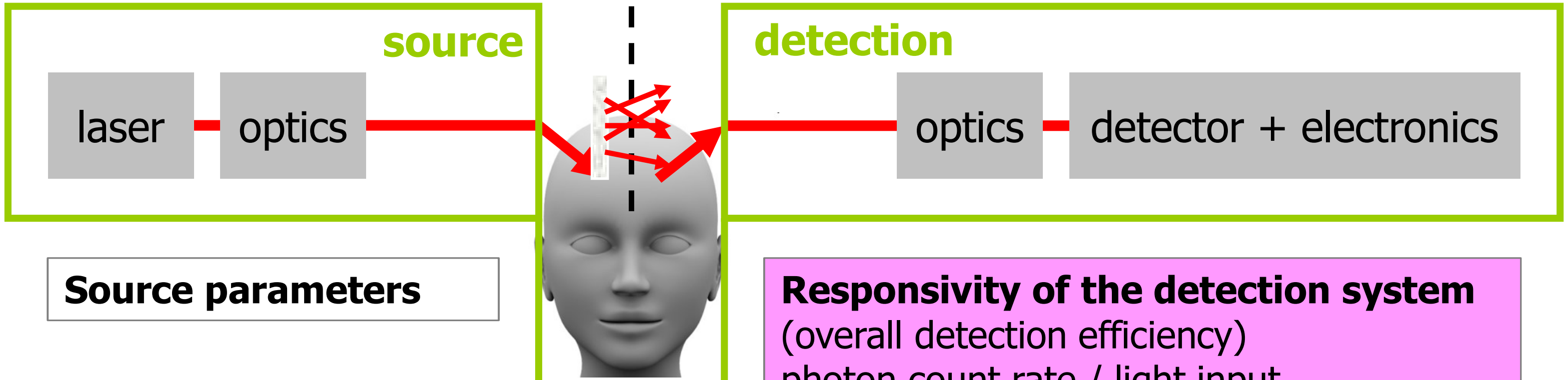

Time-domain optical brain imaging
(fNIRS - $\Delta\mu_a$)



- developments in technology and data analysis
- **performance assessment**
- clinical pilot studies
  - comparison of **instruments**
  - comparison of **methods of data analysis**
  - effect of technical improvements
  - quality assurance during clinical studies

# *Basic instrumental performance*

**Aim:** record all relevant characteristics of the instrument




**Source parameters**

**Responsivity of the detection system**
(overall detection efficiency)
photon count rate / light input

**Differential nonlinearity of timing electronics**

**Temporal instrument response function (IRF)**
← laser pulse shape
← temporal dispersion in fibers
← time resolution of detector (TTS)

*H. Wabnitz et al., "Performance assessment of time-domain optical brain imagers, part 1: Basic instrumental performance protocol," J. Biomed. Opt. 19 (2014), 086010*

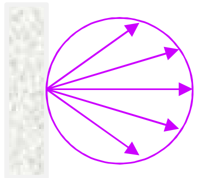
# *Definition of responsivity*

**Responsivity** (~ overall efficiency) of the **detection system**

$$s_{\text{det}}^{L}(\lambda) = \frac{S(\lambda)}{L(\lambda)}$$

signal, e.g. count rate $N$

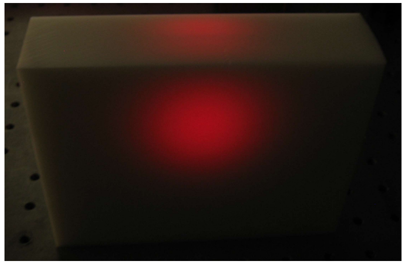
radiance (W m$^{-2}$ sr$^{-1}$)



**Required:** uniform light source

- with angular distribution ~ as from tissue (~ Lambertian)
- with known radiance $\boldsymbol{L}$

**Solution:**

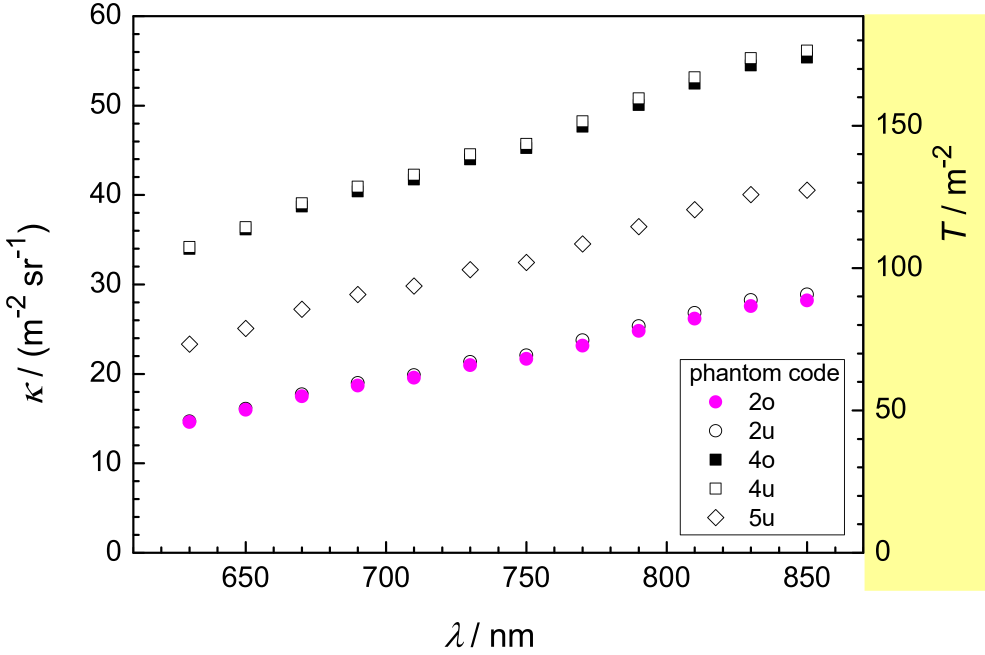


- thick slab phantom (2 cm) with known transmittance factor $\kappa(\lambda)$
- input power $\overline{P}_{\text{in}}(\lambda)$

$$\Rightarrow \quad L(\lambda) = \kappa(\lambda) \cdot \overline{P}_{\text{in}}(\lambda)$$

