Andreas Holzinger

Lecture 10 – Version WS 2013/14
Biomedical Information Systems and Medical Knowledge Management

VO 444.152 Medical Informatics

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1. Intro: Computer Science meets Life Sciences, challenges, future directions
2. Back to the future: Fundamentals of Data, Information and Knowledge
3. Structured Data: Coding, Classification (ICD, SNOMED, MeSH, UMLS)
4. Biomedical Databases: Acquisition, Storage, Information Retrieval and Use
5. Semi structured and weakly structured data (structural homologies)
6. Multimedia Data Mining and Knowledge Discovery
7. Knowledge and Decision: Cognitive Science & Human-Computer Interaction
8. Biomedical Decision Making: Reasoning and Decision Support
9. Intelligent Information Visualization and Visual Analytics
10. Biomedical Information Systems and Medical Knowledge Management
11. Biomedical Data: Privacy, Safety and Security
Learning Goals: At the end of this 10th lecture you ...

- have an overview about workflows and workflow modeling in health care;
- got an overview of typical architectures of hospital information systems for patient records as already discussed in lecture 4;
- have understood the principles of Picture Archiving and Communication PACS-Systems;
- know how important multimedia for medicine is;
- have a basic understanding of DICOM and HL7;
- are aware of the constraints of open source software in the medical domain;
- have got an idea of possible future systems solutions;
Keywords of the 10th Lecture

- Bioinformatics workflows
- Clinical workflow & management systems
- Cloud computing in healthcare
- Communication standards
- Digital Imaging and Communication in Medicine (DICOM)
- Formal methods & workflow modeling
- Health Level 7 (HL7)
- Logical Observation Identifier Names and Codes (LOINC)
- Medical multimedia
- Mobile computing in medicine
- Personal Health Record (PHR)
- Picture Archiving and Communication System (PACS)
- Quality
- Software as a Service (SaaS)
- Systems architecture
- Unified Modeling Language (UML)
Bioinformatics workflow management system = designed specifically to compose and execute a series of computational and/or data manipulation steps and/or workflows in the domain of bioinformatics;

Business process re-engineering (BPR) = analysis and design of workflows and processes within an organization (=hospital). According to Davenport (1990) a BP is a set of logically related tasks performed to achieve a defined outcome/result;

Clinical Pathway = aka care map, a tool used to manage the quality in healthcare concerning the standardization of care processes and promote organized and efficient patient care based on EBM;

Digital Imaging and Communications in Medicine (DICOM) = a standard for handling, storing, printing, and transmitting data in medical imaging (also file format definition and a network communications protocol using TCP/IP);

Evidence-based medicine (EBM) = aiming at developing mathematical estimates of benefit and harm from population-based research and apply these in the clinical routine, claiming that best research evidence on medical interventions come from experiments (e.g. randomized controlled trials);

Health Level Seven (HL 7) = a Standardization Organization accredited by the American National Standards Institute (ANSI) to push consensus-based standards representing healthcare stakeholders;
Hospital Information System (HIS) = integrated information system for (administrative, financial, clinical etc.) information management in a hospital;

Integrating Healthcare Enterprise (IHE) = initiative by healthcare professionals and industry to improve the way computer systems in healthcare share information (i.e. promotes the coordinated use of established standards such as DICOM and HL7);

National Electrical Manufacturers Association (NEMA) = holds copyright of DICOM;

Paradigm = according to Kuhn (1962) a shared view of a group of researchers, comprising 4 elements: concepts, theories, methods and instruments;

Picture Archiving and Communication System (PACS) = system for handling images from various medical imaging instruments, including ultrasound (US), magnetic resonance (MR), positron emission tomography (PET), computed tomography (CT), endoscopy (ENDO), mammmographs (MG), Digital radiography (DR), computed radiography (CR) ophthalmology, etc.;

Workflow = consists of a sequence of connected steps, succeeding the flow paradigm, where each step follows the precedent;
Key Challenges

