GePhCARD & BioMIMS: a combined platform that support research on hereditary diseases

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Difficulty & delay in diagnosis

- Partial data gathering
- No data integration
- Reduced data merging
- Few information

No data exchange

No statistical analyses

Inadequate treatments
Increase knowledge on Hereditary Diseases

• collect clinical and genealogical data of each patient/family

• increase molecular screening on blood/tissue samples

Our focus is to define a correlation between clinical data (Phenotype) and genetic screening (Genotype)
Short overview on Hereditary Rare Diseases

- less than one in 2000
- 25 million people are affected by them
- 7000 diseases are rare
- Most involve skeleton
- Mostly are not curable, chronic, life-threatening
Multiple Osteochondromas - MO

- cartilaginous caps on long bones

- huge inter/intra-familiar clinical variability (3 class each divided in 2 sub-class)

- in less than 5% of the patients a progression into a SPC

- Mutations on EXT1/EXT2 genes

- Mutated proteins for bone growth
Osteogenesis Imperfecta - OI

- heterogeneous disorder
- susceptibility to fracture, bone fragility
- 4 clinical types, expanded into 7
- caused by mutations in COL1A1 or COL1A2 genes
- mutated chains of type I collagen, structural protein of bone
IT FOR SUPPORTING RESEARCH IN HRD

• Store genomic data

• Store clinical data

• Create a data model to integrate clinical and genomic data in a standard way to allow heterogeneous application interoperability

• Correlate genomic data to clinical data in a patient centric view
GePhCARD: IT PLATFORM FOR COLLECTION

designed as services (Web Services) and developed according to SOA principles

- a relational database to store clinical, genomic and genealogic data of patients
- a relational database to store and index digital documents
- a document management system based on Alfresco 2.1 framework
- a web application
GePhCARD: IT PLATFORM FOR COLLECTION

• GENEALOGICAL DATA DOMAIN
  To store general information on each family and to guarantee the possibility to compare clinical and genomic data inside the same family

• PERSONAL DATA DOMAIN & PATIENT PANEL
  To store a complete set of private data for each patient or relative. Some fields are mandatory to identify each patient univocally
**GePhCARD: IT PLATFORM FOR COLLECTION**

- **CLINICAL CHART**
  2 sections: a left navigation panel structured as a tree with data distributed in sub-sections and a right section created to visualize the sub-section’s details

- **DOCUMENTAL DATA DOMAIN**
  an existing professional open source CMS Alfresco for storing document and a full index based searching system to perform both full text and metadata searches way
BIOMIMS: IT PLATFORM FOR COLLECTION

- relational DB for archiving clinical and genetic data
- a Light MPI Server (Master Patient Index) for interoperability
- a Content Manager for storage of clinical and genetic raw data
- an innovative tool for pedigree analysis and clustering
- a Web based UI interface
- a Medical Imaging Repository (CMO) (secure DICOM based communication)

Hospitals (PACS, Clinical and Genetic Labs) - Physicians and Researchers

DICOM - HL7 v2.X HL7 v3.0

CMO - GePh-CARD (Phenotype Genotype) - Analytics Service

Healthcare BUS - HL7 v2.X, HL7 v3, WS, IHE profiles

PIX/PDQ Service - Pedigree Service
BIOMIMS: IT PLATFORM FOR COLLECTION

DICOM COMMUNICATION
To collect and integrate medical images (upload and retrieve from the appropriate system service in DICOM format)

MASTER PATIENT INDEX
To ensure the correct identification of patients and their data in a standard manner
BIOMIMS: IT PLATFORM FOR COLLECTION

PATIENT IDENTIFIER

IHE patient identifier Cross-Reference (PIX) and Patient Demographic Query (PDQ) transactions. To enable interoperability and cross-institutional information sharing (preserving security and privacy)

PEDIGREE ANALYTICS

to manage genealogic trees for an healthcare related pedigree creation, management and analysis
They work in concert to:

- collect data
- support a set of sophisticated and federated queries (include a combination of different types of information)
- store interesting queries
- extrapolate data
- analyse data
PATIENT DATA ACCESSIBILITY

![GephCard - orto20 orto20 (Bologna - 20) - Orthopedician - DEMO](image)

<table>
<thead>
<tr>
<th>Lab. ID</th>
<th>Surname</th>
<th>Name</th>
<th>Family Id</th>
<th>Gender</th>
<th>Birth Date</th>
<th>Hospital</th>
</tr>
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<tbody>
<tr>
<td>OIS0001</td>
<td>NERI</td>
<td>FRANCO</td>
<td>NERI(3)</td>
<td>MALE</td>
<td>01/01/1944</td>
<td>OSPEDALE PADOVA - 30</td>
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<tr>
<td>FEXS0004</td>
<td>NERI</td>
<td>MARIA</td>
<td>ROSSI(1)</td>
<td>FEMALE</td>
<td>01/01/1951</td>
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<tr>
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<td>ROSSI</td>
<td>FRANCO</td>
<td>ROSSI(2)</td>
<td>MALE</td>
<td>01/01/1943</td>
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<td>FRANCO</td>
<td>ROSSI(1)</td>
<td>MALE</td>
<td>01/01/1943</td>
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<tr>
<td>FEXS0002</td>
<td>ROSSI</td>
<td>MARIO</td>
<td>ROSSI(1)</td>
<td>MALE</td>
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<td>OSPEDALE MODENA - 10</td>
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<td>PAOLA</td>
<td>ROSSI(1)</td>
<td>FEMALE</td>
<td></td>
<td>OSPEDALE MODENA - 10</td>
</tr>
</tbody>
</table>
PATIENT’S FAMILY INTERFACE
PATIENT PANEL

