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VO 709.049 Medical Informatics
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Lecture 10

Biomedical Information Systems and Medical Knowledge Management

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http://hci-kdd.org/biomedical-informatics-big-data

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Status as of 15.12.2015 08:30

Dear Students, welcome to the 10th lecture of our course. Please remember from the last lecture the importance of visualization and a few examples of data visualization methods, including: Parallel Coordinates, RadViz, StarPlots, and have a basic understanding on human-computer interaction.

Please always be aware of the definition of biomedical informatics (Medizinische Informatik):
Biomedical Informatics is the inter-disciplinary field that studies and pursues the effective use of biomedical data, information, and knowledge for scientific inquiry, problem solving, and decision making, motivated by efforts to improve human health (and well-being).

Schedule

- 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
- 12. Methodology for Info Systems: System Design, Usability & Evaluation

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)

Advance Organizer (1/2)

- **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;

Advance Organizer (2/2)

- **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), mammographs (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;

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 HL 7;
- are aware of the constraints of open source software in the medical domain;
- have got an idea of possible future systems solutions;

Slide 10-1 Key Challenges

- Lack of Integrated Systems
- Clinical Workplace efficiency
- Cloud Computing
  (Privacy, Security, Safety, Data Protection…)
- Service oriented computing
  (as electricity is already!)

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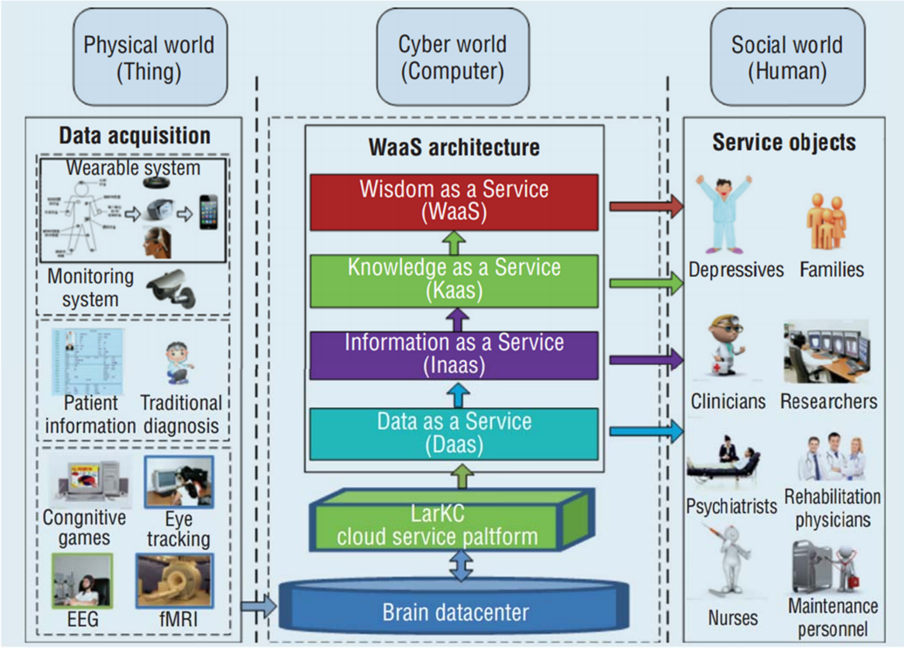
Software as a Service (as electricity is already)

Although we write the year 2014 – and we are now in the computing business since 1970 – for more than four decades – there is still the lack of integrated systems, moreover the lack of data integration. A major issue is in data fusion. The next problem is in the clinical workplace efficiency. It is not enough just to deliver more and more data to the clinician – they are already overwhelmed by the masses of data. They are interested in relevant data, and relevant information to support knowledge and decision making. There is a lot to do in the next years.

Service-oriented computing example Zhong et al. (2015)



Zhong, N., Yau, S. S., Ma, J., Shimojo, S., Just, M., Hu, B., Wang, G., Oiwa, K. & Anzai, Y. 2015. Brain Informatics-Based Big Data and the Wisdom Web of Things. *Intelligent Systems, IEEE,* 30, (5), 2-7.

This cycle is implemented by processing, interpreting, and integrating multiple forms of the
“brain big data” obtained from molecular and
neuronal circuitry levels via advanced neuroimaging technologies, such as functional magnetic resonance imaging (fMRI), magnetoencephalography (MEG), electroencephalography (EEG), functional
near-infrared spectroscopy (fNIRS), positron
emission tomography (PET), and wearable, portable micro and nano devices. Brain big data not
only help scientists improve their understanding of human thinking, learning, decision making, emotion, memory, and social behavior, but
such data also help cure diseases, assist in mental healthcare and well-being, and encourage further development of brain-inspired intelligent
technologies.

What is a clinical pathway?

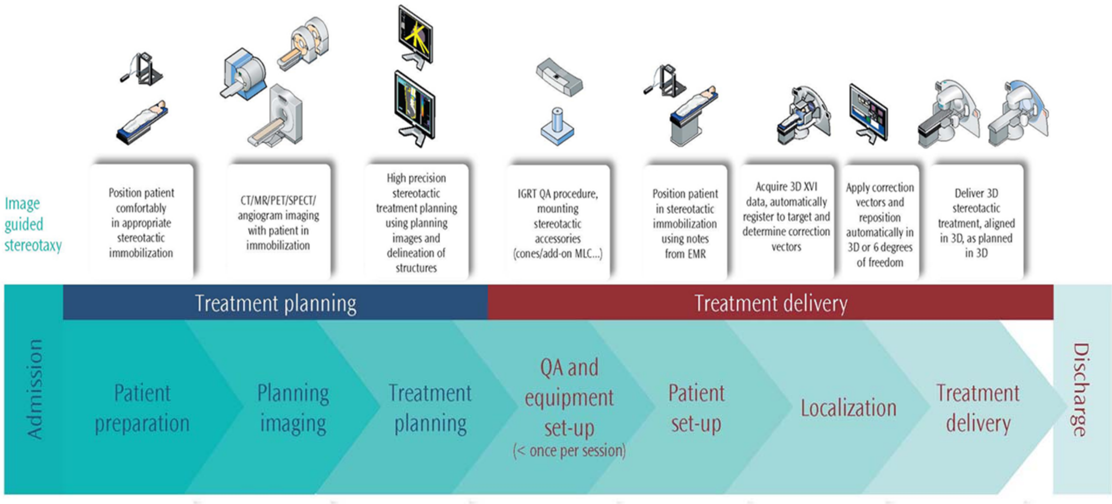
What is a clinical workflow?

Clinical pathways aka critical pathways, integrated care pathways, care maps, are one of the main tools used to manage the quality in healthcare related the standardization of care processes and is closely connected with evidence based practice.

Example

http://www3.gehealthcare.co.uk/~/media/images/specialty/cardiology/acute-caronary-syndrome-pathway.jpg