- Lack of Integrated Systems
- Clinical Workplace efficiency
- Cloud Computing (Privacy, Security, Safety issues)
- Software as a Service (as electricity is already)
What is a clinical pathway?
What is a clinical workflow?
SRT = stereotactic radiation therapy
SRS = stereotactic radiosurgery

http://www.elekta.com/
Workflow modeling is the process of **simplifying the real-world**;

Modeling is based on facts gathered during **observations** and we need to accept that this representation can never be perfect;

Expectations from a model should be **limited** to the intentions with which it is designed for, be it problem solving or understanding of system intricacies (=elaborately complex details);

A workflow is defined as a process that contains tasks $T$, and the respective rules on how those tasks are executed:

**Workflow $W := (T, P, C, A, S_0)$ where**

- $T = \{T_1, T_2, \ldots, T_m\}$ A set of tasks, $m \geq 1$
- $P = (p_{ij})_{m \times m}$ **Precedence matrix of the task set**
- $C = (c_{ij})_{m \times m}$ **Conflict matrix of the task set**
- $A = (A(T_1), A(T_2), \ldots, A(T_m))$ Pre-Condition set for each task
- $S_0 \in \{0, 1, 2, 3\}_m$ is the initial state

Example:

Formal workflow modeling 2/2

\[ T = \{T_1, T_2, \ldots, T_8\}, \]
\[ A(T_1) = \emptyset, A(T_2) = \{\{T_1\}, \{T_6\}\}, A(T_3) = \{\{T_4\}\}, \]
\[ A(T_4) = \{\{T_2\}\}, A(T_5) = \{\{T_4\}\}, \]
\[ A(T_6) = A(T_7) = \{\{T_5\}\}, A(T_8) = \{\{T_3, T_7\}\}. \]
\[ S_0 = (1, 0, 0, 0, 0, 0, 0, 0). \]

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\begin{bmatrix}
0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\
0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\
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<table>
<thead>
<tr>
<th>Name</th>
<th>Modify a wellness data entry</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Purpose</strong></td>
<td>The user edits the value of an existing wellness data entry</td>
</tr>
<tr>
<td><strong>Summary</strong></td>
<td>Clicking on an entry’s row in the list of all wellness entries (except clicking on the info-icon) opens an input form allowing the user to modify and store the selected entry. After storing the entry on the server, an info message tells about success or possible failure. Instead of modifying the data, the user can also delete the entry using a button in this form.</td>
</tr>
<tr>
<td><strong>Pre-conditions</strong></td>
<td>The user is authenticated. The user has chosen an existing wellness data entry.</td>
</tr>
<tr>
<td><strong>Post-conditions</strong></td>
<td>The entry is updated or deleted on the server.</td>
</tr>
</tbody>
</table>

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For Stakeholders use case diagrams describe sequences of actions, providing measurable values to actors.

Class diagrams show interrelationships, inheritance, aggregation, association, operations and attributes.

Communication/Collaboration diagrams show the message flow between objects and imply the relationships between classes.

Component diagrams are used as an architecture-level artifact.

Sequence diagrams are interaction diagrams which details how operations are carried out, which messages are sent and at which time.

Deployment diagrams model the static view of the run-time configuration of processing nodes and the components that run on those nodes; this shows also hardware & software requirements.

Activity Diagrams for modelling the logic and State Machine diagrams show to analysers the possible states of objects and transitions that causes changes.

