Future images of medical applications
A perspective for Electrical Engineering

Prof.dr.ir. Peter H.N. de With

With contributions from
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Intro: Grand developments in Health

- Demographic change in upcoming decades
  - Enormous growth of elderly people (5M in NL in 2040)
  - Elderly people require much more care
  - Health "career" of average person explodes in last 5-10 years of human life

- Saturation of population in Western world
  - At best modest growth of GDP

- Limited growth/freezing/reduction of health budgets
  - Need multiple revolutions, or scale down budget per person
Intro: Grand developments in Health

- To serve all people, we have to become factors smarter
- Need multiple revolutions, or scale down budget per person

<table>
<thead>
<tr>
<th>QUALITY of LIFE</th>
<th>COST BENEFITS</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>€1 - €10</td>
</tr>
<tr>
<td>0%</td>
<td>€100 - €1,000</td>
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</tbody>
</table>

- Healthy, active living
- Chronic disease management
- Doctor’s office
- Community clinic
- Assisted living
- Skilled nursing facility
- Specialized clinic
- Community hospital
- ICU

- PREVENTION
- HOME CARE
- RESIDENTIAL CARE
- ACUTE CARE

Intro: Developments health ICT/Electronics

- Mobile phone is crucial breakthrough
  - Smartphone is personal device
  - Increasingly personalized with apps and local settings and data
  - Communications gateway: speech, video conf., data storage

- Consumer devices in healthcare is just starting
  - Revolution of consumer electronics for health has yet not occurred (just starting)
  - Only basic devices still, heart rate, blood pressure, temperature
  - Intelligence in devices at infancy stage

- ICT infrastructure for patient comm. at immature stage
  - Market segmentation/fragmentation into multiple players / country
  - Even fragmentation within large hospitals....
  - Relatively small companies with dedicated solutions
  - Urgent need for standardization, common health frameworks
Presentation overview

• Introduction: grand developments
  • Demographics, smartphone

• Smart processing & analysis
  • New inform. extraction, learning algorithms

• Smart sensing
  • New sensing principles, materials

• Smart interventions, systems
  • Robots, computer-based systems, ultimate control

• Smart eHealth comm.: ICT applications in home care
  • Emerging personalized devices, embedded, software

Benefit of signal processing / Real case

• A real image processing case study

Early detection of cancer based on visual endoscopy

Fons vd Sommen, Sveta Zinger, Erik Schoon, Peter H.N. de With
Esophagus cancer / research questions

Goal: computer-aided detection of esophageal cancer

1. Can we develop a system that detects early cancer in Barrett’s Esophagus?
2. Can this system produce annotations that cannot be distinguished from expert annotations?

Esophagus cancer / Spectral analysis – (1)

- **Spectral analysis** of image patches
- Gabor filters have a specific scale and orientation
Esophagus cancer / Spectral analysis – (2)

- **Spectral analysis** of image patches
- Gabor filters have a specific scale and orientation
- How should we scale these filters? (*frequency*)
  - Analyse spectrum of labeled image patches:

Image annotated by medical expert

Split the image in $50 \times 50$ blocks

Esophagus cancer / Annotation system

- **Annotation system** for endoscopic images
Long-term processing view cancer detection

Detection and quantification of tumour characteristics for accurate grading and prognosis of breast cancer

Detection of small aneurysms for early diagnosis of diabetes

Detection of small aneurysms for early diagnosis of diabetes

Deep learning

Quantification of alignment error of follow-up images for evaluation of disease progression

Deep learning

Observations on smart processing case

- Digital Image processing forms a very powerful tool
  - Analysis, Modeling and Classification toolset available
- Field is still expanding: Deep Learning of features
  - Automated finding of essential information, extraction
  - Offers also possibilities for Data Mining, Data Analytics
- Bridge of 2 disciplines (DSP & Health) offers tremendous possibilities for success and help
  - Definition of useful data, properties/models for know-how
- Large gain in memorizing and objective reproduction
  - Computer is an assistant and never gets tired
  - When well developed: much faster decision making!
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Smart sensing / Real case

- A case study with smarter sensing

  Early detection of cancer based on Optical Coherence Tomography
  
  - New principle of sensing
  - New scanning
  - Explore depth of the tissue!