Slide 10-2 Typical Workflow in a hospital: Example Radiology

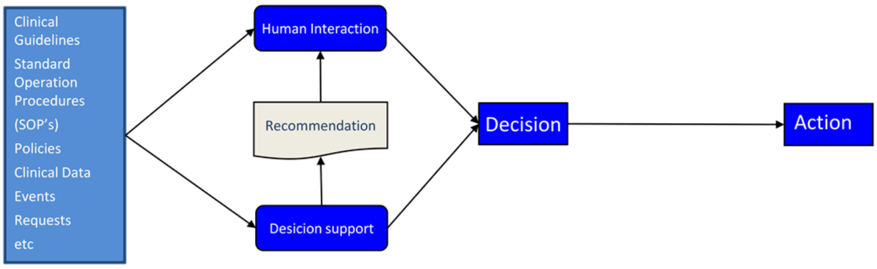


SRT = stereotactic radiation therapy
SRS = stereotactic radiosurgery

http://www.elekta.com/

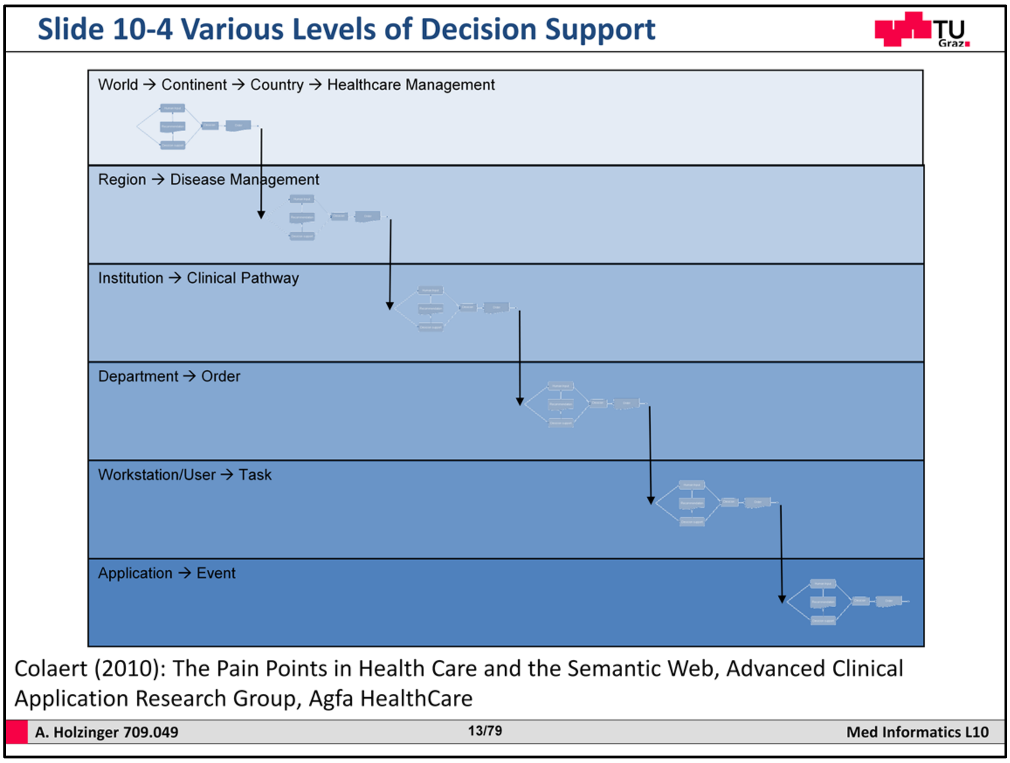
We have already heard about workflows and how important they are. Please remember that a Von-Neumann machine is a mathematical processor, hence is good in processing numbers - mathematically. Modelling is an approach to mathematize our world. What cannot be modelled in a mathematical way cannot be processed by a computer. In this slide we see a typical medical workflow on the example of radiology – from admission of the patient to the discharge.
Use case diagrams describe sequences of actions, providing measurable values to actors. A good overview is given by (Juan, Ma & Chen, 2005).

Slide 10-3 Workflow > Interaction > Decision > Action



Colaert (2010): The Pain Points in Health Care and the Semantic Web, Advanced Clinical Application Research Group, Agfa HealthCare

Remember what we learned about the relationships of data, information and knowledge and that the knowledge gained is the essential part in decision making, which results in an appropriate action. Do never forget that clinical medicine is not a theoretical, but an action science (in German: "Handlungswissenschaft"). In this slide on the left we see the "knowledge elements" (gained clinical information, policies, standard operating procedures, clinical guidelines, etc.) as a basis for decision making.



The core element of Slide 10-3 is applied in every stage of workflows from the large scale (world health management, country policies etc.) to the small scale (event handling).

Slide 10-5 Workflow modeling in a nutshell

- 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);

Malhotra, S., Jordan, D., Shortliffe, E. & Patel, V. L. (2007) Workflow modeling in critical care: Piecing together your own puzzle. *Journal of Biomedical Informatics, 40, 2, 81-92.*

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A workflow consists of a sequence of connected steps, with the emphasis on the flow paradigm. A workflow can be seen as an abstraction of the real world. Workflow modeling is basically the process of simplifying reality (with all the problems and dangers of oversimplification involved). The 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. A workflow management system is designed specifically to compose and execute a series of computational and/or data manipulation steps. In the research area there is the vision of e-Science, i.e. distributed scientists being able to collaborate on conducting large scale experiments and knowledge discovery applications using distributed systems of computing resources, data sets, and devices. 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, i.e. elaborately complex details (Malhotra et al., 2007).

Slide 10-6 Example: Formal workflow modeling 1/2

- 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, … T_m} A set of tasks, m≥ 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), …,A(T_m)) Pre-Condition set for each task
  - $S_0 \in \{0, 1, 2, 3\}_m$ is the initial state

J. Wang, D. Rosca, W. Tepfenhart & A. Milewski (2006) Dynamic Workflow Modeling and Analysis, Monmouth University

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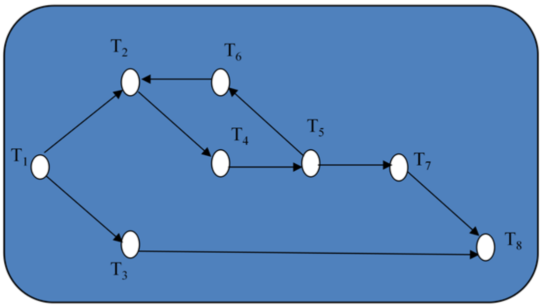
A = A(T1), A(T2), …, A™) Pre-Condition set for each task

$S_0 \in$ {0, 1, 2, 3_m } is the initial state

For more information please refer to: (Wang et al., 2008)

Slide 10-7 Example: Formal workflow modeling 2/2



$T = \{T_1, T_2, \ldots, T_8\}$,

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

$$P = \begin{bmatrix} 0 & 1 & 1 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 1 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix} \qquad C = \begin{bmatrix} 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 0 & 0 \end{bmatrix}$$

J. Wang, D. Rosca, W. Tepfenhart & A. Milewski (2006) Dynamic Workflow Modeling and Analysis, Monmouth University

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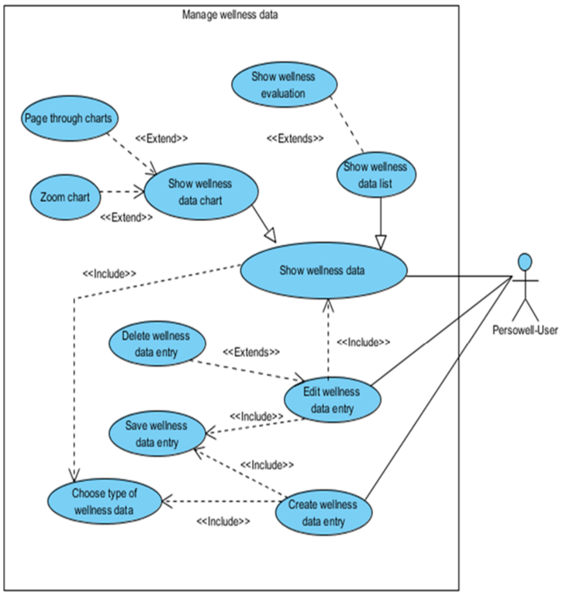
Here you can see the model of the defined workflow from Slide 10-6 and the mathematical representation (Wang et al., 2008).
P = (pij)m x m Precedence matrix of the task set
C = (cij)m x m Conflict matrix of the task set

Slide 10-8 Example: Modeling in UML – Use Case Diagram

Name	Modify a wellness data entry
Purpose	The user edits the value of an existing wellness data entry
Summary	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.
Pre-conditions	The user is authenticated. The user has chosen an existing wellness data entry.
Post-conditions	The entry is updated or deleted on the server.



Holzinger, A., Dorner, S., Födinger, M., Valdez, A. C. & Ziefle, M. (2010) Chances of Increasing Youth Health Awareness through Mobile Wellness Applications. In: *Lecture Notes in Computer Science (LNCS 6389). Berlin, Heidelberg, Springer, 71-81.*