Time = Money
Example: WF-Optimization with mobile comp

Holzinger et al. (2011)
### Important: Macrolevel – the view of the Manager

**Rechenmodell zum Ausfüllen eines Fragebogens in einer Ambulanz**

<table>
<thead>
<tr>
<th>ohne MoCoMed (Szenario 1)</th>
<th>Schreibkraft bzw. Schalter (1 B)</th>
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<tbody>
<tr>
<td>Eingebendes Personal</td>
<td>Arzt (1 A)</td>
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<tr>
<td>Personalkosten/h</td>
<td>€ 44.0</td>
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<td>Personalkosten/min</td>
<td>€ 0.73</td>
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<td>Anzahl Patienten/Tag</td>
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<td>Zeitbedarf pro Fragebogen</td>
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<td>Jahreskosten Personal</td>
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<tr>
<td>Personalkosten/h</td>
<td>€ 44.0</td>
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<tr>
<td>Personalkosten/min</td>
<td>€ 0.73</td>
</tr>
<tr>
<td>Anzahl Patienten/Tag</td>
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<tr>
<td>Zeitersparungspro Fragebogen in %</td>
<td>90%</td>
</tr>
<tr>
<td>Zeitbedarf pro Fragebogen</td>
<td>1.00</td>
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<tr>
<td>Geräteinstallationzeiten pro Fragebogen in min</td>
<td>1.00</td>
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<tr>
<td>Ambulanztag</td>
<td>250</td>
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<td>Jahreskosten Personal</td>
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### Entwicklungs- und Betriebskosten MoCoMed

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<tr>
<th>Summe Entwicklungskosten</th>
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<tr>
<td>Kosten pro Personenmonat Entwicklung (EU-Satz)</td>
<td>€ 4.000</td>
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<td>Anzahl Personenmonate Entwicklung einmalig</td>
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<tr>
<td>Kosten Personal Entwicklung</td>
<td>€ 28.000</td>
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<tr>
<td>Investkosten pro Gerät</td>
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<tr>
<td>Anzahl Geräte</td>
<td>2</td>
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<td>Kosten Geräte</td>
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### Ergebnis

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<th>Einsparungspotential/Jahr in EUR unter den o. Annahmen</th>
<th>€ 37.325</th>
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<td>147</td>
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Slide 10-14 MoCoMED-Graz in operation

Holzinger et al. (2011)
This project was evaluated from a three level perspective: **patients – doctors – managers**

- Theoretical Background: Bronfenbrenner model
- Project demonstrates how both workflows and information quality can be optimized;
- thereby raising both medical quality and patient empowerment;
- Success factors for applications within the hospital include: **simplicity, usability, reliability**

- A data-driven procedure consisting of one or more transformation processes -> nodes;
- Can be represented as a directed graph;
  - Direction is time – i.e. the order of transformations;
  - A set of transformation rules;
- The data flow origins from a source to a destination (or result) via a series of data manipulations;
- The specification is designed in a Workflow Design System (modeling component) and then run by a Workflow Management System (execution component).

Def.: WMS = a system that defines, creates and manages the execution of workflows. Its main components include:

1) a graphical interface for composing workflows, entering data, watching execution, displaying results;
2) an data archive to store workflow descriptions, results of executions and related traces;
3) a registry of available services, either local or remote,
4) a scheduler able to invoke services included in the workflow at the appropriate time,
5) a set of programming interfaces able to dialogue with remote services,
6) a monitor tool for controlling the execution of the workflow,
7) a set of visualization capabilities for displaying different types of results.

Hospital Information Systems
1970+ **“Vertical Approach”** – monolithic mainframes
Central computer systems mainly for accounting,
typical “data processing” (“EDV”)

1985+ **“Horizontal Approach”** – evolutionary systems
Departmental clinical information systems,
local area networks, distributed systems

2000+ **“Integrated Approach”** – open, distributed systems
Hospital Intranets, electronic patient/health record,
mobile computing, “information quality focus”

Basic architecture of a standard HIS

Multimedia in the Hospital
Data Standards for Communication and Representation
- 1) a set of protocols for network communication;
- 2) a syntax and semantics for commands and info;
- 3) a set of media storage services (standard compliant);

HL 7 - Health Level 7
- 1) HL 7 v2.x messaging protocol, to provide exchange of textual healthcare data between hospital information systems;
- 2) Reference Implementation Model (RIM) contains data types, classes, state diagrams, use case models, and terminology to derive domain-specific information models;
- 3) Clinical Document Architecture (CDA) is a document markup standard to specify structure and semantics of clinical documents in XML;

LOINC - Logical Observation Identifier Names and Codes
- 1) Laboratory data (e.g. molecular pathology observations used for identification of genetic mutations, tumor genes, gene deletions, etc.
- 2) Clinical Observations (e.g. non-laboratory diagnostic studies, critical care, nursing measures, patient history, instrument surveys, etc.
- 3) Claims attachments (e.g. handles the definition of new LOINC terms and codes to manage claims-related data

Each data element is uniquely identified by its corresponding tag composed of a group number and an element number. Pixel data of the image is stored in element 0010 within group 7FE0.

