Towards bedside monitoring at the subcellular level

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Biosensing

Biosensing is the conversion of biological processes into useful information.

Incorporating “a variety of means, including electrical, electronic, and photonic devices; biological materials (e.g., tissue, enzymes, nucleic acids, etc.) and chemical analysis”

PATIENT MONITORING

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The heart of the hospital

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Bedside monitoring

Heart rate
ECG
Arterial blood pressure
PA/wedge pressure
Central venous pressure
Respiratory rate / etCO$_2$
Arterial oxygen saturation
Body temperature
Bloodgas analysis

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Additional information

- Microbiology
- Virology
- Clinical chemistry
- Laboratory tests
- Organ specific tests
- Imaging

*BUT*: invasive and / or takes time to get results
Limitations of monitoring

- Conditio sine qua non
- No information about:
  - Microcirculatory function
  - Tissue oxygenation
  - Cellular metabolism

(a) Sphincters open

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Focus on microcirculation

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Septic Shock

Infection → Sepsis → Septic Shock

30-60% mortality

Blood pressure and cardiac output

Laser doppler / speckle / MicroScan

No direct bedside monitoring exists

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Metabolism

Oxygen

Carbohydrates

\[ \text{CO}_2 \]
\[ \text{H}_2\text{O} \]

Energy for life

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Mitochondria

- Energy producing organelles
- Destination of oxygen

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How to monitor the mitochondria?

Pulse oximetry  
O2C/NIRS

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The breakthrough ...

Mitochondrial PO2 measured by delayed fluorescence of endogenous protoporphyrin IX

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RECEIVED 14 JUNE; ACCEPTED 10 AUGUST; PUBLISHED ONLINE 23 OCTOBER 2006; DOI:10.1038/nmeth940

NATURE METHODS | VOL. 3 NO.11 | NOVEMBER 2006 | 939

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A mitochondrial oxygen sensor

MITOCHONDRIA

ALA

PpIX

Haem

PO$_2$ DEPENDENT QUENCHING

cytochrome c

haemoglobin

myoglobin


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Induction of protoporphyrin IX
Mitochondrial PO$_2$ measured by delayed fluorescence of endogenous protoporphyrin IX

Egbert G Mik$^{1,2}$, Jan Stap$^3$, Michiel Sinaasappel$^4$, Johan F Beek$^4$, Jacob A Aten$^3$, Ton G van Leeuwen$^{4,5}$ & Can Ince$^1$
Thus ...

ALA induces PpIX

PpIX localized in the mitochondria

PpIX has oxygen-dependent optical properties

**Mitochondrial oxygen sensor**
Basic implementation

Pulsed tunable laser

Fiber

Integrator

PMT

Mono-chromator

Lens

Tissue

reset

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Application on tissues

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In vivo rat liver: mitoPO$_2$ vs FiO$_2$

EG Mik et al., Biophys. J. 95: 3977-3990, 2008

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Optical biopsy

Penetration depth ≈ 500 µm
Small tissue volume
From oxygen to metabolism

Sham

$V_{\text{max}} = 4.3 \text{ mmHg s}^{-1}$
$P_{50} = 26.6 \text{ mmHg}$

CLP

$V_{\text{max}} = 3.2 \text{ mmHg s}^{-1}$
$P_{50} = 24.2 \text{ mmHg}$

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Optical bedside monitoring

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Summary

MACRO

Standard monitoring

Conditio Sine Qua Non

MICRO

Microcirculation

NANO

Subcellular / organelle

Cellular function