# *Characterization of responsivity phantoms*

**Diffuse transmittance factor $\kappa$ and**
**CW transmittance $T$**



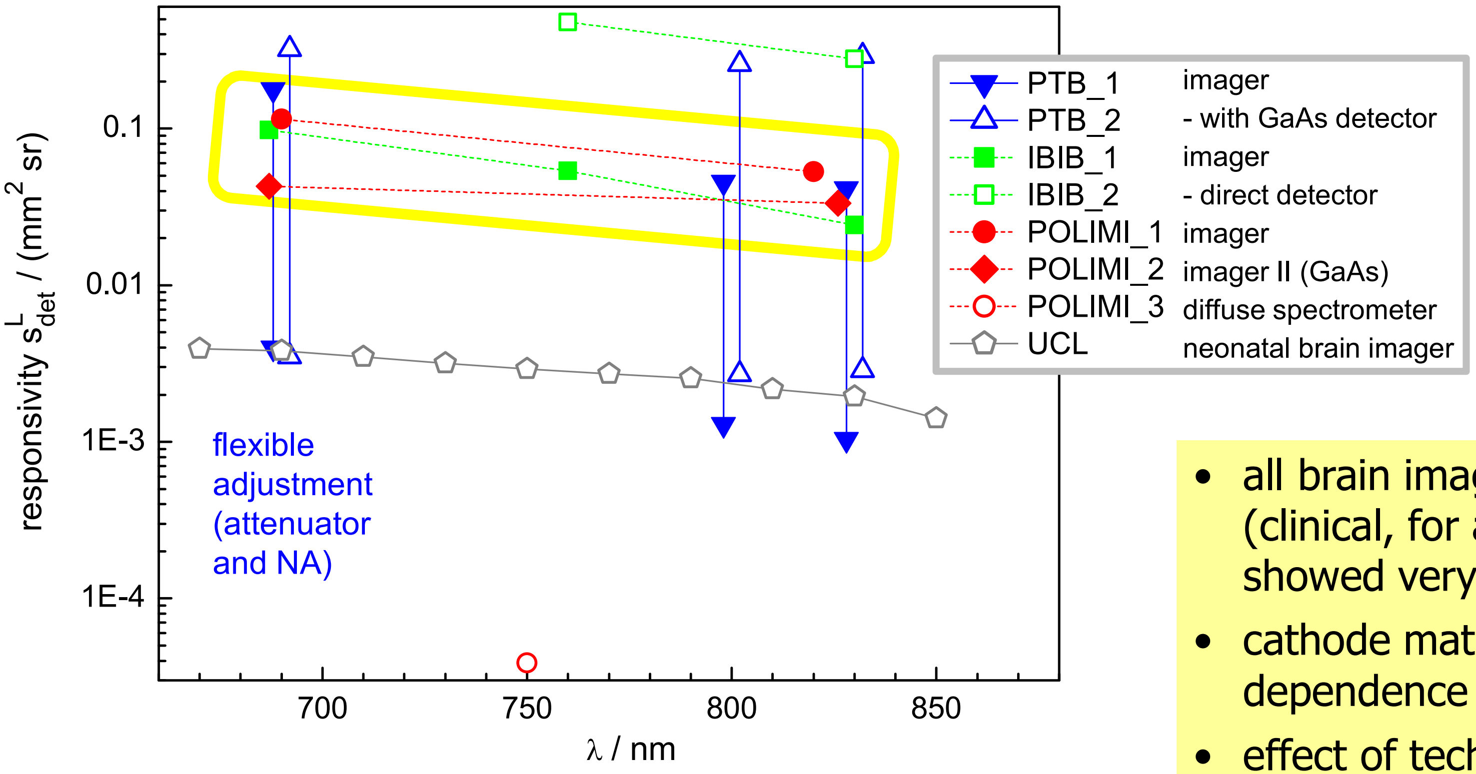


$$T\,(\lambda) = \pi\,\kappa(\lambda)$$

(radiation into full hemisphere, integrated over Lambertian angular distribution ~ cos Θ)

*H. Wabnitz et al. JBO 19 (2014), 086010 (BIP)*

# *Responsivity: Results*




*H. Wabnitz et al.*
*JBO 19 (2014), 086010 (BIP)*

- all brain imagers (clinical, for adults, with fiber bundles) showed very similar responsivities!
- cathode material → wavelength dependence
- effect of technical improvements on responsivity easily checked

# *nEUROPt protocol*

**Tests**

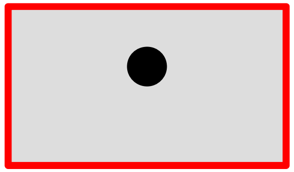
**Sensitivity**
- Contrast
- Contrast-to-noise ratio

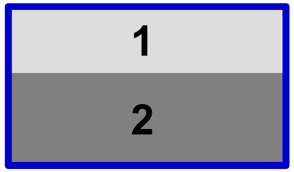
**Spatial resolution**
- Lateral spatial resolution
- Depth selectivity

**Quantification**
of absorption changes
- Accuracy
- Linearity

*H. Wabnitz et al.*
*JBO 19 (2014), 086012*
*(nEUROPt)*

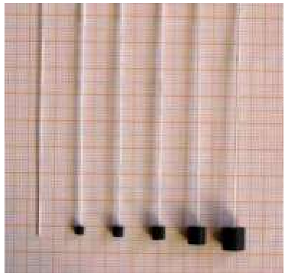
**Phantoms**

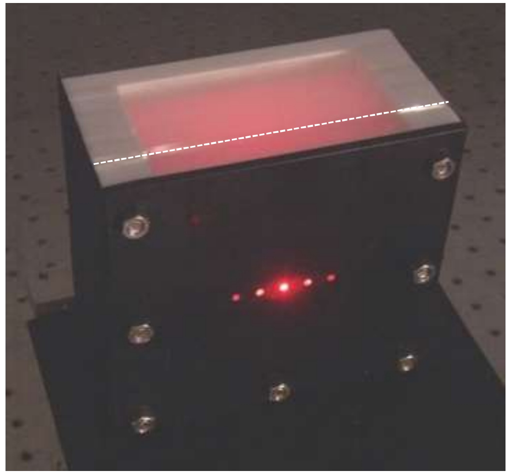




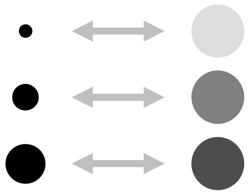

+Mylar foil

*Del Bianco et al,*
*Opt. Expr. 2004*





equivalence

size  $\Delta\mu_a$

*F. Martelli et al., JBO 2013*
*F. Martelli et al., JBO 2014*

+intralipid and pre-diluted ink accurately characterized

*P. Di Ninni et al., OE 2010*
*P. Di Ninni et al., PMB 2011*

multilaboratory (12 institutions):

*L. Spinelli et al., BOE 2014*

# *Intrinsic optical properties of Intralipid and India ink*

## Inter-laboratory comparison

$$\mu_a = \boxed{\varepsilon_{a\mathrm{ink}}}\, \rho_{\mathrm{ink}} + \mu_a^{\mathrm{BKG}}, \qquad \mu_s' = \boxed{\varepsilon_{\mathrm{sil}}}\, \rho_{\mathrm{il}}$$

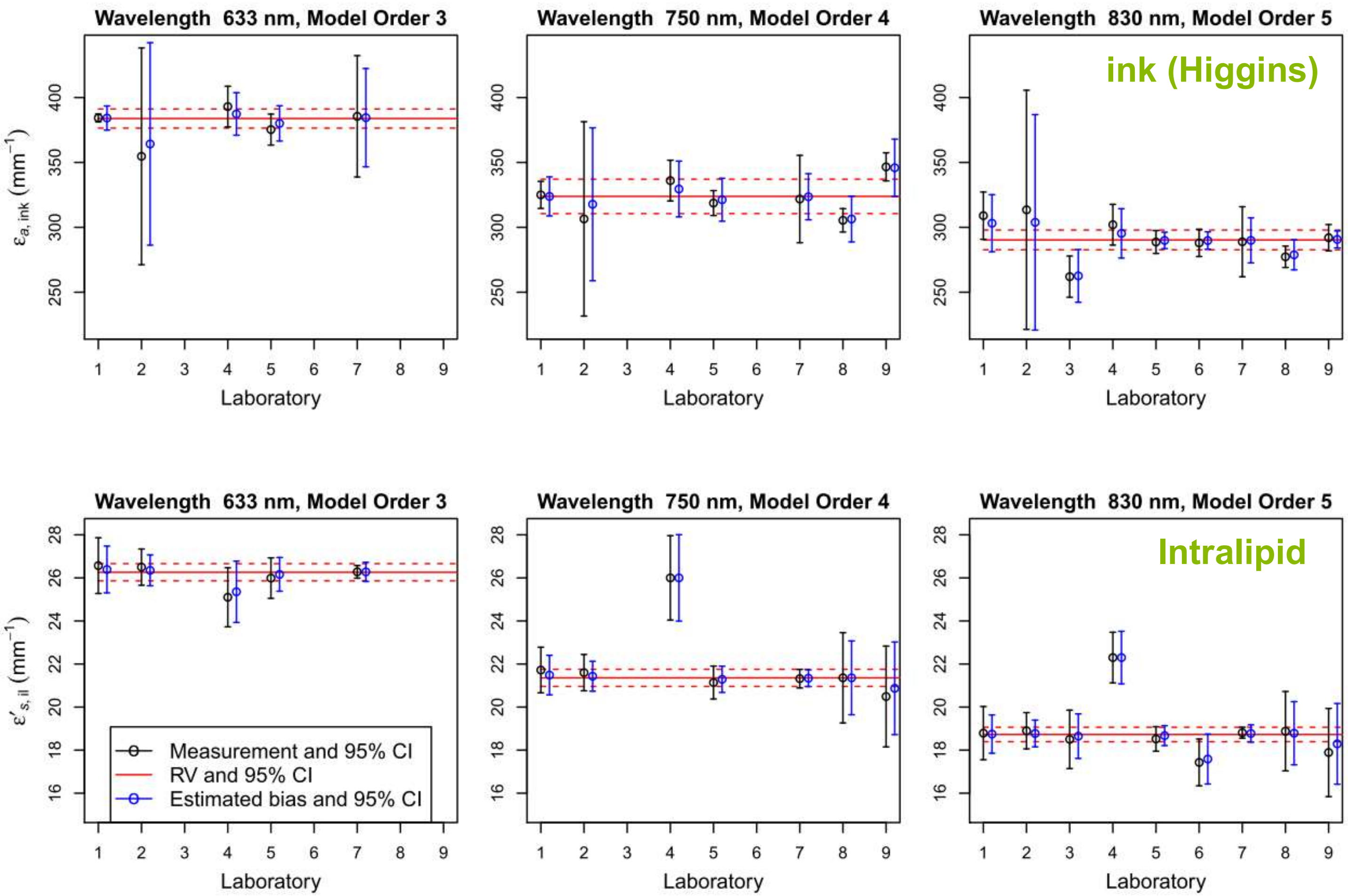
reduced scattering and absorption coefficients of dilute mixtures of Intralipid and India ink (linear regime)