A DICOM file consists of a file meta-information header and an information object (image data set). The file meta-information header is made of a file preamble, a DICOM prefix, and multiple file meta-elements.

Result delivered by Dr. Howard H. Hippocrates. The lab test was ordered by Dr. Patricia Primary for patient Eve E. Everywoman. The use case takes place in the US Realm.

Examples: http://www.ringholm.com/docs/04300_en.htm
Example: Application of VR in medical imaging

Faggioni et al. (2011)
Attention: Medical certifications such as FDA in the US and CE marking in Europe **do not apply** to Open Source software;

These certifications require a legal commercial entity to be identified as the owner of the product and warrant the legal liability of its distribution and commercial support.

Open Source software being often developed outside commercial enterprises; such as academic groups or university research labs, do not have the proper legal structure to apply for such certifications.

Also, most Open Source products being distributed free of charge lack the legal binding between the provider and the user that is required for software distribution under FDA and CE certification.

Ratib et al. (2011)
For sure the future hospital information systems will have three components:

1) the world (even the hospital world) of tomorrow will be mobile.

2) the data will be stored in the cloud as well as software-as-a-service will be used (Key problem: Privacy, Security, Safety and Data Protection).

3) Content Analytics will be integrated as tools within the clinical workplace.
Ratib et al. (2011)
Future System Architecture: Cloud Ultrasound

Future: Software as a Service (SaaS)

What about the masses of content within such systems?
IBM Content and Predictive Analytics for Healthcare
Thank you!
Sample Questions (1)

- How is a workflow defined?
- How can a workflow be described formally?
- Why is workflow modeling important in health care?
- Please describe the different tools of the Unified Modeling Language (UML) on some medical examples!
- Which benefits can be gained by optimization of workflows?
- Which three stakeholders have which interests within an Hospital?
- Please describe the basic idea of a typical bioinformatics workflow management system!
- What is the difference of system quality versus information quality?
- What are the advantages/disadvantages of the three basic system architecture approaches of hospital information systems?
- Which functional parts does the classic conceptual model of a HIS include?
- In which aspects does the process-oriented health information systems model differ from the classic conceptual model?
- Please describe the typical workflows within a PACS System?
- What are the typical modalities of a PACS System?
Sample Questions (2)

- What are the generic PACS components and the respective data flows?
- What are the typical advantages/disadvantages of the six PACS implementation models?
- Why are communication standards important for biomedical informatics?
- Please describe the purpose and advantages of DICOM?
- What is the basic idea of HL7?
- Why is open source software problematic in the medical domain?
- What are the advantages/disadvantages of cloud computing for health care?
- What are the advantages/disadvantages of the paradigm “Software as a Service”?
- What is an electronic Personal Health Record?
- Which is still the biggest problem of such PHRs?
Appendix: Bioinformatics Workflow Management Systems

- **BioExtract** = for creating and customizing workflows; you can query online sequence data, analyze it using an array of informatics tools, create and share custom workflows for repeated analysis, and save the resulting data and workflows in standardized reports; [http://www.bioextract.org](http://www.bioextract.org)

- **CellProfiler** = open source modular image analysis software developed at the Broad Institute; algorithms for image analysis; [http://www.cellprofiler.org](http://www.cellprofiler.org)

- **Discovery Net** = was one of the earliest examples of scientific workflow systems (e-Science project by the Imperial College London), having many features, e.g. chemical compounds represented in the widely used SMILES (Simplified molecular input line entry specification) format can be imported and rendered using three-dimensional representation or the structural formula, of historic interest, see: [http://www.computer.org/portal/web/csdl/doi/10.1109/HPDC.2002.1029946](http://www.computer.org/portal/web/csdl/doi/10.1109/HPDC.2002.1029946)

