EPoSS MedTech Working Group position paper on Healthcare

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**Definition**: Personalized medicine is a young but rapidly advancing field of healthcare that is informed by each person's unique clinical, genetic, genomic, and environmental information. Because these factors are different for every person, the nature of diseases (onset, their course, and how they might respond to drugs or other interventions) is as individual as the people who have them.

- **Multi criteria and multimodal diagnosis**
- **Narrow disease definition**
- **Personalized treatments**
  - Drugs
    - Specific appropriate treatment
    - Specific therapy regimen
  - Medical devices
    - Implantable & adjusted & parameterized
    - Active and regulated local therapy

**Medicine**
- Disease specific

**Personalized Medicine**
- Target specific combinations of diseases
Personalized Medicine

- New and Future Impact: Personalized Medicine is playing a Growing Role in Biopharmaceutical and Medical Devices development
  - 94% biopharmaceutical said that
    - they are investing in personalized medicine
    - See 75% increase in personalized medicine Investment
    - Personalized medicine is changing the way they do research in new medicines and increasing partnership with the external organization
  
- Survey performed by Tufts center for the Study of Drug Development (Tufts University in Boston, Massachusetts) - 2010
Personalized Medicine

- Biomarkers mostly measured in serum, plasma, urine
  - BONE DISEASE >7
  - CARDIOVASCULAR >26
  - CNS >13
  - DIABETE >5
  - GI DISEASE >7
  - HEMATOLOGY >1
  - INFLAMMATION >27
  - MEN'S HEALTH >10
  - NEPHROPATHY >5
  - THYROIDE >8
  - WOMEN's HEALTH >28
- ONCOLOGY
  - 1261 candidates
  - 9 FDA approved cancer biomarkers
Personalized Medicine

- Needs

  Narrow
  - Connected smart healthcare system:
    - In vitro Lab-on-Chip, Multiplexing markers diagnosis
      - DNA, Transcriptome, RNA, peptide
      - Biomarkers, Biology, others
    - In vivo & Implantable & multiplex diagnostic
      - Continuous & in time
      - biomarkers, biology, hemodynamic, pH
    - Standalone, wearable or implanted sensors
    - Remote monitoring with automated follow up

  Personalized
  - Automated alerts: go to physician
  - Active implantable MD
    - Individualized
    - In time adaptive
  - In vitro/vivo automated personalized drug delivery system

- Technology offers

- Unmet needs

- New & emerging technology
Personalized Medicine

- **Unmet needs**

**High sensitivity / specificity / mass production**

- **In vitro**
  - Multiplex PoC IDV
    - Biomarker multiplexing > 10
    - Easy sample preparation
    - High practicability / no final user maintenance
    - At once and easily interpretable multiplex results
    - Turn around PoC testing < 2 to 5 mn

- **In vivo**
  - In vivo implantable diagnosis sensors
    - Multiplex/combined biomarkers/sensors
    - Long term efficiency/performance > 6 years
    - 100% biocompatibility
  - Active implantable MD
    - Idem + in time adaptative functions
  - Micro/nano controlled/adaptative drug delivery system

**Blood:**
- Not serum, plasma

**Sensitivity:**
- Troponin I
  - Myocardial infarction
  - 0.1µg/l
- B-type natriuretic peptide
  - Congestive heart fail
  - 8pg/ml

**Specificity:**
- Multiple biomarkers
- Clinical studies

**Mass use:**
- Wearable
- Easy to use
- Low cost
- Ideally Reimbursed
Personalized Medicine

- New emerging technology: wireless universal smart drug-delivery

- Conventional drug delivery techniques: pills and injections
  - often not suitable:
    - for new protein-based, DNA-based or other therapeutic compounds
    - for personalized medicine
- Alternative: using the skin as alternative route for administering systematically active drugs
  - advantages of transdermal (across skin) drug delivery:
    - absence of degradation in the gastrointestinal tract and of firstpass
    - effects in the liver (oral drug delivery) + elimination of pain and inconvenience of intravenous injections
- MEMS-based drug delivery:
  - regulation of drug doses to be adapted based on physical activity, food ingestion, circadian rhythms -> exm: insulin delivery
  - lower risk of infections
  - lower non-uniformity and better localization
Personalized medicine delivered by implanted devices is exploding

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**Neurostimulation applications**

- Motor cortex recording
- Basal ganglia stimulation
- Diaphragm stimulation
- Sacral roots stimulation for urologic applications
- Paralyzed muscles functional electro-stimulation
- Nerve signal recording for sensitive feedback
- Visual cortex stimulation
- Cochlear implants
- Vagus nerve stimulation (epilepsy)
- Spinal cord stimulation (chronic pain)
- Electromyogram recording for artificial hand control
- Limb amputation
- Nerve impairment
- Implanted patients in Europe

