TOWARDS A DECREASE OF THE DELAY
BETWEEN LABORATORY INNOVATIONS AND
THEIR CLINICAL EVALUATION

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GRENOBLE?  9845km from NAGOYA
WHY BEING INTERESTED IN ACCELERATING THE TRANSFER FROM LABORATORY TO CLINICAL SETTING?

*Computer Assisted Medical Interventions (CAMI)*

- **Improvement of the care** delivered to our patients
  - Added-value? Demonstration?

- **Innovative Technology (Medical Device - MD)**
  Many innovations in the field
  - Drug ≈ 10 patent // MD ≈ 2000 patents
    - Short to enter the market

- **Usability**: MD use ≠ Drug Use
NEED TO TAKE INTO ACCOUNT THE PARTICULARITIES OF THE MEDICAL DEVICES TO IMAGINE NEW APPROACHES FOR ACCELERATING THE ESTIMATION / DEMONSTRATION OF ITS MEDICAL SERVICE
A MEDICAL SERVICE... for a MEDICAL DEVICE?

Medical service associated to a medical device:

How the medical device is contributing to:

• the improvement of the care of a patient

• The improvement of the care of a population of patients
I - Formalization of the maturation cycle of a Medical Device

II - Formalization of the maturation cycle of the Medical Service

III - Examples of acceleration of the demonstration of the Medical Service
TALK OUTLINE

I - Formalization of the maturation cycle of a Medical Device

II - Formalization of the maturation cycle of the Medical Service

III - Tools for accelerating the demonstration of the Medical Service
The Grenoble Experience

Augmented surgery in Grenoble: a series of premieres

- 1989: Robotized Brain Stereotaxic Surgery
  S. Lavallée, Pr. A L Benabid

  Pr. B. Raphael

- 1997: Navigation of Knee Ligamentoplasty
  Dr. R. Julliard

- 1999: Navigation of Total Knee Prosthesis
  Pr. D. Saragaglia

- 2000: Compact motorized scope holder for advanced laparoscopic surgery

- 2003: MRI/sonography fusion for prostate curietherapy
  Pr. Bolla, Dr. Fourmeret, J-Y. Giraud, Pr. Descottes

- 2006: Prostate Biopsy 3D reconstruction
  Dr. Mozer, Pr. Richard
I - Maturation of a MD

New Medical Problem

Idea

Medical Problem + Idea

Need

Prototype

Product

Pre-product maturation

(Pre)-product

Clinical prototype maturation

Clinical prototype

Prototype

Prototype Maturation

Concept product

Patent

Proof Of Concept

Idea Formalization & Maturation

Medical Problem

I - Maturation of a MD
Figure 2 – Steps of development of a medical device in France (IRBM journal, 2010, courtesy L Pazart, A Moreau-Gaudry), CIC-IT network
IDEAL approach

*No surgical innovation without evaluation: the IDEAL recommendations*
Peter McCulloch and all. Lancet 2009

- Stage 1: **Innovation** (Proof of concept)
- Stage 2a: **Development**
- Stage 2b: **Exploration** (Learning)
- Stage 3: **Assessment** (Assesment)
- Stage 4: **Long-term study** (Surveillance)
Maturation cycle of a medical device

Maturation cycle of

an **Innovative Technology** in Health

↓

Maturation cycle of the **MEDICAL SERVICE**

of an Innovative Technology
Delivered Medical Service

Expected Medical Service
Three examples of Medical Services of Innovative Medical devices from the CAMI field

- **HEMOCARD**
  - Research project (CHU Grenoble)

- **Light Endoscope holder Robot (LER)**
  - VICKY® (Endocontrol)

- **GPS tool for CT-Assisted Interventional Radiological Procedures**
  - IMACTIS GPS system (IMACTIS)
HEMOCARD

brevet UJF du 08/02/2008 - FR 08/00676

Dominique Blin
Grenoble
HEMOCARD

An innovative approach to control bleeding with vacuum device

Innovative Medical Device

Class III

Not CE marked

**Expected** Medical Service (2008)
- To control bleeding
  - rapidly
  - In a safer way
  - In stressless conditions
- Bench experiments
- Animal experiments
HEMOCARD

- An innovative approach to control bleeding with vacuum device
- Innovative Medical Device
- Class III
- Not CE marked
- **Expected** Medical Service
  - To control bleeding
    - rapidly
    - In a safer way
    - In stressless conditions
  - Bench experiments
  - Animal (sheep) experiments

*Estimate the Expected Medical Service*
*An active wound → a dry wound*
HEMOCARD

- An innovative approach to control bleeding with vacuum device
- Innovative Medical Device
- Class III
- Not CE marked

- **Delivered** Medical Service
  - Biomedical research protocol
  - Risk analysis, CPP, AFSSaPS

- First estimation (2010 - Clinical trial)
  - EJCTS (Heart transplant surgery with ECC)
  - Towards a startup?

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**European Journal of Cardio-thoracic Surgery**

How-to-do-it

An innovative technique to control bleeding with vacuum device

Karen Guerrero, Alexandre Moreau-Gaudry, Paolo Porcu, Dominique Blin

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*Cardiac Surgery Department, University Hospital Grenoble, Grenoble, France*

Received 21 June 2010; revised 29 September 2010; accepted 30 September 2010
Light Endoscope holder Robot (ViCKY ®)

Background
2000 : New concept of Light Endoscopic holder Robot
2001-2004 : Maturation of the Expected Medical Service
2005 : Start-Up Endocontrol created
2007 : CE Mark
2008 : FDA approved
What medical service?