$\varepsilon$... coefficients of the pure substance, $\rho$ - weight concentration

| Institution | Country | Measurement Tech. | Analysis Tech. | Wavelength (nm) |
|---|---|---|---|---|
| POLIMI | ITALY | Time Resolved | Linear method | 633, 750, 830 |
| INO | CANADA | Time Resolved | Non-linear fitting, MC RTE model | 633, 750, 830 |
| IBIB | POLAND | Time Resolved | Method of moments | 830 |
| Université de Sherbrooke | CANADA | Integrating sphere, direct method (abs only) | Inverse adding doubling, linear method (abs only) | 633, 750, 830 |
| UNIFI | ITALY | Continuous Wave | Linear method | 633, 750, 830 |
| ICFO | SPAIN | Time Resolved | Non-linear fitting, DE model | 687, 785, 830 |
| ILM | GERMANY | Spatially Resolved | Non-linear fitting, MC simulations | 633, 750, 830 |
| PTB | GERMANY | Time Resolved | Linear method | 750, 830 |
| ULUND | SWEDEN | Time Resolved | Non-linear fitting, MC simulations | 750, 830, 916 |

*L. Spinelli et al., “Determination of reference values for optical properties of liquid phantoms based on Intralipid and India ink”, Biomed. Opt. Expr. 5, 2037–2053 (2014)*

# *Intrinsic optical properties of Intralipid and India ink: Results*




**Statistical analysis** (PTB):
"fixed effects model" (accounts for inconsistency in dataset, bias)

→ uncertainty
$\leq$ 2% for $\varepsilon_{a,\text{ink}}$
< 1% for $\varepsilon_{s,\text{il}}$

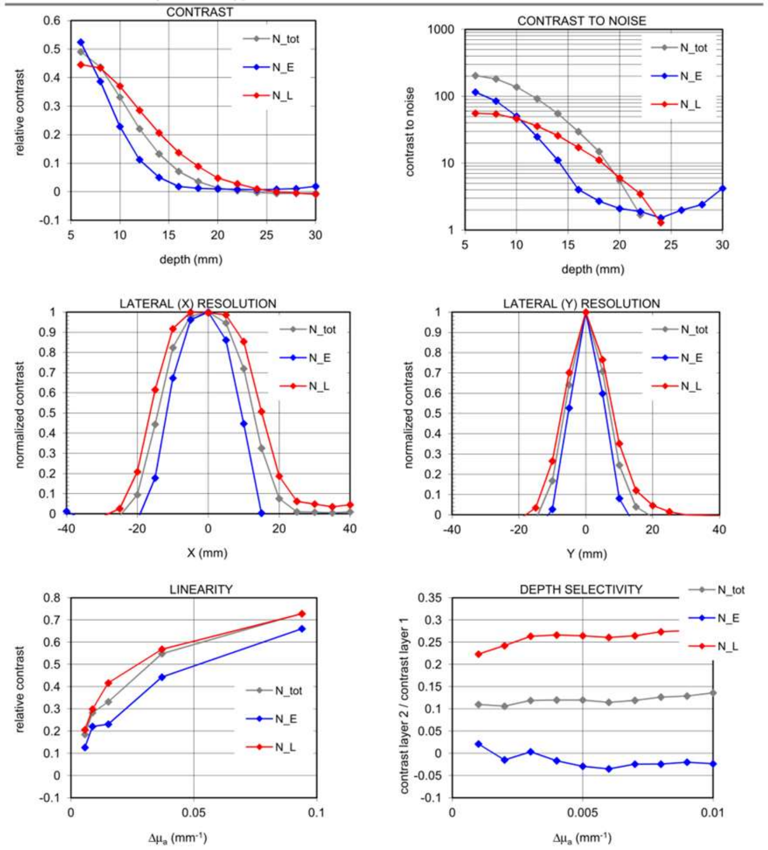
*L. Spinelli et al., BOE 2014*

# *nEUROPt protocol: Reporting sheet*

**nEUROPt PROTOCOL for Assessment of Time-Domain Optical Brain Imagers - REPORT** Ver.1.1

Group POLIMI  Setup FOXY  Name Time-Resolved Functional Oximeter  Date 30.09.11

$\lambda$ 830 nm  $\rho$ 3 cm  $\mu_a$ 0.01 mm$^{-1}$  $\mu_s'$ 1 mm$^{-1}$  $V_0$ 1000 mm$^3$  $z_0$ 10 mm  d 10 mm



