Medical electronic devices: present and future system and chip requirements

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Active electronic devices for medical use

1. Large medical devices

MRI scanner, X-Ray tool, dialysis apparatus,...

2. <u>Medium to small medical devices: portable – table top devices</u>

- In direct contact with people, often portable but not very small: ie. blood pressure, oxygen saturation in blood, clinical EEG recording,...
- Not in direct contact with people but with collected body tissue or fluid: diagnostic tools for bio- or chemical analysis, lab-on-chip systems

3. <u>Miniaturized medical devices: wearable – implantable devices</u>

- ie. pacemaker, cochlear implant, active drug delivery device
- ie. smart contact lens, active drug delivery device piercing through skin, smart camera-pill (digestive track)
- ie. small ECG monitor (chest band or patch, NOT the wrist bands!)



skin

Patient safety (correct device functioning)



skin

Patient safety (correct device functioning)



skin

Patient safety (correct device functioning)



Requirements for the final medical electronic device (no requirements for each component)

- **Functional requirements** of the device (basic functionality): examples
 - sensor: required sensitivity and specificity
 - computational unit: speed, computational power, low energy consumption
 - telemetry: wireless device needs transmission of signals and energy,...
- Environmental requirements, esp. for wearable devices and implants
 - biocompatibility
 - biostability
 - no biofouling (esp. problem for sensors)
 - limited device heating (power consumption)
 - material resorption (if required)
 - suitable sterilization technique for all device components and materials
 - also requirements related to transport (temp., shock,..)
- Specific requirements for superior device performance:
 - miniaturization: esp. for implants
 - flexible/ stretchable device
- <u>Risk assessment based requirements</u>
 - for life-saving devices: redundancy for essential parts (hardware, software)
 - strongly dependent on individual device

Strongly dependent

on type and duration

of contact between

device and body

Outline

- Introduction
 - types of medical electronic devices
 - always smarter devices
 - specific requirements for medical electronics
- medical electronics: future trends and related issues
 - 'Big data' issues
 - device miniaturization
 - biocompatibility and biostability
 - device powering
- what is a medical device?
- conclusions

Big data issues

Some medical applications need lots of data – some examples:

large medical imaging tools
 acquire a lot of 2D information
 → calculation needed to obtain 3D information



 Lab-on-chip technology enables huge amount of 'parallel processing', Lot of information simultaneously available, often visual information (pictures of cell culture,..). Image comparison is often needed.
 A interpretation of data by computer is essential.

 \rightarrow interpretation of data by computer is essential.

- Wearable devices produce a lot of information for doctor / hospital
 → Automatically sorting of incoming data is needed. Medical staff has to look
 only at data highlighted by computers.
- Surgery assisted by superior imaging possibilities.
 → During surgery: superior interpretation of tissue possible by dedicated imaging tools and high performant image processing techniques

Big data issues

- Need for huge calculation power
- Need for high performant GPU's (GPU : Graphical Processing Unit)
- Need for huge memory capacity combined with fast data access
- Realization: optimized combination of hardware and software

Hardware:

- fast chips with huge calculation power
- If possible: fast chip enabling data processing should have sufficient memory on chip
- Big memory chips with very efficient access, ie. by stacking of logic and memory chips to allow for fast data transport

Software:

- realize very efficient parallel processing of all CPU's (in one computer) and of various computers
- Realize efficient data /signal transport

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Trends for electronic implants

Always smarter device, more functionality



Device miniaturization

- Minimal invasive surgery
- Smaller FBR, less infection risk
- Small implantation site possible (retinal implant, sensing electrode in nerve,..)



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Built-up of pacemaker



Most recent pacemakers (FDA approval in spring 2016)



Result of excellent system engineering

- Small battery (120mAh) + ultra low power device
- Smart electronics integration
- Metal housing is also electrode and antenna
- no traditional welding of Ti housing

Replaces only the single lead pacemakers

Micra: 6.7mm diameter 25.9mm long 1.75grams 1.5T and 3T MRI compatible

120mAh battery Very low power electronics

Technology requests for small medical devices

Typical electronic circuit of wearable / implantable system:



Communication with doctor, hospital using external device (smart phone, laptop,..)