- To come back to the initial idea
  - Robot = mechanical hand
  - Robust, but not smart

- Complications
  - Per-operative, post-operative, long-term complication

- Operating duration, length of hospitalization

- Improvement of the visual comfort?

- Device reliability?

- Learning curve?

- Preferential surgical indication?

- Others?
Materials and Method

Biomedical Research

Equivalence trial

« In term of number of “Hands”, the robot may be considerer as a mechanical hand « equivalent » to those of the operator who holds the laparoscope?»

Multicentric (Grenoble, Lyon, St Etienne)

Prospective

Comparative (Conventional vs Robot)

Randomized

Open-label trial

=> Results to be published
An Electromagnetic-localizer navigation system for CT-Based Radiological Interventions
CT Nav : step 1

→ Expected medical service

A prototype for needle navigation :

1/ Position and orientation of the sterile needle holder are displayed in real-time on 2D reconstructed CT-images extracted from the 3D CT volume

2/ The radiologist can explore the anatomy of the patient in any plane

3/ The radiologist can visualize in real-time the needle trajectory in this plane

Background

- Prototype developed during SurgiMaG
- Ex vivo evaluations
  – Risk Analysis + Bench results
- Expected Medical Service
  - To be more precise than Conventional Procedure
CTNav: step 2

→ First estimation of the delivered medical service

Innovative Medical Device

❖ Class IIa

❖ Not CE marked

→ Biomedical research protocol

→ Risk Analysis, CPP, AFSSaPS
CTNav : step 2

→ First estimation of the delivered medical service

Innovative Medical Device

- Class IIa
- Not CE marked

Materials & Methods

- IRB approved, open, comparative, prospective, randomized controlled trial (ClinicalTrials.gov NCT00828893).
- N=120 patients randomized
  - standard procedure (CT group) or navigated procedure (NAV group)
  - stratified according to predictable difficulty before intervention
- Main outcome
  - accuracy of the needle initial placement, defined as
    - the maximal distance between planned and realized trajectory
    - The maximal angle between planned and realized trajectory
- Worse case scenario intention-to-treat (ITT) and per protocol (PP) data analysis.
CTNav : step 2

→ First estimation of the delivered medical service

<table>
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<tr>
<th></th>
<th>CT</th>
<th>NAV</th>
<th>p</th>
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<tr>
<td>population</td>
<td>n=60</td>
<td>n=60</td>
<td>-</td>
</tr>
<tr>
<td>distance (mm)</td>
<td>8.9 [4.9; 15.1]</td>
<td>4.1 [2.7; 9.1]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>angle (°)</td>
<td>7.9 [5.9; 13.2]</td>
<td>4.7 [2.4; 8.2]</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Towards a multicenter clinical trial

→ national PHRC

→ Materials & Methods

- IRB approved, open, comparative,
- prospective, randomized controlled trial
  - CT vs Conventional
- Main criteria (combined criteria) :
  - SECURITY
    Number of complication directly linked to the puncture gesture
  - EFFICICENCY
    Number of touched target
  - PERFORMANCE
    Number of CT-scan performed to put in place the needle

CTNav : step 3
→ to refine the delivered medical service

III – 3 Examples
Challenges

To evaluate:
- as soon as possible
- following an high quality methodology

To facilitate the transfer: Laboratory → Clinical Practice

To guide the maturation process in the best possible manner
- Of the medical device
  - The time to market
- Of the medical service
- the time to “delivered medical service”
What are tools are our disposal?

To use according to the degree of maturity of the Medical Device

- **Expected Medical Service**
  - In Silico Experiment (Expected medical service)
  - Ex Vivo Experiment (Expected Medical Service)
  - In Vivo Experiment (animals – Expected Medical Service)

Risk Analysis (CE? FDA?)

- **Delivered Medical Service**
  - Biomedical research
  - “soins courant”
  - “Observationnelle”
Are we totally satisfied?

- **Clinical Evaluation**

- **In current practice**:
  - Complex
  - Difficult to implement, especially in the surgical field,
  - With a consistent supply,
  - With a significant cost,
  - To be achieved over a suitable time window of the maturing process of the IT,
  - With a “small” number of patients (around hundred)
  - Etc…

- « There is a dearth of such studies ». 

Are we totally satisfied?

- **Biomedical research**: YES, NECESSARY!!

- **BUT NOT ONLY**: 

  - **REGISTRIES**
    - To “capitalize” on the surgeries performed by the Medical Device
      - To access to “Big Data” on medical devices,
      - To share these data,
      - To refine the Medical Service,
      - To better “design” clinical studies,
      - To facilitate Research Program,
      - To facilitate “Post market” follow-up
      - To better structure the knowledge field related to an application
A CAMI Observatory

Access to objective data about medical practice.

About the impact of new technology

Access to a tool to facilitate the regulatory compatibility (post market surveillance)

Access to high volume data and to realistic models

Medical Issues

Medical Device Observatory

Research Issues

Industrial Issues
Conclusion

To understand the maturation cycle of IT in Health may have advantages:

- to anticipate the next step
- to shorten the maturation cycle
- to guide the maturation of the medical service

To demonstrate the medical service

- Through “Biomedical Research » Tool,
- Through « CAMI observatory » tool