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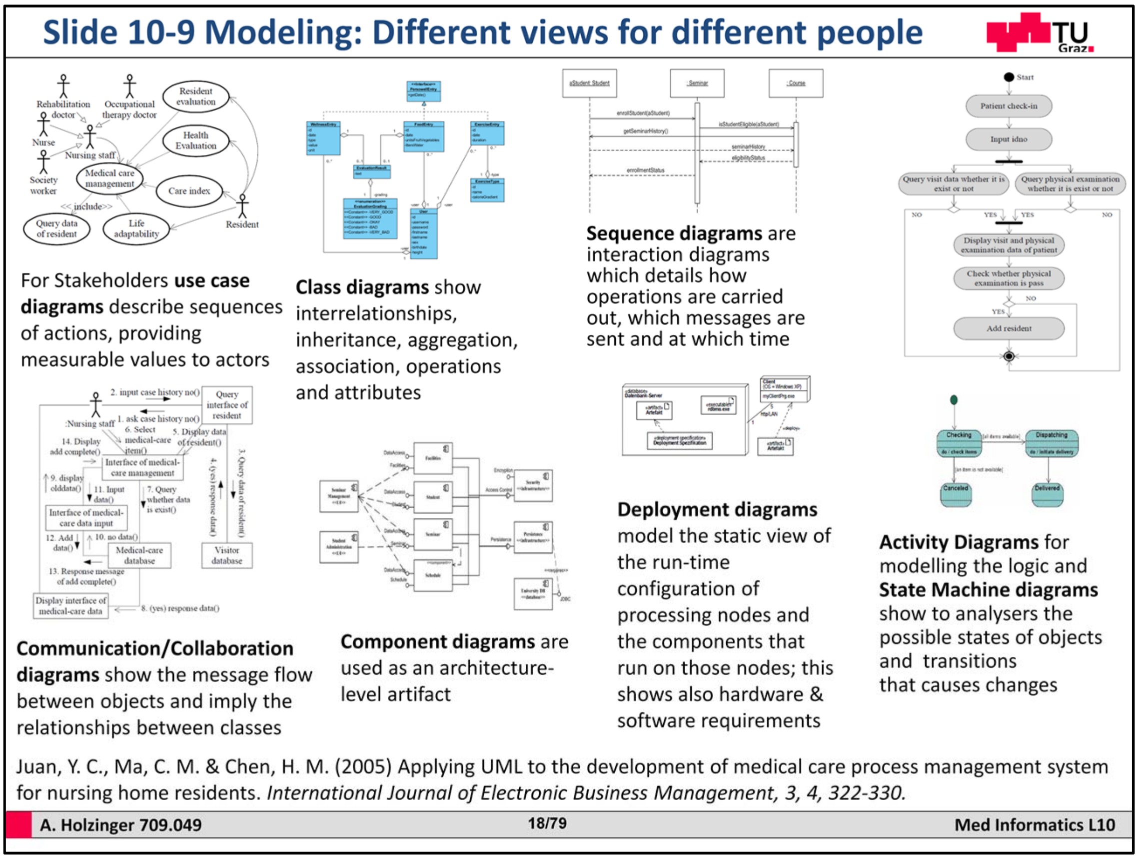
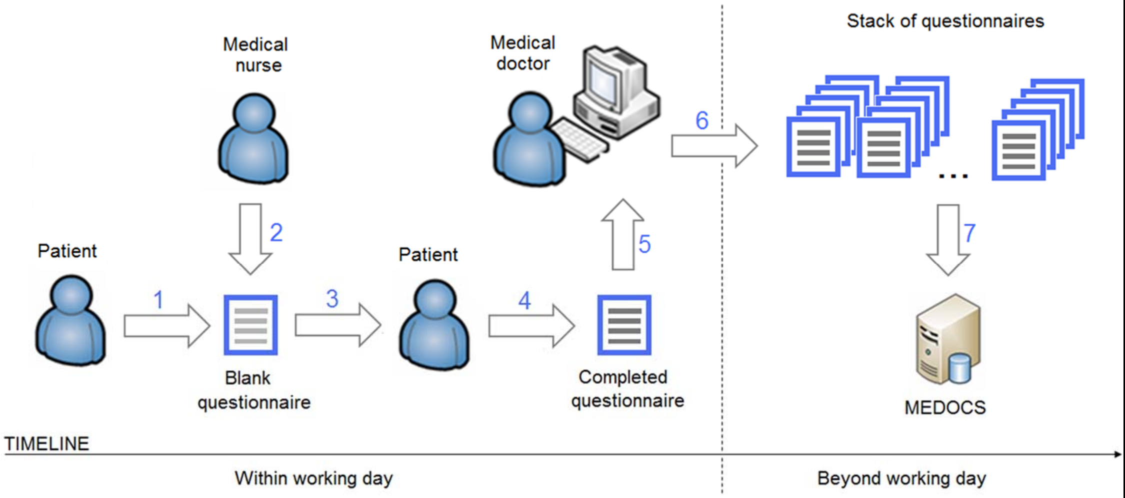
In this slide you see the description of a real-world example by the use of the UML and a corresponding use case diagram (Holzinger et al., 2010).
The Unified Modeling Language (UML) is a standardized (ISO/IEC 19501:2005), modeling language developed from the software engineering domain (Oestereich, 1999). UML includes a set of graphic notation techniques to create visual models of object-oriented systems. Originally, it was developed by (Booch, 1994) and (Booch, Rumbaugh & Jacobson, 1999). It was adopted as a standard in 1997 by the OMG (Object Management Group) and has been managed by this organization ever since. The current version of the UML is 2.4.1 published by the OMG in August 2011.



Although this slide is overcrowded and hard to read – the advantage is having a good overview on the usage of different diagrams – enabling different views for different people.
For Stakeholders use case diagrams describe sequences of actions, providing measurable values to actors.
Class diagrams show interrelationships, inheritance, aggregation, association, operations and attributes.
Sequence diagrams are interaction diagrams which details how operations are carried out, which messages are sent and at which time.
Communication/Collaboration diagrams show the message flow between objects and imply the relationships between classes.
Component diagrams are used as an architecture-level artifact
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 analysts the possible states of objects and transitions that cause changes.

Time is money. Nowhere else this comes out so clearly as in the medical area. Interestingly enough, your very last minutes of life are the most expensive ones. Maybe we should invest more in prevention, quality of life, wellness and wellbeing …

Slide 10-10 Example Clinical Workflow



Holzinger, A., Kosec, P., Schwantzer, G., Debevc, M., Hofmann-Wellenhof, R. & Frühauf, J. (2011) Design and Development of a Mobile Computer Application to Reengineer Workflows in the Hospital and the Methodology to evaluate its Effectiveness. *Journal of Biomedical Informatics, 44, 6, 968-977.*

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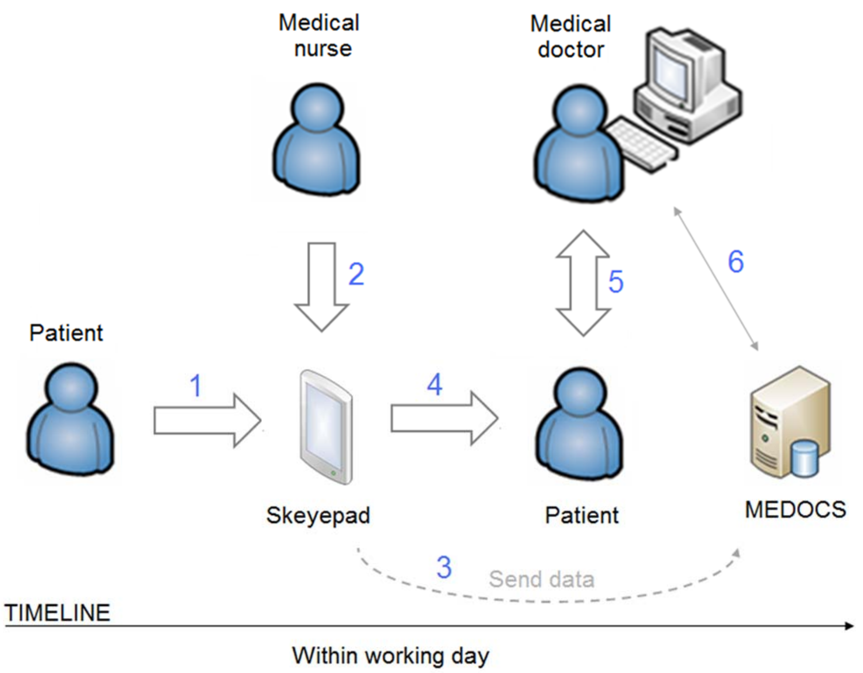
This is an example of how a typical hospital workflow looks like and in the following we will see what computer science can do to help to make such a workflow much more effective. This example is from an outpatient university clinic where questionnaires are very important for supporting research in fighting skin cancer (Holzinger, Sammer & Hofmann-Wellenhof, 2006), (Holzinger et al., 2011).

Look at the slide:

When the patients arrive at the central administration desk of the outpatient clinic, a medical nurse hands them over a paper questionnaire. The patient is asked to complete the questionnaire alone and return it to the nurse, where they are collected together for the medical doctor. Theoretically, the doctor can peruse the paper questionnaire during the treatment, but concentration is usually limited to the patient and the Electronic Patient Record (EPR) displayed on the clinical workplace monitor. Most often, the questionnaires are just gathered and manually typed into a separate electronic database after the clinic is closed – in the spare time of the doctor. Moreover, the separate data base has no direct connection to the electronic patient record of the Enterprise Hospital Information System (EHIS). Consequently, a lot of effort is spent just on typing. Let us look to the next slide, what we can do from a computer science perspective to save time and effort.