- **Ergatis** = to create, run, and monitor reusable computational analysis pipelines, contains pre-built components for common bioinformatics analysis tasks. These components can be arranged graphically to form highly-configurable pipelines. Each analysis component supports multiple output formats, including the Bioinformatic Sequence Markup Language (BSML), [http://ergatis.sourceforge.net](http://ergatis.sourceforge.net)

- **GenePattern** = genomic analysis platform that provides access to 150+ tools for gene expression analysis, proteomics, SNP analysis, flow cytometry, RNA-seq analysis as well as standard data processing tasks. A web-based interface provides easy access to these tools and allows the creation of multi-step analysis pipelines that enable reproducible in silico research; [http://www.broadinstitute.org/cancer/software/genepattern](http://www.broadinstitute.org/cancer/software/genepattern)

- **Triana** = open source problem solving environment developed at Cardiff University that combines an intuitive visual interface with powerful data analysis tools. Already used by scientists for a range of tasks, such as signal, text and image processing, Triana includes a large library of pre-written analysis tools and the ability for users to easily integrate their own tools. is an open source problem solving environment developed at Cardiff University that combines an intuitive visual interface with powerful data analysis tools; [http://www.trianacode.org](http://www.trianacode.org)
Some useful links

- [http://www.gimias.org/download/sampledata](http://www.gimias.org/download/sampledata) (some useful sample data)
- [https://www.biomedtown.org/biomed_town/MSV/reception/wikis/Data](https://www.biomedtown.org/biomed_town/MSV/reception/wikis/Data) (on-line community open and free to anyone has a professional or educational interest in biomedical research & practice)
- [http://rad.usuhs.edu/medpix/index.html](http://rad.usuhs.edu/medpix/index.html) (Medical Image Database)
- [http://www.incits.org](http://www.incits.org) (International Committee for Information Technology Standards)
- [http://medical.nema.org](http://medical.nema.org) (about DICOM)
- [http://www.openehr.org](http://www.openehr.org) (Open HER – good UML examples)
- [http://www.wfmc.org](http://www.wfmc.org) (Workflow Management Coalition)
Appendix: Open Source in medical imaging

I DO IMAGING
FREE MEDICAL IMAGING SOFTWARE

Dicom Viewer Fast, flexible, complete medical image viewer, free demo. [www.idoimaging.com](http://www.idoimaging.com)


Pressure Imaging Systems Tacillo Pressure Imaging Systems for Medical, Industrial, Commercial [www.Tacillo.com/Pressure-Imag](http://www.Tacillo.com/Pressure-Imag)

If you work with medical imaging files, this site can help you. Looking for a free DICOM viewer, DICOM converter, or PACS client? You’ll find them here. Idoimaging.com tracks free medical imaging applications and resources: conversion programs, image display and analysis, surface and volume rendering, PACS clients and servers. Many programs are classified by a specialty to allow you to find similar programs by imaging modality, medical specialization, or similar. Half of all the programs listed here work with DICOM files, but there are over 25 file formats covered.

All the programs included are free and intended for distribution; there are no "demo" versions of commercial applications. If you are involved in programming, many of the programs are open-source, and provide APIs and SDKs for radiology programmers.

http://www.idoimaging.com
Appendix: OsiriX Open Source component architecture

http://www.osirix-viewer.com

Example: Drug Target Identification

Galaxy/PacBio Integration

http://screencast.g2.bx.psu.edu/pacBio-demo


Experts consider health IT key for improving efficiency and quality of health care processes.