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Sensing of bio-signals: signal frequency is low!!

- Bio-signals (electrical, chemical, pressure, ..) are varying slow in comparison with the speed of signals in advanced CMOS
- Highest speed: EMG signals frequency below 5 kHz (EMG: electrical signals driving muscle movements)



- No need for fast sensor read-out, no need for fast CMOS
- Advanced CMOS is even disadvantageous:
 - Higher power consumption (due to higher gate leakage current)
 - More noise (gain/Id is lower)
 - Matching (between transistors) is less good

Technology requests for small medical devices

Typical electronic circuit of wearable / implantable system:



PMU & AFE (yellow): no need for fast signal processing

- → No gain with CMOS scaling !
- \rightarrow Scaling will result in higher power consumption and more noise

DBE & Radio & MEM (blue): fast signal processing is better
→ CMOS scaling is requested

Technology requests for small medical devices

Typical electronic circuit of wearable / implantable system:



Traditional: 5 different chips

Now: request for miniaturization:

- \rightarrow integrate various chips into 1 chip (not ideal regarding power, noise,..)
- → Combine 2 technologies: 1 chip using 'older' CMOS technology 1 chip using advanced technology
- \rightarrow Use multiple chips and smart integration (ie. stacking)

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Tissue / body and implant interact with each other

Implant → tissue: implant should be <u>hermetic and biocompatible</u>:

- No diffusion of toxic materials towards tissue
- Mild tissue reaction upon implantation
 Organism will always react towards implanted material (foreign body reaction (FBR))
- tissue → implant: implant should be <u>hermetic and biostable</u>

prevention of:

- leaching of body fluids/ into implant
- chemical degradation i.e. oxidation (super-oxides during FBR!)
- Adverse response to mechanical stress (i.e. wear, fatigue)
- These issues have to be addressed by the system package, not by the individual components



Biocompatibility and biostability of standard CMOS chips to be used in implants?

- Various conventional materials used in chips are not biocompatible (ie. Cu)
- Several materials used in chips are not biostable, they dissolve or corrode in (certain) biofluids (ie. Cu, TiW, W,..)
- Conventional passivation materials (SiO₂, Si₂N₃) are slowly dissolving in (certain) biofluids
- Ideal biocompatible metallization of an implantable device consist of platinum and gold, which are not welcome in a cleanroom

Conventional chip processing does not result in biocompatoble chips!

On top of this: also common assembly materials for electronic components are not suitable for implantation (material chemistry + quantity) !!

Most often not the components but the total device is encapsulated

- All materials in direct contact with tissue should be biocompatible & biostable
- The device encapsulation should act as a bi-directional diffusion barrier

Biocompatibility and biostability of electronic implants by encapsulation

- Conventional Ti housing → rather large encapsulation
- Ti housing but with adjusted welding technique for hermetic closure (most recent pacemakers)
- Glass encapsulation
 → can be small but is
 less shock resistant



 Polymer based encapsulation flexible encapsulation, needs

extra barrier layers (ie. ALD) for hermeticity.

(currently used for neural sensors, smart contact lenses)





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Miniaturization by smart electronic integration developments ongoing @ CMST (ultrathin flexible packages)

Length = 15.38 µm

Length = 15.85 µm

Length = 18.46 µm

Si die

<u>UltraThin Chip Package (UTCP) for wearable devices</u>

- \succ Off-the-shelf dies, thinned down to \pm 30 μm
- thin die packaged between two polyimide foils
- Cu metallisation for fan-out

'UTCP' :

- Flexible package
- Thin : 50-70 µm

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- <u>Currently under development :</u> <u>Flexible Implantable Thin Electronic Package (FITEP):</u>
- \succ conventional processed dies thinned down to \pm 30 μm
- die packaged between a stack of biocompatible polyimide and ALD layers as bidirectional diffusion barriers
- Metallisation made from platinum and gold