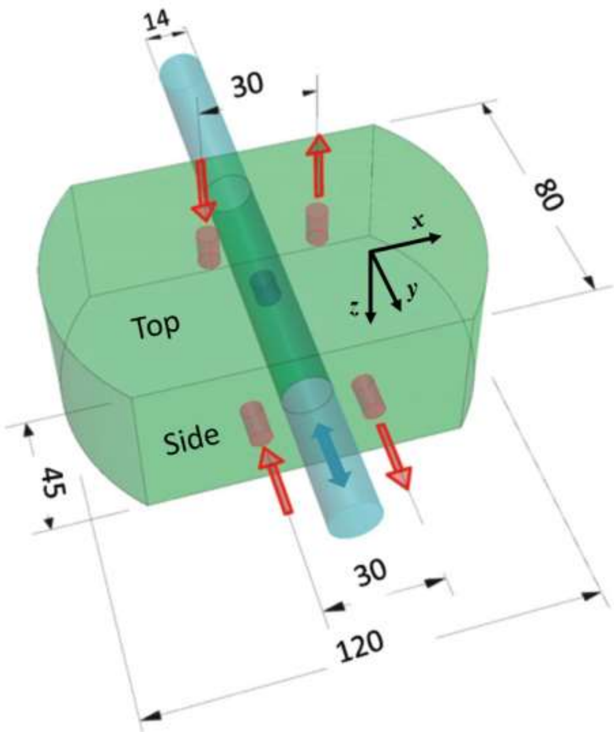

**SYNTHETIC DESCRIPTORS**

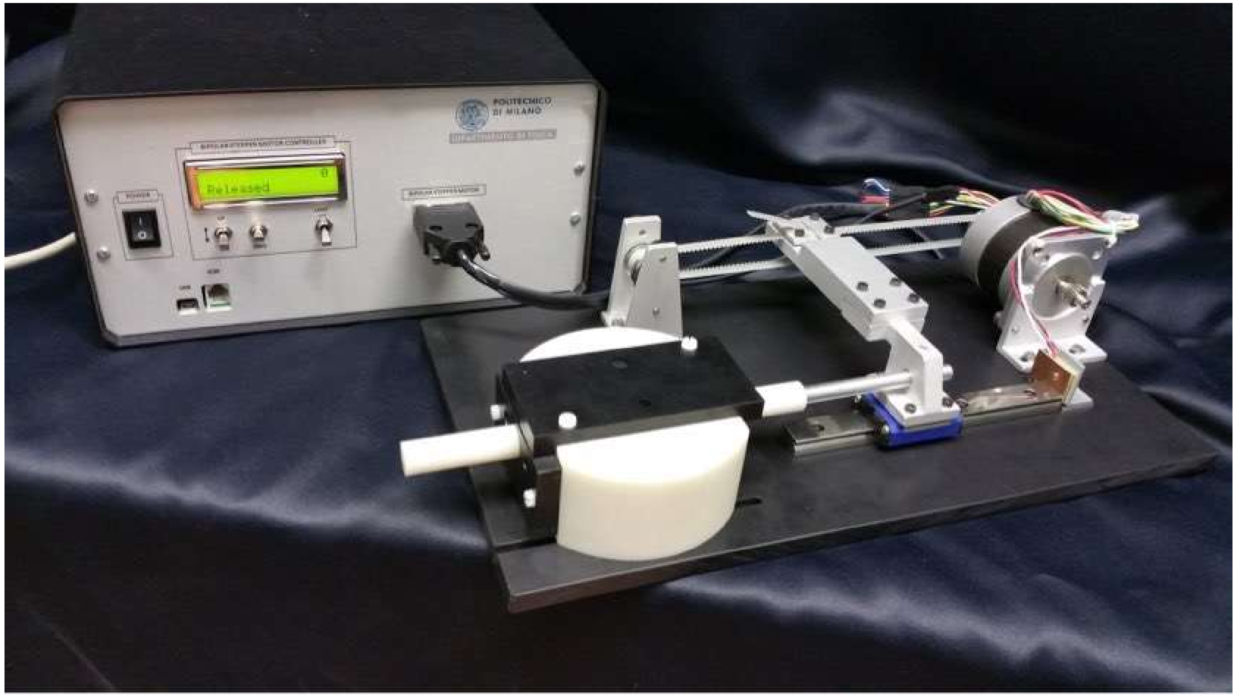
| parameter | target | unit | output | unit | N_tot | N_E | N_L |
|---|---|---|---|---|---|---|---|
| contrast | 15 | *mm* | contrast | | 10.2% | 3.4% | 17.2% |
| CNR | 10 | | z | *mm* | 19.0 | 14.3 | 18.4 |
| X-resolution | 50% | | resolution | *mm* | 27 | 21 | 32 |
| Y-resolution | 50% | | resolution | *mm* | 14 | 11 | 16 |
| depth selectivity | 0.004 | *mm*$^{-1}$ | selectivity | | 0.12 | -0.02 | 0.27 |

- consolidated presentation of results
  - contrast, contrast to noise ratio as function of depth
  - lateral spatial resolution
  - linearity
  - depth selectivity
- synthetic descriptors
- actual implementation of the nEUROPt protocol, definition of measurands, conditions for analysis and reporting

*H. Wabnitz et al., A. Pifferi, "Performance assessment of time-domain optical brain imagers, part 2: nEUROPt protocol," J. Biomed. Opt. 19 (2014), 086012*

# Switchable solid phantom



*A. Pifferi et al., "Mechanically switchable solid inhomogeneous phantom for performance tests in diffuse imaging and spectroscopy," J. Biomed. Opt. 20 (2015), 121304*

# SOLUS: diffuse optics + ultrasound phantom development

SOLUS | SMART OPTICAL AND ULTRASOUND DIAGNOSTICS OF BREAST CANCER

**Grant Agreement:** 731877
**Call identifier:** H2020-ICT-2016-1
**Topic:** ICT-29-2016 Photonics KET 2016

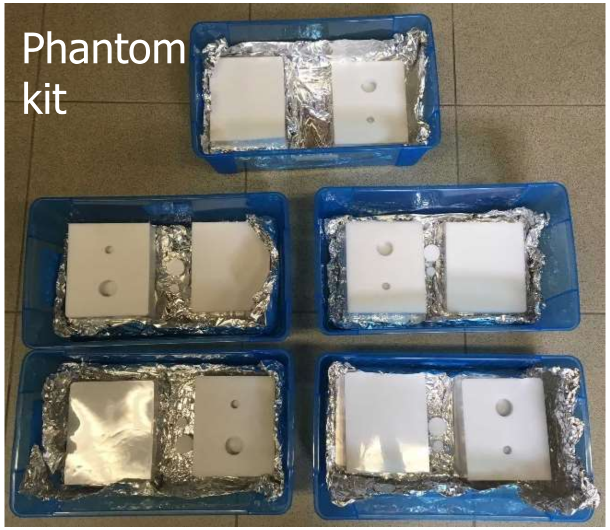
- Politecnico di Milano, Dipartimento di Fisica, Italy
- SuperSonic Imagine SA, France
- VERMON SA, France
- Ospedale San Raffaele, Italy
- Commissariat à l'énergie atomique et aux énergies alternatives, France

Contact:
alberto.dallamora@polimi.it

www.solus-project.eu/deliverables
*Deliverable 4.1: Design of multi-modal phantoms for DOT-US*

*L. Di Sieno, Proc. SPIE 11075 (2019)*

- long-lasting silicone-based phantoms
- **bulk:** new silicone material for diffuse optics and ultrasound (Ecoflex 00-30)
  **inclusions:** Sylgard 184
  (different echogenicity, same speed of sound,
  no influence of light absorbing and scattering powders on US properties)
- independent tuning of optical and acoustical properties




*Courtesy A. Dalla Mora (Politecnico di Milano)*

## Performance tests and phantoms in the ISO/IEC standards

- fNIRS
- Tissue oximetry

# *How were these international standards developed?*

| | | IEC 80601-2-71 fNIRS | ISO 80601-2-85 cerebral tissue oximeters |
|---|---|---|---|
| **NP** | new work item proposal * | **2011 (JP *)** | **2016 (US *)** |
| **WD** | working draft | | **JWG (all **)** |
| **CD** | committee draft ( *1 or more* ) | | **CD1, CD2** |
| **DIS / CDV** | draft International Standard (ISO) / committee draft for vote (IEC) | | **subm. 2019-11** |
| **FDIS** | final draft International Standard | | **2020** |
| **IS** | International Standard (published) | **2015** | |

* industry driven:
market leaders are standardization leaders

** scientific community well represented (e.g. fNIRS Society)

# *Performance tests in IEC/ISO 80601-2-71 (fNIRS)*

201.12.1.101. Performance of FUNCTIONAL NIRS EQUIPMENT

2 AVERAGE OPTICAL POWER
3 PEAK WAVELENGTH
4 FULL WIDTH AT HALF MAXIMUM of spectral distribution
5 PATHLENGTH DEPENDENT HAEMOGLOBIN CHANGE
6 Signal stability
7 RESPONSE TIME
8 *SIGNAL-TO-NOISE RATIO
9 SIGNAL CROSS-TALK

no phantom

phantom with

- large, typical attenuation between emitter and detector (turbid material)
- in addition, a means to generate attenuation change $\Delta A$

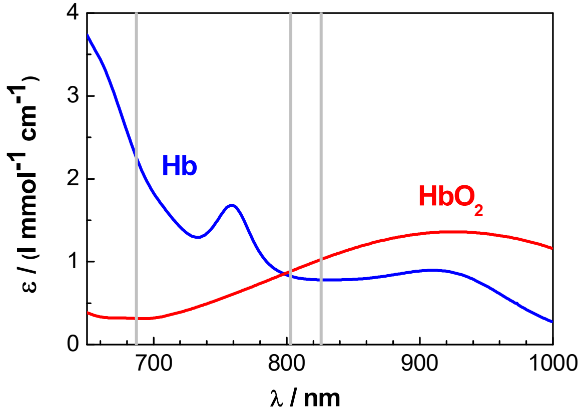
Attenuation change

$$
\begin{aligned}
-\Delta A(\lambda_i) &= \log_{10}(I_B / I_A) \\
&= \Delta\mu_a(\lambda_i) L / \log_e 10 \\
&= \varepsilon_{O_2Hb}^{(\lambda_i)} \Delta C_{O_2Hb} L + \varepsilon_{HHb}^{(\lambda_i)} \Delta C_{HHb} L
\end{aligned}
$$

$\Delta CL$ – pathlength-dependent Hb change

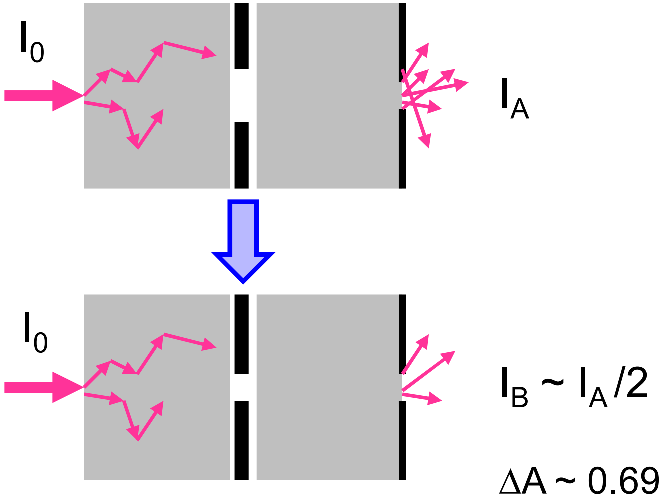
$L$ – mean optical pathlength,

assumption: $L = L(\lambda_1) = L(\lambda_2)$



# *Performance test for signal ("haemoglobin change")*

Simulation of haemoglobin change by turbid phantom with interchangeable aperture
→ specific value of intensity change




- not applicable to all-in-one probes (reflection geometry)
- CW fNIRS only

→ include elements of nEUROPt protocol in next edition?