Patient search panel

Patient navigator tree
PATIENT PANEL

Patient Tree:

- Personal Info
- Pre-Diagnoses
- Diagnoses
- Visits
- Clinical Observations
- Multiple Osteochondromas
  - 24-05-2010
  - 01-01-2007
- Samples
- Genetic Analyses
- Medical Images
- Documents
### Personal Data Domain

**Identification Info**

- **Laboratory Id**: FEX59999
- **Name**: Mario
- **Surname**: [Redacted]
- **Gender**: Male
- **Birth Date**: [Redacted]
- **Birth Place**: Italy
- **City**: Arezzo
- **Town**: Bucine
- **Fiscal Code**: [Redacted]
- **Health Insurance Card**: [Redacted]

**Contacts and Addresses**

- **Country**: Italy
- **City Of Residence**: Arezzo
- **Zip Code**: Bucine
- **Phone**: [Redacted]
- **Mobile Phone**: [Redacted]
- **E-mail**: [Redacted]

**Some Clinical Notes**

- **Institutional Clinical Chart Id**: 20455546729
- **Other Diseases**: [Redacted]
- **Notes**: [Redacted]

**Family Data**

- **Proband**: [Redacted]
- **Family Name**: [Redacted]
PEDIGREE TOOL
## OI Clinical Data

**Detailed Observations: Row 1 of 1**

<table>
<thead>
<tr>
<th>Date</th>
<th>23/11/2009</th>
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<tbody>
<tr>
<td>Deafness</td>
<td>YES</td>
</tr>
<tr>
<td>Dentin. Imper.</td>
<td></td>
</tr>
<tr>
<td>Cutis Laxa</td>
<td></td>
</tr>
<tr>
<td>Card. Lesions</td>
<td></td>
</tr>
<tr>
<td>Worm. Bones</td>
<td></td>
</tr>
<tr>
<td>Triang. Facies</td>
<td></td>
</tr>
<tr>
<td>BD</td>
<td></td>
</tr>
<tr>
<td>Notes</td>
<td>Dall’89 ha avuto fratture multiple in seguito a traumi diretti (anche se di lieve entità)</td>
</tr>
</tbody>
</table>

### Sites - Locations - Sides

<table>
<thead>
<tr>
<th>Site</th>
<th>Nº</th>
<th>Age</th>
<th>Location</th>
<th>Side</th>
<th>Nº fractures</th>
<th>Level of pain</th>
</tr>
</thead>
<tbody>
<tr>
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<td></td>
<td></td>
<td>UNKNOWN</td>
<td>unknown</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>unknown</td>
<td></td>
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</tr>
</tbody>
</table>

### Limitations
RARE HEREDITARY DISEASES

Lack of data for meaningful research

Collaboration among centres
IT PLATFORM FOR COLLABORATION

The data accessibility

→ Role Based Access Control (RBAC) system

→ enables users from different organizations with customized access rights to patients' information according the user profile or role
**GePh-CARD**
Genotype-Phenotype Correlation, Analyses, Research Database

IT PLATFORM

to organize and screen genetic, genealogical, and clinical data

genotype-phenotype patient characterization to a personalized healthcare vision

**BioMIMS**
BioMarker Imaging Management System

IT PLATFORM

to merge information from dispersed hospitals (pedigree, imaging, etc)

clinical and genealogical characterization to a personalized healthcare vision
MO RESULTS

1. Male patients have more severe manifestations than female, from an inter- and an intra-familial point of view

2. EXT1 mutations are associated with a more severe form and correlate to specific clinical manifestations

3. Class III patients usually have low height

4. Negative Familiarity refers to Class III
OIS RESULTS

1. Quantitative genetic defects (Frameshift, Duplication, Initiating methionine, Nonsense, SpliceSite, SpliceVariant) are usual for Class I patients

2. Qualitative genetic defects (In-frame insertion, In-frame deletion, In-frame insertion-deletion, Missense) are usual for Class II
OUTCOMES 1

• More accurate and precise data ➔ A statistical analyses dataset ➔ Better disease overview and help in differential diagnosis

• Increased patient and family dataset ➔ Genotype-Phenotype Correlation & Study on Hereditary

• Patient-Centric & Family-Centric Approach ➔ Patient’s quality of life
OUTCOMES 2

• Logging tool thorough an authentication system ➔ Multilevel access profile system (different roles - different domains - different datasets) ➔ Data Legal Protection

• Web-accessibility (user-friendly interface) ➔ Input from different locations

• Service Oriented Architecture (SOA) ➔ Possibility of future implementations and incorporations of configurable modules ➔ Pairing of new techniques & new modules
OUTCOMES 3

• To purpose innovative research directions ➔ To decide the future health-related strategies

• Multi-language engine and multi-organization structure ➔ Increased gathering of data and data merge

• Advanced algorithms ➔ Correlation patterns ➔ Pedigree analytics

• Articulated queries system ➔ Possibility of store queries ➔ Reload interesting results
THANKS!!!!