With
Prof.dr. J. Bergman (AMC)
Dr. W. Curvers, Dr. E. Schoon
A.F. Swager
Esoph. cancer improve: / Coming up: VLE

• Volumetric Laser Endomicroscopy (VLE)

Esoph. cancer improve: / VLE Detection

Early cancer

No cancer
Other examples smart sensing—(1)
Prostate cancer localization

M. Mischi, SPS

Modern direction: unobtrusive sensing

ExG
Accelerometry, movement
Acoustic
Optical (SpO2)

Massimo Mischi (EMG)
Chiara Rabotti (EHG)
Rik Vullings (ECG)
Pierre Cluitmans (EEG)
Ronald Aarts (all modalities)
Other examples of sensing – (2)
Pregnancy monitoring

Key pregnancy risks: premature birth; fetal oxygen deficiency.

Current monitoring techniques are unreliable and/or invasive.

Innovation: electrophysiological monitoring: uterine contractions; fetal ECG and VCG.

Other examples of sensing – (3)
Baby monitoring – Bambi belt – comfort detect.
Other example of sensing – (4)

**NeuroEngineering**

- Neurodegeneration
- Neuronal networks
  - functional
  - structural
- Neuromodulation
  - mechanisms of action
  - neurophysiological models
  - EM simulations
  - neuroplasticity

- Other example of sensing – (5)
  - Neuroactivity / brain sensing

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**Other example of sensing – (4)**

Prof. A.P. Aldenkamp, Prof. P. Boon

**Neurodegeneration**

- epilepsy
- seizures

**Neuronal networks**

- cognitive impairment

**Neuromodulation**

- TMS
- VNS
- DBS
-...

**advanced neuroimaging**

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**Other example of sensing – (5)**

**Neuroactivity / brain sensing**

- **muse™**

*Reduce stress, focus your mind and improve concentration with Muse.*

*Réduisez le stress, concentrez votre esprit et améliorez votre concentration grâce à Muse.*

**Like a heart rate monitor for your mind.**

**Change the way you respond to stress.**

**Have fun. Stay motivated. Keep improving.**

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**CES 2015**
Other example of sensing – (6)
Pressure sensing with optical fibers

- Smart sleep behavior analysis
  - Actuators for snoring stop
  - Integrated data analysis

Observations on new sensing

- New sensing principles appear and are further expanding
  - Laser, Optical Coherence Tomography, Radar
  - Narrow-band, multi-spectral, multi-modal sensing
  - Other materials: optical fiber, polymers, etc.

- Image Analysis and Visual Analytics in Health domain
  - New HQ sensors allow improved quality of detection and analysis
  - New principles allow visual modeling and visual analytics

- 3D sensing and processing is emerging
  - Advanced modeling of data, human body parts, organs

- Sensors become smaller, wearable, and go into the body
  - More precise diagnostics, use particle carriers for conditioning
  - Up to the molecular level
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Smart interventions

- A real case study with smart intervention

Detecting needles for 3D Ultrasound-guided interventions

A. Pourtaherian, Dr. E. Korsten
S. Zinger, N. Mihajlovic,
P.H.N. de With
**Needle interventions**

- In various medical procedures, *needles* are used for:
  - Taking tissue samples: biopsy (e.g. breast, liver, prostate)
  - Delivering anesthetic medicine: regional anesthesia (nerve block)
  - Delivering electric energy: radiofrequency ablations
  - Placing radioactive sources into a tumor: prostate brachytherapy

Ultrasound imaging is used to visualize needle and its tip with respect to structures inside the patient’s body.