**Procedure:**

Measure $I_B$ / $I_A$ by power meter → $\Delta A$

Calculate related signal:

$$\Delta C_{O_2Hb} L = \frac{\varepsilon_{HHb}(\lambda_2)\Delta A(\lambda_1) - \varepsilon_{HHb}(\lambda_1)\Delta A(\lambda_2)}{\varepsilon_{O_2Hb}(\lambda_1)\varepsilon_{HHb}(\lambda_2) - \varepsilon_{O_2Hb}(\lambda_2)\varepsilon_{HHb}(\lambda_1)}$$

$$\Delta C_{HHb} L = \ldots$$

concrete values depend on

- $I_B$ / $I_A$
- wavelengths $\lambda_1$, $\lambda_2$
- Hb spectra applied

**Example:**

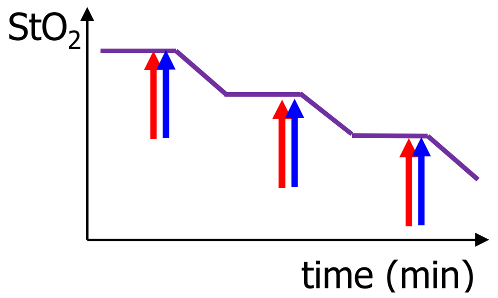
- $I_B = I_A/2$
- $\lambda_1$ = 690 nm, $\lambda_2$ = 830 nm
- spectra:
  M. Cope, PhD Thesis, London 1991

$$\Delta C_{O_2Hb} L = 204\ \mu\mathrm{M} \cdot \mathrm{cm}$$
$$\Delta C_{HHb} L = 111\ \mu\mathrm{M} \cdot \mathrm{cm}$$

# *Tissue oximeters: (Traditional) in-vivo validation*

**Controlled human desaturation study**

- breathing air with reduced $O_2$ content, stepwise decrease of arterial saturation down to 70% (→ $StO_2$ ~ 55%)
- simultaneous blood sampling form artery and jugular vein (both catheterized) → $SaO_2$, $SjvO_2$ (measured with CO-oximeter)
- ~20 healthy adult subjects




P.E. Bickler et al.,
Anesth. Analg. 117 (2013)

**Reference method:**

- no gold standard available for $StO_2$ in brain tissue
- surrogate reference saturation:

$$StO_{2,ref} = \alpha \cdot SaO_2 + (1 - \alpha) \cdot SjvO_2$$

$\alpha$ = 0.3 or 0.25

**PRO**

- representation of *in-vivo* situation including inter-subject variability
- traditionally applied and strongly advocated by major manufacturers (for most CW devices)

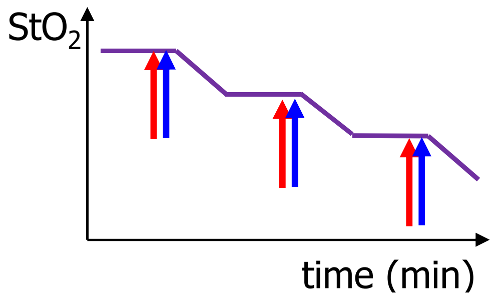
**CON**

- has not led to quantitatively comparable devices
- **ethical** concerns**!** (in a number of countries)
- healthy, adult subjects only
- limited to $StO_2$ range of ~ 55…85%
- desaturation systemic, also occurs in scalp → capability of device to selectively determine $StO_2$ in brain cannot be addressed

# *Tissue oximeters: (Traditional) in-vivo validation*

**Controlled human desaturation study**

- breathing air with reduced $O_2$ content, stepwise decrease of arterial saturation down to 70% (→ $StO_2$ ~ 55%)
- simultaneous blood sampling form artery and jugular vein (both catheterized) → $SaO_2$, $SjvO_2$ (measured with CO-oximeter)
- ~20 healthy adult subjects




P.E. Bickler et al.,
Anesth. Analg. 117 (2013)

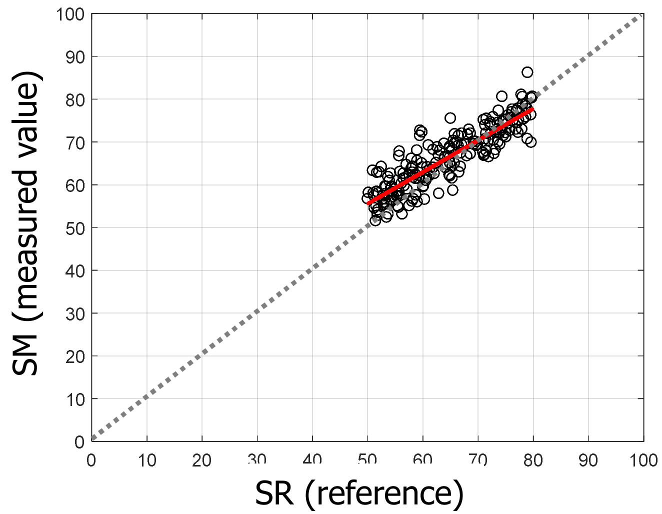
**Reference method:**

- no gold standard available for $StO_2$ in brain tissue
- surrogate reference saturation:

$$StO_{2,ref} = \alpha \cdot SaO_2 + (1 - \alpha) \cdot SjvO_2$$

$\alpha$ = 0.3 or 0.25

Result:

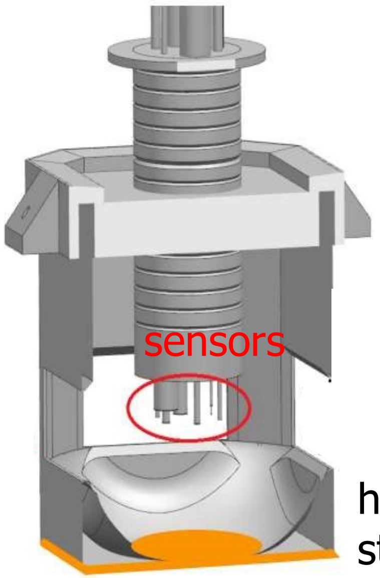



Scatter due to inter-subject variability and within-subject variation (e.g. plateau stability)

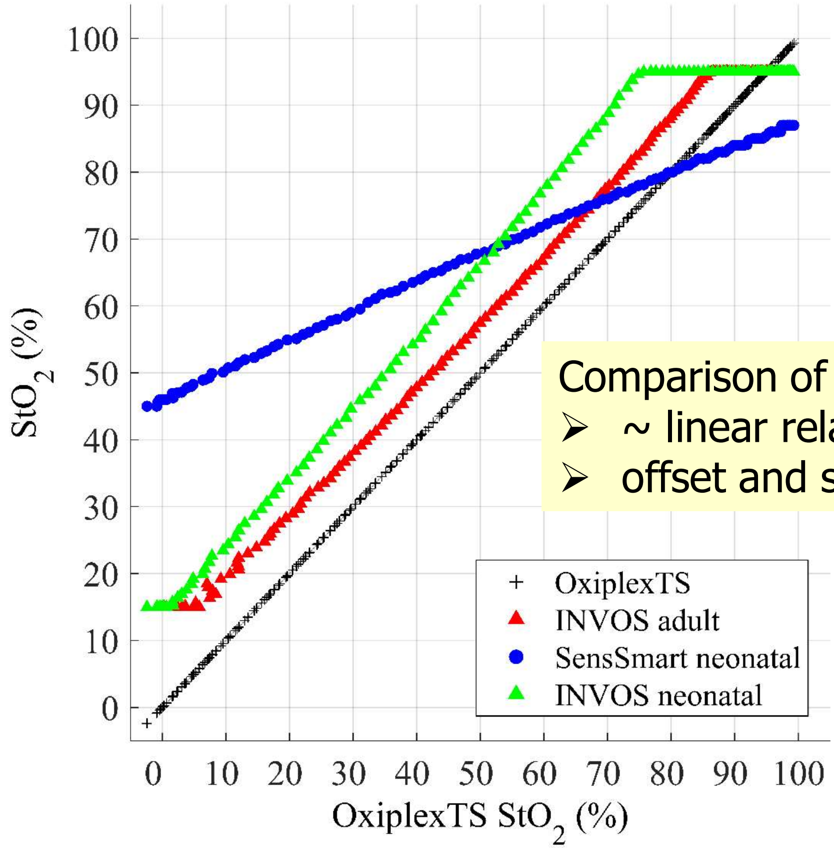
# *Alternative: Phantom-based validation*