**NeuroStimulation devices are treating an increasing number of pathologies:**

- Chronic pain
- Epilepsy
- Parkinson’s disease
- Depression, behavior disorder
- Vision deficiency
- Deafness
- Obesity
- Urologic disorder, incontinence
- Hypertension
- Cardiac arrhythmia …
Personalized medicine delivered by implanted devices is exploding but still …

- **New emerging technology:**
  - **Source of energy:**
    - Today limiting factor for longevity and size of implants
      - Numerous surgery for battery replacement or patient uncomfortable long intervention to charge the battery
    - Small size efficient and durable implanted energy scavengers
    - Batteries increase energy density, thin film batteries
    - Biofuel cells like glucose
      - Many applications like obesity…
    - New ways to have a long range of power transmission go beside inductive limited range
    - Applicable also to wearable microsystems for healthcare
Personalized Medicine

Emerging: mass remote monitoring / follow up

Current for AIMD

- Patient
- Home Monitor
- Back-office
- Web Application
- Physician & Helpdesk

**Future**
- Home monitor
  - Multiple usage
  - Wearable and wireless
  - Large autonomy
  - Smart phone / mobile phone accessory
  - Low cost
- Automated back-office, huge amount of data
Minimal invasive surgery MIS

- **Today technology**
  - Small incisions or natural orifices with microsurgical tools, catheters, endoscopes
    - Most of the present gall bladder or other urinogenital tract procedures
    - 75% of thoracic and abdominal operations can be replaced by MI procedures
  - CAD assisted surgery
  - Robotic MIS
    - Increase the surgeon's dexterity
    - Offer high-resolution three-dimensional image
    - Less trauma for the patient
    - Less risk of complications
    - Less pain and blood loss
    - Faster overall recovery time
    - A shorter hospital stay
    - A quicker return to normal activities
  - Limitations
    - Still expensive on training, purchase, maintenance and occupied area
    - Not accepted by all patients and surgeons
New emerging technology:

- Active catheters
  - Tactile feedback is essential for identifying hidden tissue planes, accurate targeting of cancerous tissues and in delineating tissue boundaries
  - Sensors with tactile or visual feedback, motion control for active steering catheters
  - Integrated sensors and actuators, active forceps, grippers, ultrasonic microscalpels with force sensors
    - Piezoelectric tactile sensors on catheter to aid in navigation through the vessels
    - PVDF tactile sensor for endoscopic graspers
    - Local blood pressure, temperature, continuous flow velocity, oxygen saturation, microcamera systems
    - 6DoF manipulation and steering of passive catheters using EAP, shape memory alloys, actuators
  - Replacement of catheters by wireless microrobots which can navigate inside the body or vessels
Commercialization bottleneck issues

How to use microsystems in healthcare?

Conduct in parallel:

The advanced technological development

&

How to clinically use the microsystem

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The validation of the clinical relevance

Market unsuccessful

If clinical relevance not validated:

- very weak market
- very low volume
- low price no ROI

If no reimbursement:

- inadequate market
- low volume

Technological breakthrough

• Demographic and
• Clinical information

• Clinical development
• Clinical relevance
• Patient cost benefit

Reimbursement of the overall clinical service or proper business model

Commercialization bottleneck issues
Commercialization bottleneck issues

- **Regulatory requirements** not enough included in the R&D specification of the prototype
  - Additional iterative R&D prototype to reach the regulatory requirements, once the collaborative program is ended

- **Industrialization & scale-up** not enough anticipated
  - How the sensitivity and the reproducibility are affected by the processing?
  - How are the controls performed during the industrialization processing: Are new metrology tools needed?
  - In which extend the processing impact the unit cost?

- **How to clinically use** microsystems for healthcare?
  - Cost-benefit issues not enough anticipated, rendering inadequate market access and market volume to weak for low cost
• Specific challenges for the medical industry:
  • Technical barriers:
    • Hermetic packaging for bio-compatibility and sterilization
    • Fluidics harsh environment
    • Highly reliable
  • Stringent regulatory control:
    • US food and Drug Administration approval process
    • CE mark
    • Clinical trial on huge patient cohort: very expensive, not included in FP funding
  • Inertia of the medical industry in order to take no patient risk—skepticism of users (doctors, patients)
  • Testing, calibration and packaging difficulties
  • High entry and facilities development cost => difficult for small companies
  • Interdisciplinary work – engineers need to understand the health care needs and the health care environment
Thank You

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