**Proposed solution: autom. needle detect**

*Image-based needle detection in 3D ultrasound*

- No additional setup, no tracking devices (extra cost, skills…)
- No modifications of signal generation or needle
- Familiar practice with coarse placement of the transducer
- Simplify manual skills as the computer returns the best vision
Methods for needle detection

Method 1.
Based on intensity and frequency (shape) of the needle voxels in 3D

- 3D Gabor transformation for $n$ Wavelet Orientations
- Classification for Needle Voxel Extraction
- RANSAC-based Axis Estimation

Method 2.
Based on shadowing traces of the needle

Experimental results

Result with mm accuracy
Few degrees angle error

(a) PVA Cryogel
(b) Heart Phantom
(c) Chicken Breast (1.47-mm needle)
(d) Chicken Breast (0.72-mm needle)
Conclusions image-guided needle detection

- Minimum manual effort from the physician to find the needle
- Faster, easier and safer procedure
- Within a few needle iterations, physician can identify target vessel/nerve and safely proceed the needle towards the target
- **Benefit:** Only half of the anesthesia is required yielding shorter recovery time and less hospital days for the patient

Smart interventions

- A real case study with smart intervention

Robot-assisted microsurgery
Problem without solution

Lymphatic-Venous Anastomosis (Lymfoedeem)
- 25% of cancer patients
- Chronic disease
- Frequent & expensive treatment of symptoms
- Cure not possible

Direct care costs € 2 Billion/year (USA and EU)
Treatment of Lymphatic-Venous Anastomosis

Method
- Early phase of disease
- 0.3 – 0.8 mm vessels
- 1-2 cm incisions
- Directly under the skin
- Redirection of thin vessels

Cannot be treated manually
Possible cost savings 50% of € 1 Billion (USA and EU)

Solution Microsure platform

- Performance:
  - Accuracy (0.3 mm vessels)
  - Stability
  - Safety
- Fits/embeds in existing workflow
- Compatible with microscope and intervention tools
- Modular
- Affordable in purchase and maintenance cost
Demonstration of Microsure platform

Impact and multitude of applications

- Lymphatic-Venous Anastomosis (Lymfoedeem)
- Reconstructions after tumor removal
- Nerve and hand surgery
- Pediatrics
- Neurosurgery
- Others

In 5 years, 30% of all surgery is performed by robots (Reuters, 2015)
Smart interventions

- International developments

3D printing and minitaturization Labs

CES 2017 / Small low-cost 3D printer

- 3D printing becomes available for local labs
- Opens multiple applications for health
  - Body parts printing for education
  - Optimal personalized prostheses
  - Bone part replacement
CES 2017 / 3D printing

- Stockbridge robotics 3D printing
  - Facilitates advanced applications (hand prosthesis)
  - Enables normal living
Biochemical testing

• Menno Prins

in-vitro point-of-care testing

in-vivo patient monitoring

Next level:
On-body
In-body

Handheld
Small laboratory

Biochemical monitoring - devices

• Various device formats

• Non-invasive
  • Light absorption

• Minimally invasive
  • Subcutaneous probe
  • Patch on the skin
  • Mucosal analysis, e.g. eye fluid

• Invasive
  • Catheter in a blood vessel
  • Microprobe inside the body
## Medical conditions and biomarkers

<table>
<thead>
<tr>
<th>Conditions / problems</th>
<th>Relevant markers for monitoring</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes</td>
<td>glucose, insulin</td>
</tr>
<tr>
<td>Therapy management (drug level, drug effectiveness, drug resistance, compliance)</td>
<td>drug, drug metabolite, therapeutic effect, side effect</td>
</tr>
<tr>
<td>Peri-operative patient monitoring</td>
<td>coagulation, kidney function, cardiac function, intestine status</td>
</tr>
<tr>
<td>Early warning of patient deterioration in the hospital general ward</td>
<td>lactate (hypoxia), CRP (inflammation), PCT (inflammation), ( \text{CO}_2 ) (respiratory)</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>cardiac strain (BNP), cardiac damage (cTn), kidney function (urea, creatinine), electrolytes (K)</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>immunosystem, liver function, kidney function</td>
</tr>
<tr>
<td>COPD</td>
<td>inflammation</td>
</tr>
<tr>
<td>Inflammatory Bowel Disease</td>
<td>inflammation</td>
</tr>
<tr>
<td>Skin disorders (psoriasis, pressure ulcers)</td>
<td>skin inflammation, metabolic breakdown products</td>
</tr>
<tr>
<td>Obesity</td>
<td>impulsivity marker</td>
</tr>
<tr>
<td>Psychiatric disorder</td>
<td>stress marker (e.g. cortisol), neurotransmitters</td>
</tr>
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## Options for biomarkers