**Homogeneous turbid liquid phantoms with Hb**

| | |
|---|---|
| scattering component: | Intralipid |
| Hb component: | human erythrocytes or blood |
| oxygenation: | $O_2$ bubbling |
| deoxygenation: | yeast |
| probe placement: | (thin) silicone “window” [1] or immersed [2] |




heater
stirrer




Comparison of equipment
- ~ linear relationship
- offset and slope

*[1] S. Kleiser et al., BOE 2016 (Zurich)*
*[2] S. Suzuki et al., Proc. SPIE 3597 (1999) (Hamamatsu)*

# *Contribution to draft standard for cerebral tissue oximeters*

- phantoms introduced in the JWG discussion (2016)
- "phantom annex" written (2018)
- strong resistance of major manufacturers
- now accepted as possible method of performance evaluation of cerebral tissue oximeters

**Annex DD**
(informative)

**Characteristics of a *tissue haemoglobin phantom* for the *verification* of the *accuracy* of *cerebral tissue oximeter equipment***

**DD.1 General**

This annex is provided as a guideline for the construction and use of phantoms that can be applied by *manufacturers* to assess the performance and, in particular, to verify the $StO_2$ *accuracy* of *cerebral tissue oximeter equipment* in a standardized and reproducible manner, without the need to perform in-vivo tests. For a detailed comparison of in-vivo and phantom-based *verification* approaches see Annex II.

Haemoglobin-containing turbid phantoms have been used by a number of research laboratories for decades, to validate equipment and algorithms in diffuse optical spectroscopy, in particular in the context of tissue oximetry [Kurth[56], Franceschini[44], Suzuki[80], Kleiser[53], Lange[58]]. Such phantom measurements have also been part of evidence for approvals of *cerebral tissue oximeters* in Europe, Japan and the US. The main component of a tissue haemoglobin phantom is a turbid liquid that contains, in particular, erythrocytes and a scattering material. The level of haemoglobin oxygen saturation in the tissue
Oxyge
Anyon
phanto

**Annex II**
(informative)

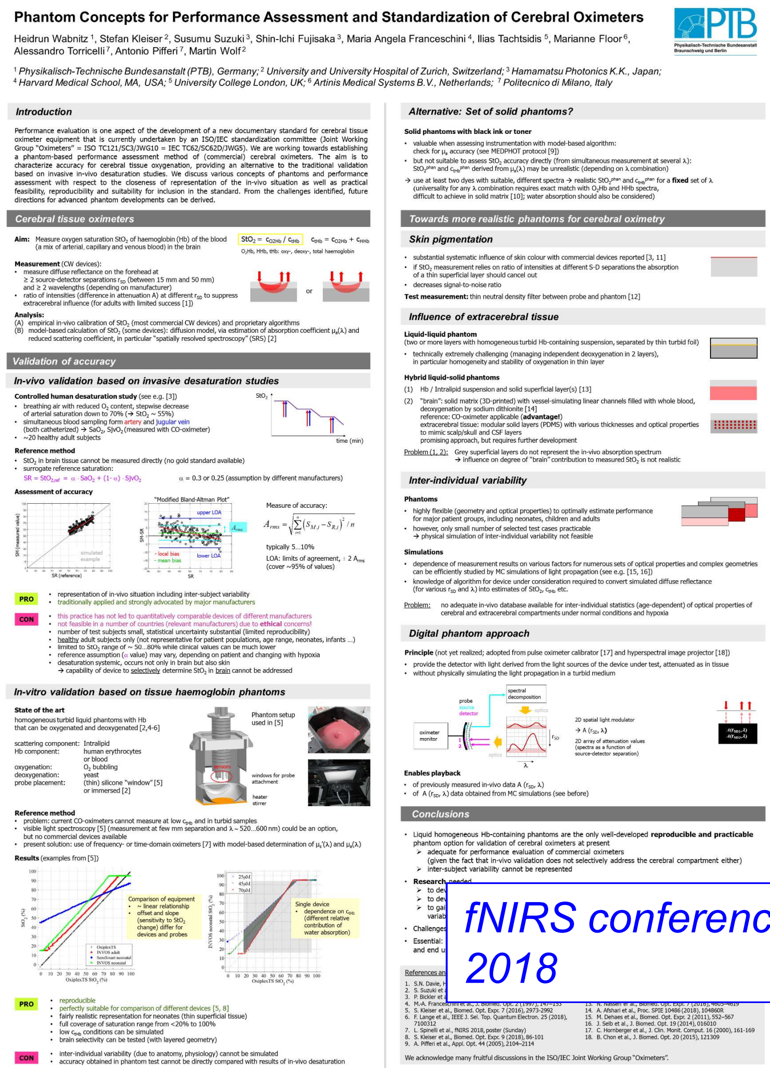
**Comparison of methods of performance evaluation**

# *Phantoms for tissue oximetry - open questions*

- How to provide an opportunity for manufacturers to gain experience with tissue hemoglobin phantoms (site, funding)?
- How to find a (commercial) provider for tissue hemoglobin phantoms?
- How to design more realistic phantoms that include
  - skin pigmentation?
  - extracerebral tissue layers?
  - inter-individual variability?
- How to obtain the necessary input parameters (optical properties $\mu_s'(\lambda)$, $\mu_a(\lambda)$ and geometry) for all relevant tissue compartments including their variability?

Promising novel approach (FDA):

*A. Afshari et al., "Cerebral oximetry performance testing with a 3D-printed vascular array phantom," BOE 10 (2019), 3731 (2019)*


Phantom Concepts for Performance Assessment and Standardization of Cerebral Oximeters

Heidrun Wabnitz [1], Stefan Kleiser [2], Susumu Suzuki [3], Shin-Ichi Fujisaka [3], Maria Angela Franceschini [4], Ilias Tachtsidis [5], Marianne Floor [6], Alessandro Torricelli [7], Antonio Pifferi [7], Martin Wolf [2]

Introduction

Cerebral tissue oximeters

Validation of accuracy

In-vivo validation based on invasive desaturation studies

In-vitro validation based on tissue haemoglobin phantoms

Alternative: Set of solid phantoms?