Slide 10-11 Example: WF-Optimization with mobile comp



Holzinger et al. (2011)

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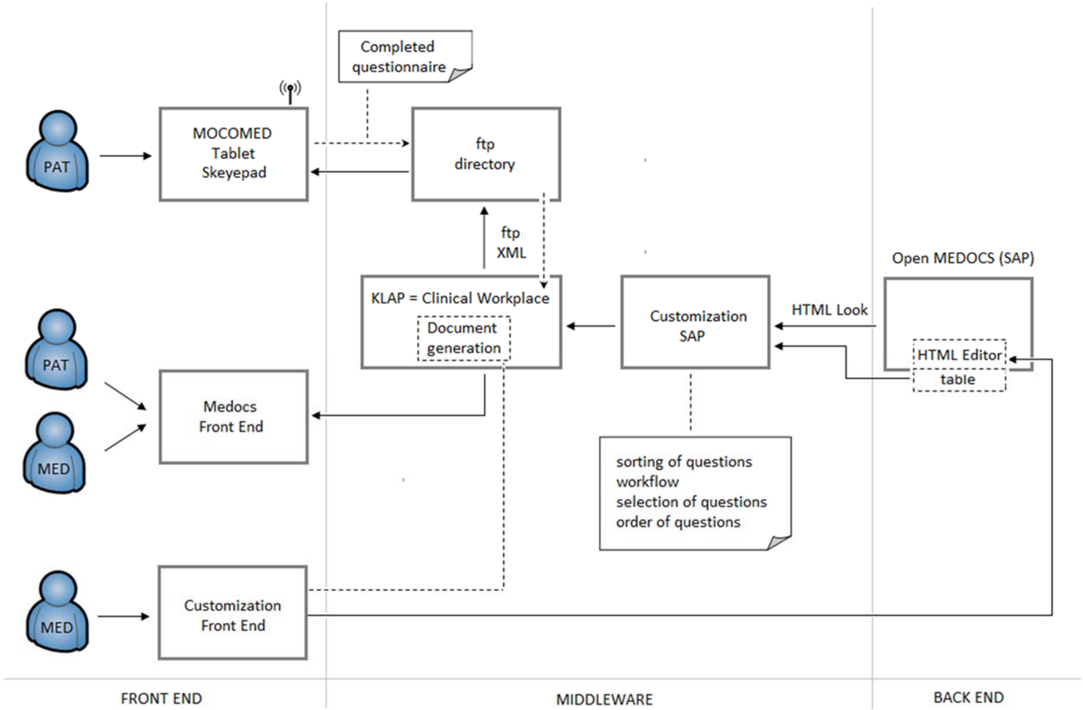
In the new workflow, the patient reports to the central administration desk of the outpatient clinic. There, they are registered anyway via the MEDOCS hospital information system administration program. This will now be used as an patient identifier. At the clinical workplace, a list of the waiting patients, who have been registered already in the system but not yet released by a medical doctor, is displayed, flagged to show whether or not they have already filled out a questionnaire. This is indicated by means of text and/or a symbol and differentiates between a questionnaire which has been made available to the patient, a questionnaire filled out on the current day; and a questionnaire, which was completed by the patient during a previous visit (non-current date) and is still available. When no questionnaire is available the flag column remains empty. The medical doctor or the nursing staff of the clinic can decide whether the patient should complete a questionnaire and whether this should be the long or the short version. Clicking on the relevant icon generates the empty questionnaire and registers it in MEDOCS using a unique identification code which identifies the patient unequivocally as the user. Using an XML communication, the patient identification number (PID), the unique number of the document (document number at the top of the questionnaire) and any further data (e.g. name, date of birth) considered necessary by MoCoMED-Graz, are transmitted. At the terminal, the patient is equipped with a touch based Tablet PC and a code, with which he/she can login to MoCoMED-Graz and complete the questionnaire following a touch based application. The authentication at MoCoMED-Graz is necessary for data security reasons, so that no patient can access other data and patients avoid mistakes or errors. The code is a unique identification number, generated by and linked with the enterprise hospital information systems patient record MEDOCS, ensuring that the proper patient enters the data. An incorrect code entry prompts an error message and the data is not accepted by the system.
After the questions have been answered and the questionnaire is completed, MoCoMED-Graz transfers the questionnaire directly into the MEDOCS system. The corresponding column in MEDOCS now shows the status "questionnaire was filled out on the current day". As soon as the patient has completed the questionnaire, the XML file containing the answers is stored on the server and subsequently transferred to MEDOCS by using a remote function call (RFC). The XML document containing all answers of a patient includes, of course, the unique identification of each. This project serves as an example of how computer application can benefit all three groups of people: patients, medical professionals and hospital managers. Patients were very satisfied with the front end of the application. Medical professionals could save up to 90 % (!) of their formerly wasted time; which ultimately saves money for the hospital manager. Most important, the quality of the medical service is increased, since the newly created workflow brings together patients and doctors in front of the clinical workplace, to check whether all entries are correct.
Since robust, reliable, light and unobtrusive, uncomplicated, appealing hardware is an essential part of the success of such an application in a real-life hospital, the selection of appropriate hardware is an essential success factor. For more details refer to (Holzinger et al., 2011).

Slide 10-12 Mobile Computing Project MoCoMed-Graz



Holzinger et al. (2011)

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Here you see the architecture of this application. PAT = Patient, MED = medical doctor. For details see (Holzinger et al., 2011).

Slide 10-13 Important: Macrolevel – the view of the Manager

Rechenmodell zum Ausfüllen eines Fragebogens in einer Ambulanz		
ohne MoCoMed (Szenario 1)		
Eingebendes Personal	Arzt (1 A)	Schreibkraft bzw. Schalter (1 B)
Personalkosten/h	€ 44,0	€ 19,0
Personalkosten/min	€ 0,73	€ 0,32
Anzahl Patienten/Tag	30	30
Zeitbedarf pro Fragebogen in min.	10	7
Ambulanztage pro Jahr	250	250
Jahreskosten Personal	**€ 55.000**	**€ 16.625**
mit MoCoMed (Szenario 2)		
Eingebendes Personal	Arzt	Schreibkraft bzw. Schalter
Personalkosten/h	€ 44,0	€ 19,0
Personalkosten/min	€ 0,73	€ 0,32
Anzahl Patienten pro Tag	30	30
Zeitersparnis pro Fragebogen in %	90%	90%
Zeitbedarf pro Fragebogen in min.	1,00	0,70
Gerätemanipulationszeit pro Fragebogen in min.		1,00
Ambulanztage	250	250
Jahreskosten Personal	**€ 7.875**	**€ 4.038**
+ Gesamtkosten MoCoMed/Jahr	€ 9.800	€ 9.800
= Jahreskosten TOTAL	**€ 17.675**	**€ 13.838**
Ergebnis		
Eingebendes Personal	Arzt	Schreibkraft bzw. Schalter
Einsparungspotential/Jahr in EUR unter den oa. Annahmen:	**€ 37.325**	**€ 2.788**
Einsparungspotential/Jahr in Std. unter den oa. Annahmen:	**848**	**147**

Entwicklungs- und Betriebskosten MoCoMed	
Kosten pro Personenmonat Entwicklung (EU-Satz)	€ 4.000
Anzahl Personenmonate Entwicklung einmalig	7
Kosten Personal Entwicklung	**€ 28.000**
Investkosten pro Gerät	€ 1.600
Anzahl Geräte	2
Kosten Geräte	**€ 3.200**
Summe Entwicklungskosten	**€ 31.200**
Kosten pro Personenmonat Wartung und Betrieb	€ 4.000
Anzahl Personenmonate Wartung und Betrieb pro Gerät pro Jahr	0,25
Anzahl Jahre (Lebenszyklus)	4
Kosten Wartung und Betrieb auf Lebenszyklus	**€ 8.000**
Gesamtkosten auf Lebenszyklus	**€ 39.200**
Gesamtkosten anteilig/Jahr	**€ 9.800**

Holzinger, A., Kosec, P., Schwantzer, G., Debevc, M., Hofmann-Wellenhof, R. & Frühauf, J. (2011) Design and Development of a Mobile Computer Application to Reengineer Workflows in the Hospital and the Methodology to evaluate its Effectiveness. *Journal of Biomedical Informatics, 44,* ***6, 968-977.***

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From the hospital managers´ point of view, this method may serve as a valuable tool to achieve extensive surveillance data with limited resources, to reduce human errors to a minimum, and to create standardized data sets for further analyses, thus improving skin cancer prevention and quality of care. As patients were actively integrated into their treatment process and provided with a useful way of spending their waiting time, this may also lead to a substantial improvement in patient care services, and therefore increased patient satisfaction., Apart from the time saving benefit, an important aspect for the health system in general, which is also relevant to the hospital managers in terms of quality of patient treatment is the increased patient empowerment. For clearly depicting the benefit for the hospital management, a scenario analysis has been made by calculating the facts in this particular outpatient clinic on the basis of N = 30 patients a day, 250 days a year.