- **Molar scale**

<table>
<thead>
<tr>
<th>glucose</th>
<th>drugs</th>
<th>proteins</th>
<th>nucleic acids</th>
</tr>
</thead>
<tbody>
<tr>
<td>mM</td>
<td>( \mu \text{M} )</td>
<td>nM</td>
<td>pM</td>
</tr>
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</table>

New sensing techniques are needed:
- sensitive, stable, accurate
- miniaturizable

**Biosensing with single-molecule resolution**

But how??
- Particle motion
- Particle color change
Biosensing based on particle motion

Finally, single-molecule biosensors

Stochastic Protein Interactions Monitored by Hundreds of Single-Molecule Plasmonic Biosensors

Michael A. Buener, Menno W. J. Prins, and Peter Zijlstra
Observations smart interventions

- Smart interventions based on adv. Processing & models
  - Detection of instruments easing the physician
  - Leads to new protocols, less medication, lower costs (gradually)

- Robots are *in the end* more accurate / less costly
  - *New electro mechanical systems, natural action control, friendly*
  - *Can do tasks which are impossible for humans*

- 3D printing opens up a whole new world of possibilities
  - Personalized and optima solutions for patients
  - Becomes market for local hospitals and centers or even home

- Diagnostics & Interventions are enriched by biosensors
  - Measurement in the body, particle levels
  - *Up to the molecular level to measure with high accuracy*

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- *Smart eHealth comm.: ICT applications in home care*
  - Emerging personalized devices, embedded, software
BHL / Vision and Ambition - elements

Wish of Slimmer Leven 2020 Foundation
- Cooperate on large-scale implementation of eHealth to live longer, independent and vital at home, hence – >> Active healthy ageing.
- Better integration between different health process stages
- Client-oriented focus for diagnosis, care and cure
- Efficient application of know-how on prevention; for example prediction models (SW based on real data) identifying high-risc patients in a city area in 2020.
BHL / IT and Data Architecture Vision

personal health platform

PHILIPS APPLICATIONS
3rd PARTY APPLICATIONS

ICT infrastructure architecture – cont. care

ICT architecture
Health APPS: Personal health systems

Virtual doctor
- Feedback/actuation
- Diagnostic inference
- Signal processing/decision support
- Remote doctor

Patient

Sensors

Home sleep monitoring PHILIPS
Remote pregnancy management

Home screening for atrial fibrillation PHILIPS

Wearable phone app with integrated monitoring
- Data analysis, fall incident alerting, GPS location
- Ear thermo
- Blood press.

CES 2017 / Philips personal health monitor
CES 2017 / Pregnant woman health analysis

Advanced breathing analysis device (Breezing)
- Multiple – chip diagnostics

CES 2015+2017 / Robots for home care

Android – based robots for personal communication and simple tasks
Example App: Sensing for home training

- Video-based sensing for heart rehabilitation training

Final conclusions / statements – (1)

- Towards personalized treatment, medication, care
  - Advanced data analysis and prediction models

- Sensing/sensors at distant, on-body and in-body
  - Many add-on sensors and related processing for standard platforms
  - New sensors on diverse materials and principles
  - Biosensors have great future for in-body diagnostics and intervention

- Robots will perform many standard surgery tasks
  - More accurate, reproducible results, will save costs in the end

- Personalized prostheses
  - Personalized and optimal per patient

- Advanced DSP analysis for replacing complicated actions
Final conclusions / statements – (2)

- Growth of standardized SW infrastructure
  - Advanced data analysis and prediction models
  - Supports personalized treatment, better participation

- Development of structured databases and data analysis
  - Per disease and contextual data (co-morbidities)
  - Also treatment process analysis or other processes in care/cure

- Explosion of Apps and devices supporting home care
  - Also integrating into smart home
  - Unobtrusive, low cost, large scale, consumer devices
  - Robot-supported actions, training, rehabilitation, etc.

- Good cooperation with physicians
  - Leads to certified local solution and enhances quality