Towards more realistic phantoms for cerebral oximetry

Skin pigmentation

Influence of extracerebral tissue

Inter-individual variability

Digital phantom approach

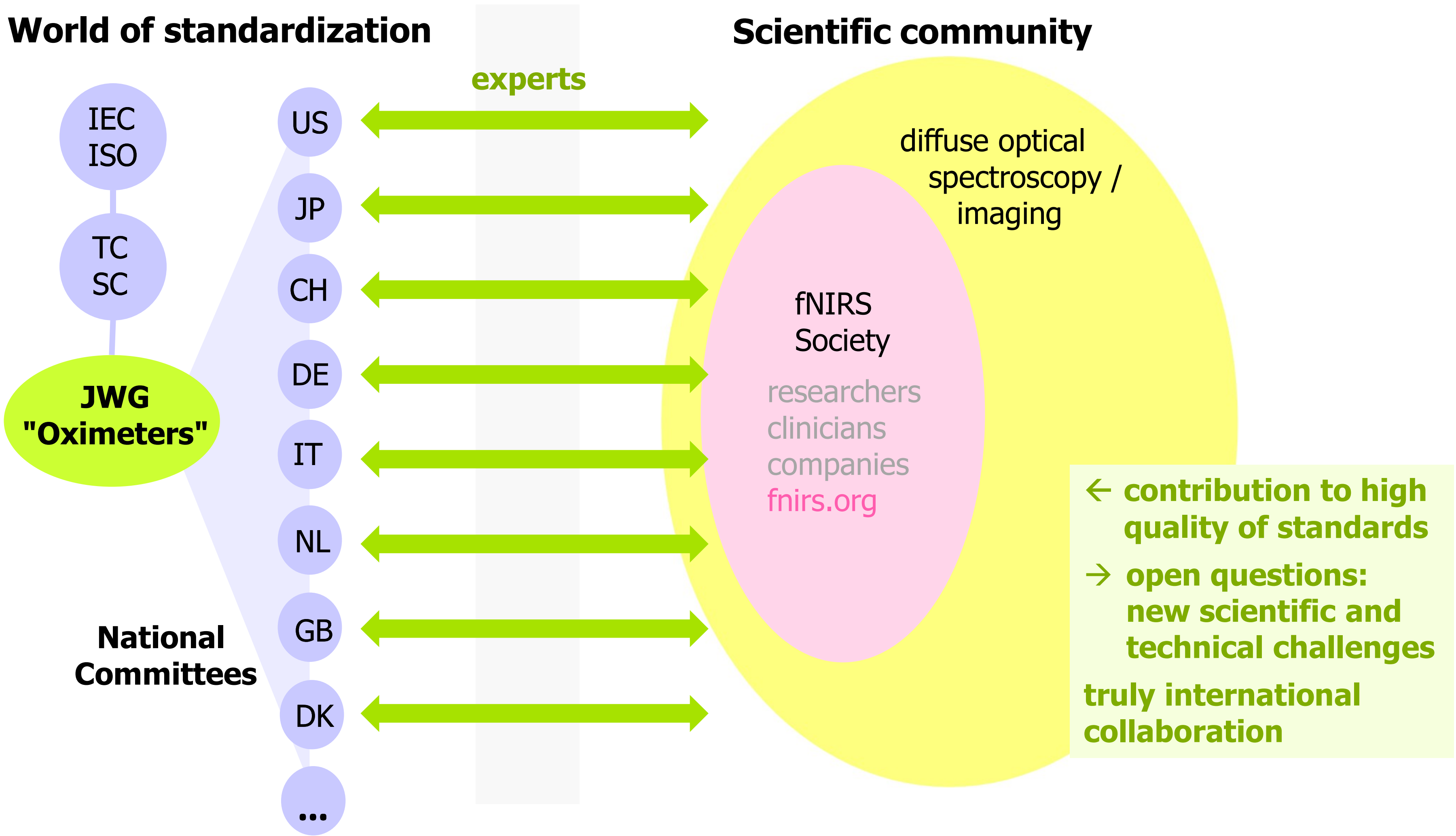
Conclusions

fNIRS conference 2018

## *Science and standardization !*

**2019**

**→ DIS Tissue oximetry**



# *Lessons learned*

**Standardization (developing new ISO/IEC standards) is not boring**

**Benefits of participation in ISO/IEC standardization**

- awareness: what is a standard, how it is developed
- valuable contribution: researchers / developers deeply understand the methodology (example: penetration depth)
- tasks for research: device technology, phantom development, simulations
- truly international collaboration: but – without funding for joint research, device comparison,…

**Are ISO/IEC standards the right place for our ambitions?**

- 60601 family (safety standards) do not cover comprehensive performance assessment
- other standard documents? - Technical Report (TR), Publicly Available Specification (PAS)
- alternatives? AAPM – Fluorescence Guided Surgery

# *Fluorescence guided surgery – AAPM* Task Group*

*B. W. Pogue, T. C. Zhu, V. Ntziachristos, K. D. Paulsen, B. C. Wilson, J. Pfefer, R. J. Nordstrom, M. Litorja, H. Wabnitz, Y. Chen, S. Gioux, B. J. Tromberg, and A. G. Yodh,*
*"Fluorescence-guided surgery and intervention — An AAPM emerging technology blue paper,"*
*Med. Phys.* ***45****, 2681–2688 (2018)*
*https://doi.org/10.1002/mp.12909*

- published documents!
- white paper in preparation

* AAPM:
American Association of Physicists in Medicine

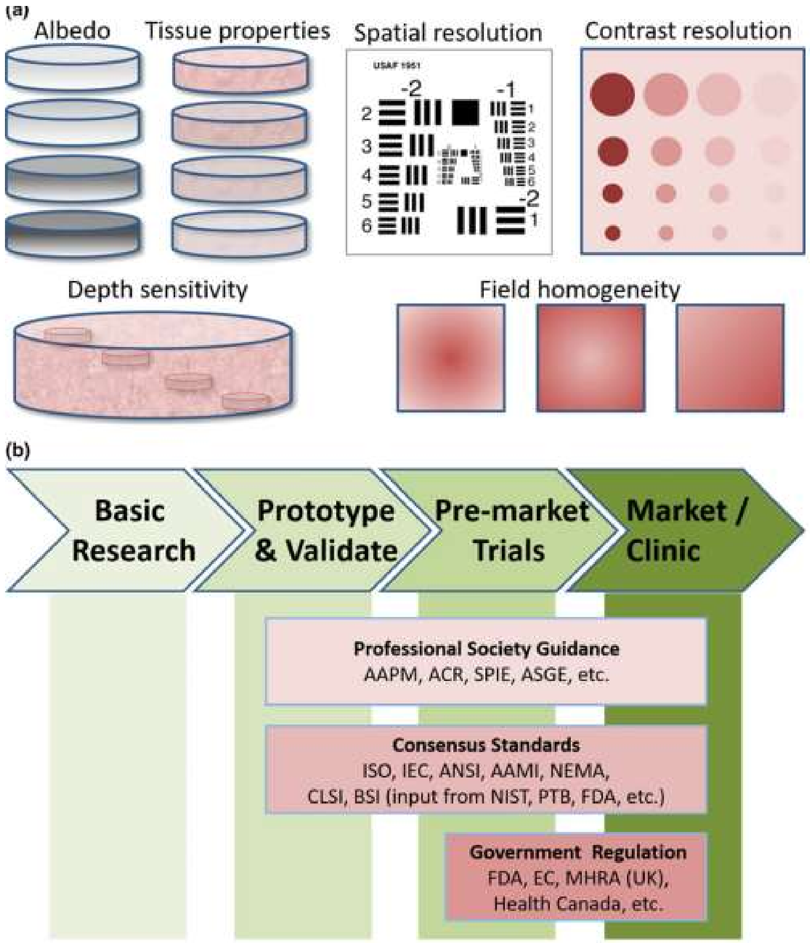



Fig. 2. The range of issues for testing are illustrated in (a) including albedo, tissue optical property performance, depth sensitivity, as well as the traditional issues of spatial and contrast resolution with field homogeneity. The relevant stages of development are listed in (b) along with the needed professional society guidance, systems standards bodies, and government regulatory bodies. [Color figure can be viewed at wileyonlinelibrary.com]

# *Save the date*

PTB

Workshops of the European Commission

Performance Assessment and Standardization in

BIOPHOTONICS

European Commission

organized by A. Pelagotti (EC),
A. Pifferi (Politecnico di Milano)

1. 2018-10-26
2. 2019-09-12
3. 2020 - ?

https://ec.europa.eu/digital-single-market/en/news/performance-assessment-and-standardization-biophotonics-back-save-date

(incl. video recordings)

SPIE BIOS – Photonics West

CONFERENCE 10870

Saturday–Sunday 2–3 February 2019 • Proceedings of SPIE Vol. 10870

**Design and Quality for Biomedical Technologies XII**

*Conference Chairs:* **Rongguang Liang,** College of Optical Sciences, The Univ. of Arizona (USA); **Jeeseong Hwang,** National Institute of Standards and Technology (USA)

*Conference Co-Chairs:* **T. Joshua Pfefer,** U.S. Food and Drug Administration (USA); **Gracie Vargas,** The Univ. of Texas Medical Branch (USA)