Scenario 1 (without mobile computers): A doctor costs the hospital approx. 44 EUR per hour = 0.73 EUR per minute. With an average of 10 minutes per patient, the 300 minutes of extra effort required by the doctors to transcribe the questionnaires are equivalent to 219 EUR per day = 55 kEUR per year and there is the additional risk of lost and missing data.

We also tested the alternative of letting copy typists transcribe the data: They are faster median = 7 minutes (min: 5 minutes; max: 8 minutes), however, since they are not medical professionals they make more errors, which cannot be corrected without extra costs. Calculating on the basis of their average hourly wages results in a cost of 19 EUR per hour = 0.32 EUR per minute, we have costs of approx. 17 kEUR per annum.

Scenario 2 (using two mobile computers):

Development Costs: 7 Person Months = 28 kEUR

Hardware Costs: 3.2 kEUR

Original cost of acquisition = 31.2 kEUR

Annual service costs: 0.5 Person mpy = 2 kEUR

The reduction to only 30 minutes of the medical doctors time per day is equivalent to 22 EUR per day or approx. 5.5 kEUR per year.

Total annual costs = 7.5 kEUR

Assuming an average life span of 4 years, this amounts to a total of 31.2+(4*7.5) = 61.2 kEUR, or 15.3 kEUR per annum.

Maximum total possible cost saving per year: 55 kEUR – 15.3 kEUR = 39.7 kEUR

Minimum total possible cost saving per year: 23.5 kEUR – 15.3 kEUR = 8.2 kEUR

You clearly see the benefit of such an application – reached through careful workflow optimization.

Slide 10-14 MoCoMED-Graz in operation

Holzinger et al. (2011)

Finally, have a view on the front-end of this application – from the patient side.

Slide 10-15 MoCoMedGraz Project – Benefit Summary

- 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**

Holzinger, A., Kosec, P., Schwantzer, G., Debevc, M., Hofmann-Wellenhof, R. & Frühauf, J. (2011) Design and Development of a Mobile Computer Application to Reengineer Workflows in the Hospital and the Methodology to evaluate its Effectiveness. *Journal of Biomedical Informatics, 44,* ***6, 968-977.***

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What can we learn out of this project: Most of all you must acknowledge that different people have different views, different expectations and different goals. To provide a clear benefit, an application should satisfy different requirements and most of all should bring a clear – measurable (!) – benefit. Time to perform a task is still a major issue, easy to measure and pays-off. Time is money. If you save time of a medical professional, you save money, but at the same time you enhance quality! For evaluation purposes the ecological systems theory by (Bronfenbrenner, 1977) is useful, which originates from child development theory and describes the interaction between various environments using a layer structure – each having an effect on a child's development. Originally, Bronfenbrenner described five such layers:

a) the microsystem, which encompasses relationships and interactions within the person's direct environment – from the individual persons' point of view.
b) the mesosystem, which describes the interaction between the microsystem and the
c) the exosystem , which defines the larger social system in which the person does not function directly.
d) the macrosystem, which includes the cultural values, customs, and laws
e) the chronosystem, which encompasses the dimension of time as it relates to a persons' environment.

The essence is that interactions at outer levels have always impact on the inner structures. For our purpose, we instrumentalized only three of Bronfenbrenners layers : microsystem, mesosystem and macrosystem and we them into our context:

1) the microsystem relates to the end user and their immediate environment (end user centered human-computer interaction: user tasks, patient empowerment, …)
2) the mesosystem relates to the medical professionals and their environment (professional process centered human-computer interaction: work tasks, medical processes, social context, i.e. discussing the medical data together with the patient – strong influence on patient empowerment, …)

Slide 10-16 Summary: Workflows in Bioinformatics

- 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).

Hasan, S., Daugelat, S., Rao, P. S. S. & Schreiber, M. (2006) Prioritizing genomic drug targets in pathogens: application to Mycobacterium tuberculosis. *PLoS Computational Biology, 2, 6, e61.*

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We can summarize: A data-driven procedure consisting of one or more transformation processes can be seen as nodes and thus can be represented as a directed graph, where the direction is time – i.e. the order of transformations and a set of transformation rules. The data flow origins from a source to a destination (or result) via a series of data manipulations and the specification is designed in a Workflow Design System (modeling component) and then run by a Workflow Management System (execution component) (Hasan et al., 2006).

Slide 10-17 Bioinformatics Workflow Management System

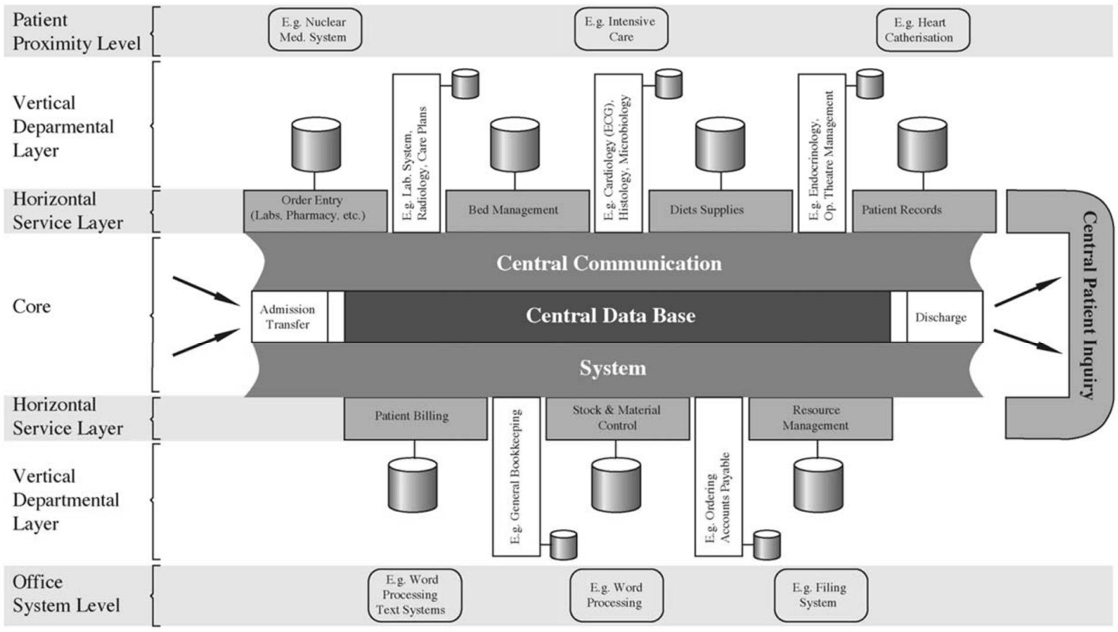
- Def.: WMS = a system that defines, creates and manages the execution of workflows. Its main components include:
- 1) a graphical interface for composing workflows, entering data, watching execution, displaying results;
- 2) an data archive to store workflow descriptions, results of executions and related 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.

Romano, P. (2008) Automation of in-silico data analysis processes through workflow management systems. *Briefings in Bioinformatics, 9, 1, 57-68.*

(Romano, 2008) described the components of a WMS in the bioinformatics domain.
Note: 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

Slide 10-18 Remember: Classic Conceptual Model of a HIS



Reichertz, P. L. (2006) Hospital information systems - Past, present, future. *International Journal of Medical Informatics, 75, 3-4, 282-299.*

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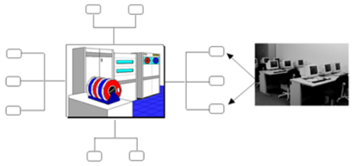
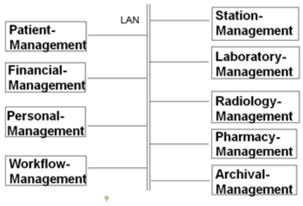
Remember the classic architecture of a Hospital Information System which we have already discussed in →Lecture 4. Managing all clinical information is a challenge implying huge constraints, because healthcare providers use technology in a ubiquitous manner. Medical information systems (e.g., Hospital Information Systems (HIS), Picture Archiving and Communication Systems (PACS), Radiology Information Systems (RIS) and Laboratory Information Systems (LIS)) are used in parallel together and are often heterogeneous. A process-oriented HIS has to be modified whenever the business process changes, i.e., it must be adjustable to process changes and to changing organizational structures very quickly and at reasonable costs (Dadam, Reichert & Kuhn, 2000).