Please, carefully determine between:
- Quality of Systems
- Quality of Data
- Quality of Information
- Quality of Knowledge
- Quality of Action

## PACS R&D Progress and R&D Topics

<table>
<thead>
<tr>
<th>Decade</th>
<th>R&amp;D progress</th>
<th>R&amp;D topics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1980s</td>
<td>Medical imaging technology development</td>
<td>CR, MRI, CT, US, DR, WS, storage, networks</td>
</tr>
<tr>
<td>Late 1980s</td>
<td>Imaging systems integration</td>
<td>PACS, ACR/NEMA, DICOM, high-speed networks</td>
</tr>
<tr>
<td>Early 1990s</td>
<td>Integration of HIS/RIS/PACS</td>
<td>DICOM, HL7, Intranet and Internet</td>
</tr>
<tr>
<td>Late 1990s – present</td>
<td>Workflow &amp; application servers</td>
<td>IHE, ePR, enterprise PACS, Web-based PACS</td>
</tr>
<tr>
<td>2000s – present</td>
<td>Imaging Informatics</td>
<td>Computer-aided diagnosis (CAD), image contents indexing, knowledge base, decision support tools, image-assisted diagnosis and treatment</td>
</tr>
</tbody>
</table>

- **CR** = Computed Radiography (vs. Direct Radiography (DR)); **MRI** = Magnetic resonance imaging; **CT** = Computed Tomography; **US** = Ultrasonography; **WS** = Web services;  
  **ACR** = American College of Radiology; **NEMA** = National Electrical Manufacturers Association;

## Pros/Cons of six PACS implementation models

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Home-grown system</td>
<td>Built to specifications, state-of-the-art technology, continuously upgrading, not dependent on a single manufacturer</td>
<td>Difficult to assemble a team, one-of-a-kind system, difficult to service and maintain</td>
</tr>
<tr>
<td>2. Two-team effort</td>
<td>Specifications written for a certain clinical environment, implementation delegated to the manufacturer</td>
<td>Specifications over ambitious, underestimate technical and operational difficulty, manufacturer lacks clinical experience, expensive</td>
</tr>
<tr>
<td>3. Turnkey</td>
<td>Lower cost, easier maintenance System will keep up with technology advancement, health center does not have to worry of the system becoming obsolete, manufacturer has long-term contract to plan ahead</td>
<td>Too general, not state-of-the-art technology Expensive to the health center, manufacturer may not want to sign a partnership contract with a lesser prominent center, center has to consider the longevity and stability of the manufacturer</td>
</tr>
<tr>
<td>4. Partnership</td>
<td>Minimize initial capital cost, may accelerate potential return on investment, no risk in technology obsolescence, provide flexible growth, no space requirement in data center Healthcare provider purchases its computer and communication equipment, use open source software, good for special PACS application server, lower cost</td>
<td>More expensive over 2–4-year time frame comparing to a capital purchase, customer has no ownership in equipment</td>
</tr>
<tr>
<td>5. ASP</td>
<td></td>
<td>Open source software may not be robust for daily clinical use, maintenance and upgrade of the software may be a problem, may not be good for a full large-scale PACS</td>
</tr>
<tr>
<td>6. Open source</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

ASP = application service provider model

Example: Images within the EPR

Ex.: The Hong Kong Hospital Clinical Information System

Therapy Imaging and Model Management System: TIMMS

Informatics platform/infrastructure for Model Guided Therapy

Therapy Imaging and Model Management System (TIMMS)

- Images and signals
- Modelling tools
- Computing tools
- WF and K+D tools
- Rep. tools
- Devices/Mechatr. tools
- Validation tools

IO Imaging and Biosensors
Modelling
Simulation
Kernel for WF and K+D Management
Visualisation Rep. Manager
Intervention
Validation

Therapy Imaging and Model Management System (TIMMS)

ICT infrastructure (based on DICOM-x) for data, image, model and tool communication for patient model-guided therapy

Data and information
Lemke & Berliner (2011)

Models (Simulated Objects)
WF’s, EBM, "cases"

Models and intervention records

Data Exch.
Control

Big Fact: Personal Health Records: Poor Usability

- 300+ different systems in the US
- Only 1% of the US population have access (2008)
- “Most EHR are 100 % bad.” (Forrester Research, 2008)
- Biggest obstacles:
  - Cost factors
  - Poor usability
- Need for UCD
- Need for proactive wellness management