Note: dedicated package adjustments needed for each specific device



Thin Si die

Polyimide 2

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Powering a wearable / implantable medical device

Providing sufficient power for a wearable/ implantable device is a concern: batteries are too big and heavy

reduction in power consumption of the device is essential

Especially for implants:

- changing batteries is not possible without surgery
- charging a rechargeable battery is often not easy (tissue absorption)
- power consumption → heating: tissue heating of 1 to 2°C is not allowed



Powering the active implant

 Implant contains primary batteries (non-rechargeable)



 Remote powering: rechargeable batteries and antenna
 > similar techniques as used for telemetry

 Internal energy harvesting: energy is harvested from energy sources in the body

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What is a medical device?

A **medical device** is any instrument (apparatus, appliance, software, material, or other article) intended to be used for humans for the purpose of:

- Diagnosis, prevention, monitoring, treatment, or alleviation of disease
- Diagnosis, monitoring, treatment, alleviation, or compensation for an injury or handicap
- Investigation, replacement, or modification of the anatomy or of a physiological process
- Control of conception

Important influence on wellness and health of people Device is controlled by national health authority

Are all devices related to wellness and health 'medical devices' ?

- NO ! Device needs to be registered as medical device, hence approval of legal authority is essential (eg. FDA, EU: notified bodies – EU label)
- Clear difference between medical market (medical device)
 'wellness & health' market (consumer product)
- > For same application: both types of devices can exist (ie. heart beat monitoring)

Regulatory path for a medical product (1)

For all medical devices:

Official approval required before introduction on the market (so-called 'regulatory path') based on risk assessment, to ensure patient safety



This approval process varies between countries!

FDA certification (USA) EMEA - CE label (Whole Europe) INMETRO certification (Brazil) etc... JPAL Quality system Certification (Japan) Health Canada SFDA (Saudi Food and Drug administration)

Currently: trend for international harmonization of this regularization

approval process is country dependent but tests to prove biosafety, device functionality, reliability etc. : often international standards

Rules for approval are constantly under discussion and changing.
 In Europe: lots of questions regarding patient safety due to PIP scandal
 MDD (medical device directive) will be replaced by MDR (medical device regulation), with stricter rules (regarding ie. proof of clinical evidence before market introduction, post market follow-up, ..)

Regulatory path for a medical product (2)

Official approval required before introduction on the market:

- a lot of testing required regarding device functionality / safety / reliability / life time tests. Tests strongly depends on individual device.
- > Some test protocols for medical devices exist \rightarrow 'guidelines'
- other test standards are 'borrowed' from 'High Rel' applications (military, space, automotive). (Rel = reliability)

Medical device manufacturer: - develops suitable test protocols, - explains rationale to regulatory people

Example: reliability testing based on thermal cycling tests: long term cycling between -50°C and + 400°C → not very relevant for an implanted electronic device





Device development including approval process

Suppose development of an entirely new electronic device (e.g. implant)

Start: concept of a solution to a medical problem

Fabrication of preliminary prototype, initiation of patent process

preliminary bench testing and animal testing

device enters a cycle of testing and redesign that typically takes several years and costs between 10 and 20 million Euro.

- Preclinical trial
- Clinical trial

Approval process for all relevant countries (EU-notified bodies, FDA,...)

Introduction into medical market, Follow up on devices FDA / EU / ... follow up

Total medical device development process: slow and expensive

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Conclusions

- No well-defined specific requirements exist for chips to be used in medical electronic devices.
- A myriad of medical device requirements exists, strongly depending on the particular medical device and its intended use.
- Future medical electronics need a solution for handling 'Big Data': huge computation power and fast accessible big memories are essential. An optimized combination of dedicated software and hardware will be essential.
- Most important current and future issues for wearable and implantable electronics are related with device miniaturization, biocompatibility and biostability, low power consumption and efficient energy & signal transfer.
- Not the subcomponents but the total medical device itself is strongly controlled before it can be introduced on the market, as well as during later usage, in order to ensure device reliability and patient safety.

This control process makes medical device development slow and expensive.

Thank you !