Slide 10-19 Architectures of Hospital Information Systems

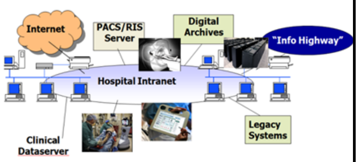
1970+ **“Vertical Approach”** – monolithic mainframes
Central computer systems mainly for accounting, typical “data processing” (“EDV”)



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



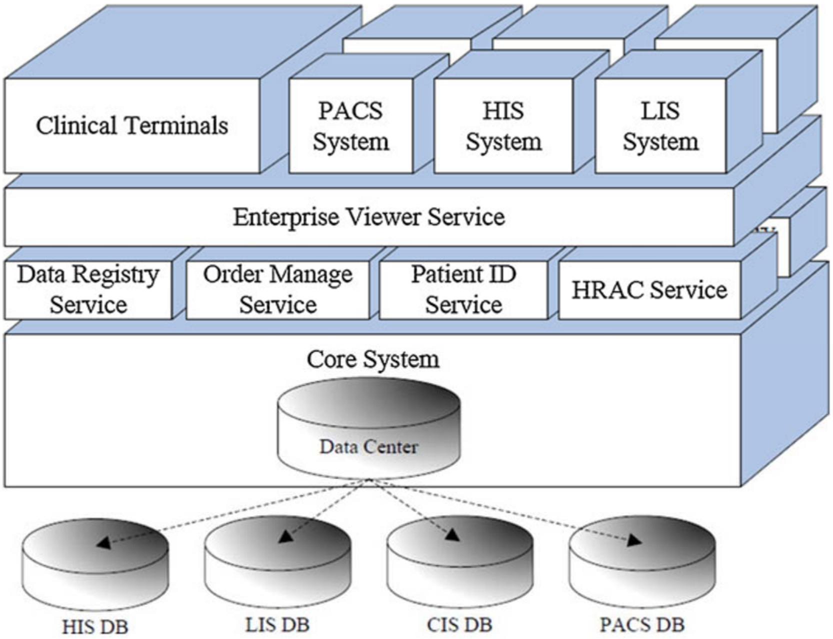
2000+ **“Integrated Approach”** – open, distributed systems
Hospital Intranets, electronic patient/health record, mobile computing, “information quality focus”



Holzinger, A. (2002) *Basiswissen IT/Informatik Band 1: Informationstechnik. Das Basiswissen für die Informationsgesellschaft des 21. Jahrhunderts. Wuerzburg, Vogel Buchverlag.*

There is a need to integrate the various theoretical frameworks and formalisms for modeling clinical guidelines, workflows, and pathways, in order to move beyond providing support for individual clinical decisions and toward the provision of process-oriented, patient-centered HIS that formally model guidelines, workflows, and care pathways (Gooch & Roudsari, 2011).
Historically, we determine between three different system architectures:
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, networked electronic patient/health record, mobile computing, “information quality focus” (Holzinger, 2002).

Slide 10-20 Basic architecture of a standard HIS



El Azami, I., Cherkaoui Malki, M. O. & Tahon, C. (2011) Integrating Hospital Information Systems in Healthcare Institutions: A Mediation Architecture. *Journal of Medical Systems, (in print), 1-12.*

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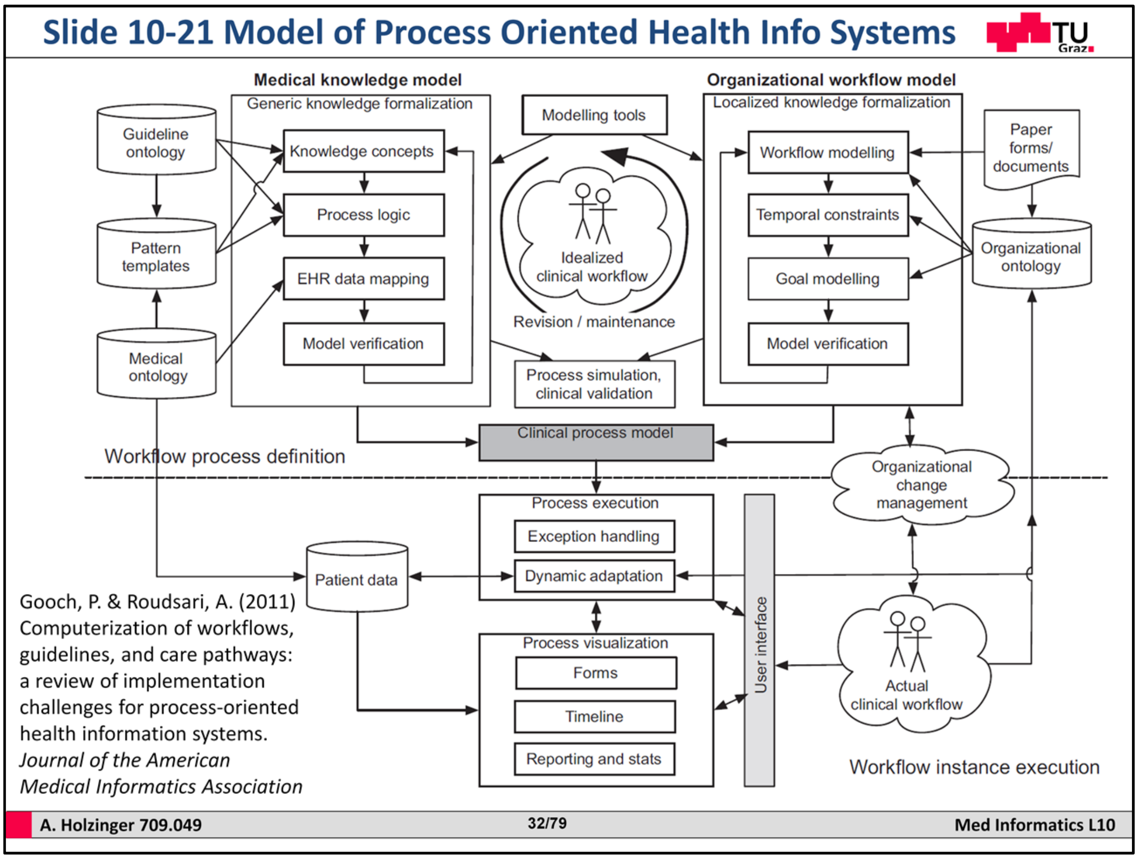
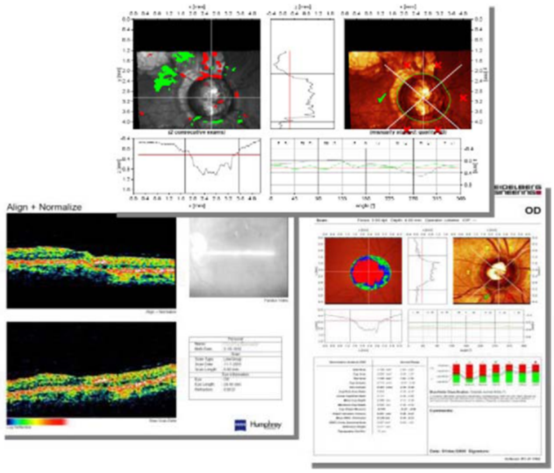
A standard universal integrated architecture contains a data center – fusing together the data from the main data bases (patient records, laboratory information system, PACS storage, etc.) and a integrated view in terms of a clinical workplace (El Azami, Cherkaoui Malki & Tahon, 2012).



Coming back to a grand challenge: data integration and data fusion in the life sciences: There is a need to integrate the various theoretical frameworks and formalisms for modeling clinical guidelines, workflows, and pathways, in order to move beyond providing support for individual clinical decisions and toward the provision of process-oriented, patient-centered HIS that formally model guidelines, workflows, and care pathways. One approach can be seen in this slide, where different workflow models and data models and knowledge models are combined and used for the overall clinical process model (Gooch & Roudsari, 2011).