*Program Committee:* **David W. Allen,** National Institute of Standards and Technology (USA); **Anthony J. Durkin,** Beckman Laser Institute and Medical Clinic (USA); **Robert J. Nordstrom,** National Institutes of Health (USA); **Ramesh Raghavachari,** U.S. Food and Drug Administration (USA); **Eric J. Seibel,** Univ. of Washington (USA); **Behrouz Shabestari,** National Institutes of Health (USA); **Gracie Vargas,** The Univ. of Texas Medical Branch (USA); **Rudolf M. Verdaasdonk,** Vrije Univ. Medical Ctr. (Netherlands); **William C. Vogt,** U.S. Food and Drug Administration (USA); **Heidrun Wabnitz,** Physikalisch-Technische Bundesanstalt (Germany)

- phantoms, performance,…
- cross-sectional

# Thanks

## Performance assessment (EU project "nEUROPt")

**PTB**
A. Jelzow, M. Mazurenka, O. Steinkellner, R. Macdonald, R. Taubert

**Politecnico di Milano** (IT)
A. Pifferi, A. Torricelli, D. Contini, R. Re, L. Zucchelli, A. Farina, I. Bargigia, M. Caffini, L. Spinelli, R. Cubeddu

**U Florence** (IT)
F. Martelli, G. Zaccanti, P. Di Ninni

**IBIB Warsaw** (PL)
A. Liebert, N. Zolek, D. Milej, M. Kacprzak, P. Sawosz, R. Maniewski

**UCL** (UK)
J. Hebden, S. Magazov, R. Cooper

nEUROPt
Non-invasive imaging of brain function and disease by pulsed near infrared light

## JWG "Oximeters"

**Manufacturers**
CasMed (US) – B. Kopotic (Co-Convenor)
Hamamatsu Photonics (JP) – S. Suzuki, S. Fujisaka
Medtronic (US) – K. Buxton, D. Milkes
Nonin (US) – C. Smith
Artinis (NL) – M. Floor

**Research – technology, phantoms**
FDA (US) – J. Pfefer, S. Weininger (Secretary)
Politecnico di Milano (IT) – A. Pifferi, A. Torricelli
Univ-Spital Zürich (CH) – M. Wolf, S. Kleiser
MGH (US) – M.-A. Franceschini
UT Southwestern (US) – D. Busch
UCL (UK) – I. Tachtsidis
U Rostock (DE) – J. Kraitl, U. Timm
GPI (JP) – H. Eda (Co-Convenor)
AIST (JP) – Y. Tanikawa

**Research – clinical**
U Lübeck (DE) – M. Heringlake
Rigshospitalet Kopenhagen (DK) – G. Greisen
UCSF (US) – P. Bickler

… and many others

***Thank you!***

**Physikalisch-Technische Bundesanstalt**
**Braunschweig und Berlin**
Abbestr. 2-12
10587 Berlin

Dr. Heidrun Wabnitz
Dept. Biomedical Optics

Phone: +49 30 3481 7293
Email: heidrun.wabnitz@ptb.de
www.ptb.de

2019-11

# *Literature*

**Performance assessment in diffuse optics**

Pifferi, A., Torricelli, A., Bassi, A., Taroni, P., Cubeddu, R., Wabnitz, H., Grosenick, D., Möller, M., Macdonald, R., Swartling, J., Svensson, T., Andersson-Engels, S., van Veen, R.L.P., Sterenborg, H.J.C.M., Tualle, J.-M., Nghiem, H.L., Avrillier, S., Whelan, M., Stamm, H., 2005.
Performance assessment of photon migration instruments: the MEDPHOT protocol.
Appl. Opt. 44, 2104–2114. https://doi.org/10.1364/AO.44.002104

Wabnitz, H., Taubert, D.R., Mazurenka, M., Steinkellner, O., Jelzow, A., MacDonald, R., Milej, D., Sawosz, P., Kacprzak, M., Liebert, A., Cooper, R., Hebden, J., Pifferi, A., Farina, A., Bargigia, I., Contini, D., Caffini, M., Zucchelli, L., Spinelli, L., Cubeddu, R., Torricelli, A., 2014.
Performance assessment of time-domain optical brain imagers, part 1: Basic instrumental performance protocol.
J. Biomed. Opt. 19, 086010. https://doi.org/10.1117/1.JBO.19.8.086010

Wabnitz, H., Jelzow, A., Mazurenka, M., Steinkellner, O., Macdonald, R., Milej, D., Zolek, N., Kacprzak, M., Sawosz, P., Maniewski, R., Liebert, A., Magazov, S., Hebden, J., Martelli, F., Di Ninni, P., Zaccanti, G., Torricelli, A., Contini, D., Re, R., Zucchelli, L., Spinelli, L., Cubeddu, R., Pifferi, A., 2014.
Performance assessment of time-domain optical brain imagers, part 2: nEUROPt protocol.
J. Biomed. Opt. 19, 086012. https://doi.org/10.1117/1.JBO.19.8.086012

**Liquid phantoms**

Di Ninni, P., Martelli, F., Zaccanti, G., 2010.
The use of India ink in tissue-simulating phantoms.
Opt. Express 18, 26854. https://doi.org/10.1364/oe.18.026854

Di Ninni, P., Martelli, F., Zaccanti, G., 2011.
Intralipid: towards a diffusive reference standard for optical tissue phantoms.
Phys. Med. Biol. 56, N21–N28. https://doi.org/10.1088/0031-9155/56/2/N01

# *Literature*


Spinelli, L., Botwicz, M., Zolek, N., Kacprzak, M., Milej, D., Sawosz, P., Liebert, A., Weigel, U., Durduran, T., Foschum, F., Kienle, A., Baribeau, F., Leclair, S., Bouchard, J.-P., Noiseux, I., Gallant, P., Mermut, O., Farina, A., Pifferi, A., Torricelli, A., Cubeddu, R., Ho, H.-C., Mazurenka, M., Wabnitz, H., Klauenberg, K., Bodnar, O., Elster, C., Bénazech-Lavoué, M., Bérubé-Lauzière, Y., Lesage, F., Khoptyar, D., Subash, A.A., Andersson-Engels, S., Di Ninni, P., Martelli, F., Zaccanti, G., 2014.
Determination of reference values for optical properties of liquid phantoms based on Intralipid and India ink.
Biomed. Opt. Express 5, 2037–2053. https://doi.org/10.1364/BOE.5.002037

**Black inclusions**

Martelli, F., Pifferi, A., Contini, D., Spinelli, L., Torricelli, A., Wabnitz, H., MacDonald, R., Sassaroli, A., Zaccanti, G., 2013.
Phantoms for diffuse optical imaging based on totally absorbing objects, part 1: Basic concepts.
J. Biomed. Opt. 18, 066014. https://doi.org/10.1117/1.JBO.18.6.066014

Martelli, F., Ninni, P. Di, Zaccanti, G., Contini, D., Spinelli, L., Torricelli, A., Cubeddu, R., Wabnitz, H., Mazurenka, M., Macdonald, R., Sassaroli, A., Pifferi, A., 2014.
Phantoms for diffuse optical imaging based on totally absorbing objects, part 2: experimental implementation.
J. Biomed. Opt. 19, 076011. https://doi.org/10.1117/1.jbo.19.7.076011

Pifferi, A., Torricelli, A., Cubeddu, R., Quarto, G., Re, R., Sekar, S.K. V., Spinelli, L., Farina, A., Martelli, F., Wabnitz, H., 2015. Mechanically switchable solid inhomogeneous phantom for performance tests in diffuse imaging and spectroscopy. J. Biomed. Opt. 20, 121304. https://doi.org/10.1117/1.jbo.20.12.121304

**Tissue haemoglobin phantoms**

Suzuki, S., Takasaki, S., Ozaki, T., Kobayashi, Y., 1999.
A Tissue Oxygenation Monitor using NIR Spatially Resolved Spectroscopy.
SPIE Proc. 3597, 582–592. https://doi.org/277-786X/99

Kleiser, S., Hyttel-Sorensen, S., Greisen, G., Wolf, M., 2016.
Comparison of Near-Infrared Oximeters in a Liquid Optical Phantom with Varying Intralipid and Blood Content.
Adv. Exp. Med. Biol. 876, 413–418. https://doi.org/10.1007/978-1-4939-3023-4_52