Multimedia in the Hospital

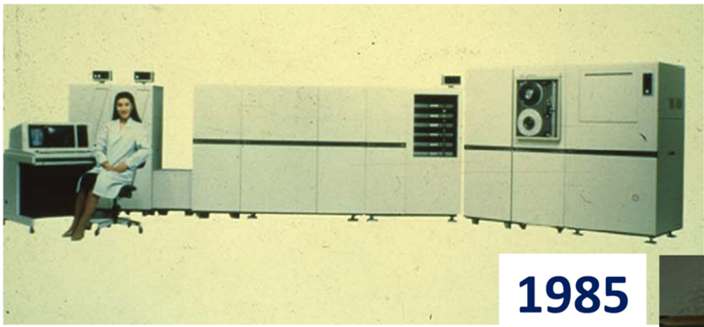
Slide 10-22 Multimedia throughout the Hospital



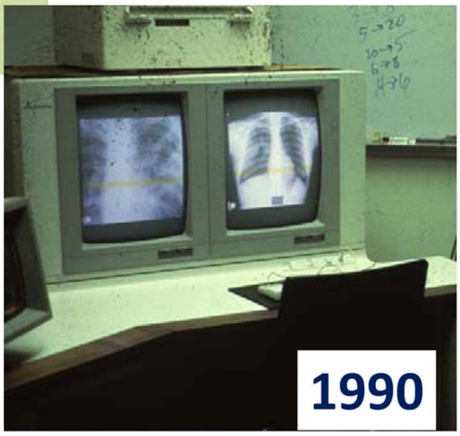
Bellon, E., Feron, M., Deprez, T., Reynders, R. & Van den Bosch, B. (2011) Trends in PACS architecture. *European Journal of Radiology, 78, 2, 199-204.*

Various medical departments generate images or videos for medical documentation. Although these images are lightweight from a technological perspective, the workflows for image generation and viewing are very diverse (Bellon et al., 2011).
In primary diagnosis images must often be acquired in a separate step before diagnosis is possible, e.g. when images are generated using ionizing radiation, radio waves, laser beams (e.g. optical coherence tomography, retinal thickness analysis, etc.) or fluorescence (fluorescein angiography, etc.). In contrast, in pathology using visual light microscopy diagnosis can be performed by direct observation, but even for this application there are advantages obtaining an image first by using the computer as a digital microscope. Such "virtual microscopy" images contain many thousand pixels along each direction. This huge storage (much higher than in radiology) makes routine use difficult. Workflows in many cases are similar to radiology, however, not in the completely different class of applications in which images or short video sequences are not needed for primary diagnosis, but are obtained for later reference, e.g. to facilitate discussion with colleagues, to document the case, or for communication with the patient (left in the Slide). For such "reference images, quality usually is not a concern and technological needs are low. In many cases the acquisition devices are consumer products such as digital photo cameras that do not support DICOM related concepts. For example, many systems in ophthalmology output reports in the form of a document containing text, numbers, graphs, and some images (right in the Slide). Even if some new equipment might be able to generate a DICOM structured report, most systems just generate output on paper. An easy but efficient way to capture the latter documents into an electronic system is to replace the traditional paper printer by a virtual printer that generates PDF. In a third class of applications there is a real-time aspect, for example in surgery (endoscopic cameras for keyhole surgery, fluoroscopic imaging equipment, vital signs monitors, surgical robots, image processing applications for intra-surgical guidance etc.).

Slide 10-23 1st commercial Picture Archiving & Comm. System



1985



Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

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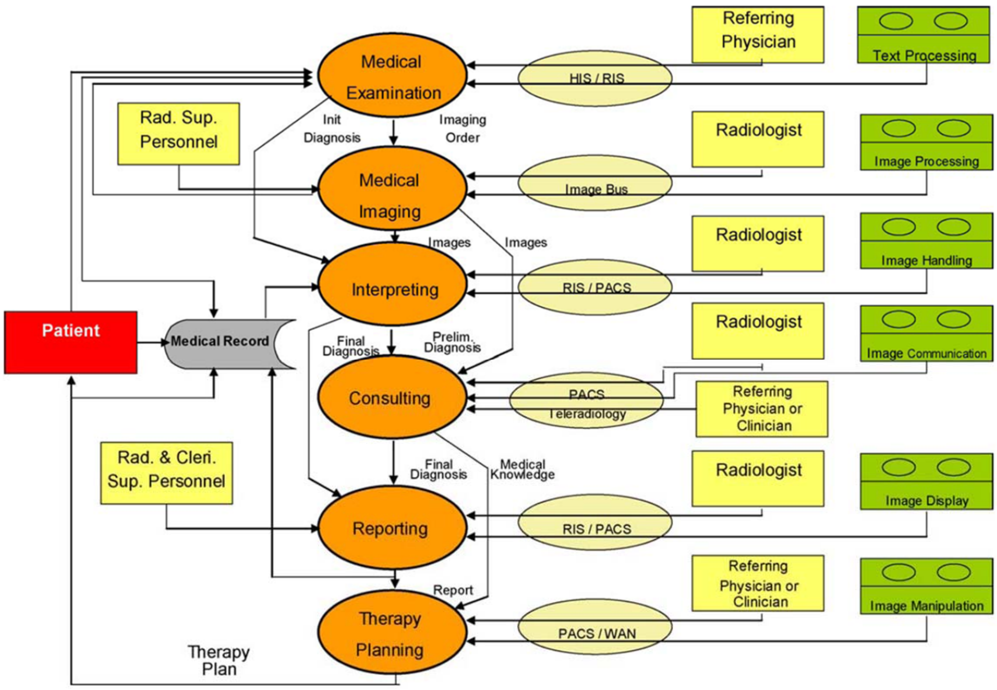
A PACS (Picture Archiving and Communication System) is still primarily associated with radiology, but can handle images from various medical sources, including ultrasound (US), magnetic resonance (MR), positron emission tomography (PET), computational tomography (CT), endoscopy (ES), mammograms (MG), etc. In the Slide above we see the first commercial PACS installation in the US – a Fuji CR-101 system at the Osner Clinics, New Orleans. Below we see a PACS console from 1990 (Huang, 2011).

Note: Although the concept of PACS was developed in Europe during the late 1970s, no commercial system was completed at that time. The first PACS implementations took place in the United States in the early 1980s, e.g. at Pennsylvania University, UCLA, Kansas City University and the Osner Clinics, New Orleans. Some more or less successful PACS developments also took place in Europe in the 1980s – and Graz was amongst the first PACS installations. Most systems could be characterized by their focus on a single department, such as radiology or nuclear medicine. Hospital-wide PACS evolved in the early 1990s in London (Hammersmith Hospital) and Vienna (SMZO) (Lemke, 2003), (Lemke, 2011).

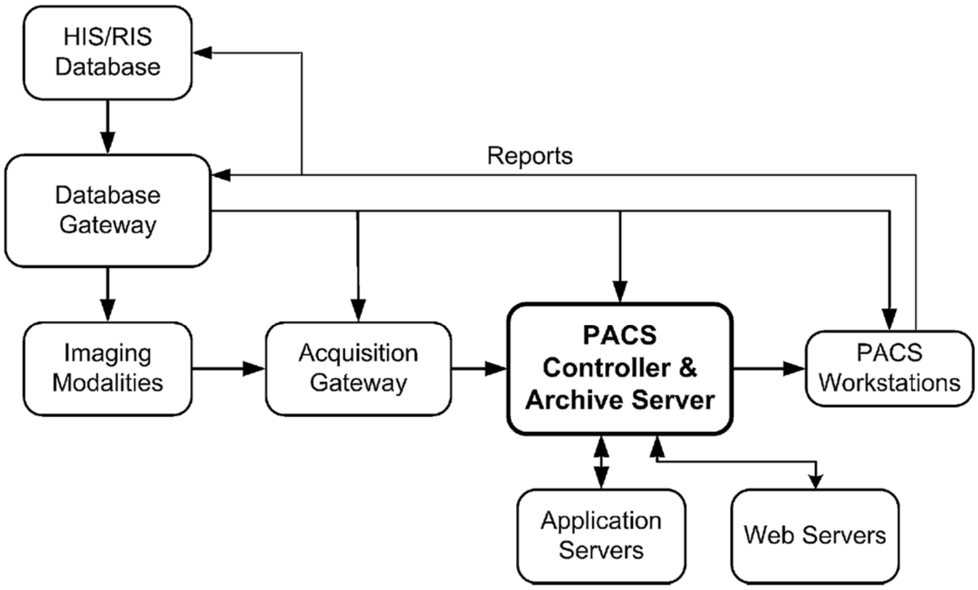
Slide 10-24 Typical Workflow in a European PACS



Lemke, H. (2011) Short history of PACS (Europe). *European Journal of Radiology, 78, 2, 177-183.*

A typical workflow can be seen in this slide: The dark oval symbols indicate the activity steps of the clinical process from examination to therapy planning on a low granulation level. Bright rectangular symbols indicate the personnel involvement in the activity steps, light beige oval symbols indicate IT system support for the given activities, and dark rectangular symbols indicate the functionalities of medical workstations supporting the given activities (Lemke & Berliner, 2011), (Lemke, 2011).

Slide 10-25 Generic PACS components and data flow



Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

In this slide we see the PACS basic components and data flow; HIS: Hospital Information System; RIS: Radiology Information System. System integration and clinical implementation are two other necessary components during the implementation after the system is physically connected. Application Servers and Web Servers connected to the PACS controller enrich the PACS infrastructure for other clinical, research and education applications (Huang, 2011).
Note: Imaging modalities are the different image generating devices, e.g. CT, PET, MR, etc.
(has nothing to do with the modality known from multimedia theory)

Data Standards for Communication and Representation

Remember that we already learned about the importance of standards for both technology and data.

Slide 10-26 Data Standards for Comm. & Representation

- **DICOM 3.0 – Digital Imaging and Communication in Medicine** (1993)
  - 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, ant 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

Bui, A. A. T. & Taira, R. K. (2010) *Medical Imaging Informatics. New York, Heidelberg, London, Springer.*

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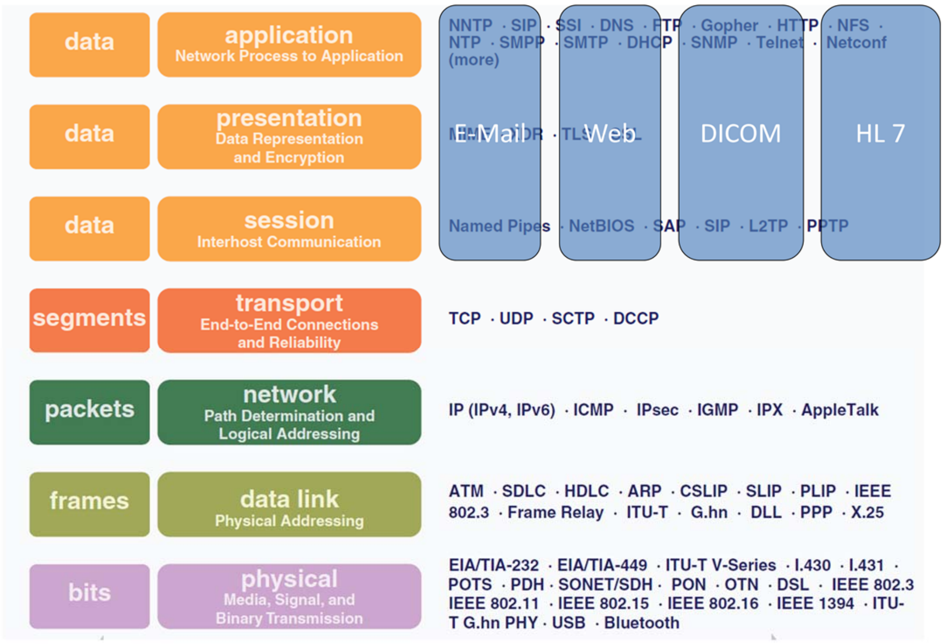
In the context of hospital information systems in general and with medical imaging in particular, three standards have a significant importance: DICOM, HL7 and LOINC (Bui & Taira, 2010):
DICOM 3.0 – Digital Imaging and Communication in Medicine (1993) is …
1) a set of protocols for network communication;
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 is a 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, ant 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 is used for …
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 etc.).

Slide 10-27 DICOM and HL 7



Williams, R. (2011) Network Concepts.
In: *An Introduction to Trading in the Financial Markets. San Diego, Academic Press, 201-225.*

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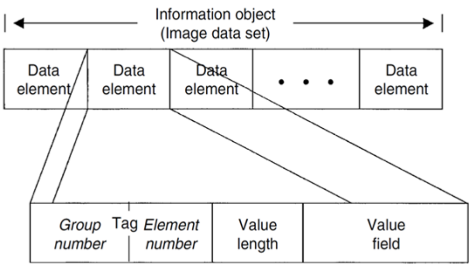
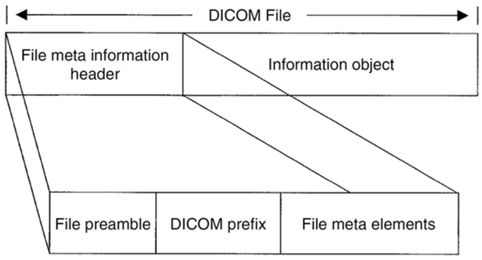
In this compact overview we see the ISO OSI Reference Layer model showing the most common protocols and data standards, from the physical level up to the application level (= level 7).
HL7 (Health Level 7) is both an organization and a standard, which was founded in 1987 aiming at a general standard for hospital information systems. The organization was accredited in 1994 by the American National Standards Institute. The name is a reference to the seventh layer of the ISO OSI Reference layer model aka application layer and indicates that it focuses on that layer, independent of the layers. All relevant information can be retrieved from the Website: http://www.hl7.org

Slide 10-28 DICOM Object containing multiple data elements





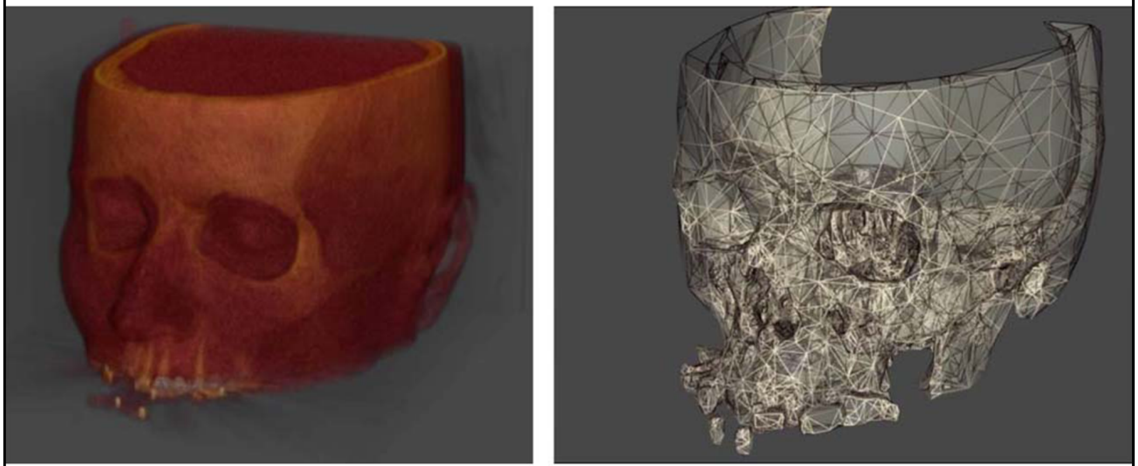
Each data element is uniquely identified by its corresponding tag composed of a group number and an element number. Pixel data of the image is stored in element 0010 within group 7FE0.

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.

Wong, A. & Lou, S. L. (2009) Medical Image Archive, Retrieval, and Communication. In: Isaac, N. B. (Ed.) *Handbook of Medical Image Processing and Analysis (Second Edition). Burlington, Academic Press, 861-873.*

Communication of images between medical imaging systems and among their applications has always been difficult because of the multiple platforms and vendor-specific communication protocols and data formats.
The DICOM standard, developed in 1992 by a joint committee formed by the American College of Radiology (ACR) and the National Electrical Manufacturers Association (NEMA), is intended to provide connectivity and interoperability for multivendor imaging equipment, allowing communication of images and exchange of information among these individual systems. Medical images are defined in DICOM as information objects or datasets. An information object represents an instance of a real-world information object (i.e., an image) and is composed of multiple data elements that contain the encoded values of attributes of that object. Each data element is made of three fields: the data element tag, the value length, and the value field. The data element tag is a unique identifier consisting of a group number and an element number in hexadecimal notation and is used to identify the specific attribute of the element (Wong & Lou, 2009).
Look at the slide (left side): 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. Look at the right side: 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. (Wong & Lou, 2009).

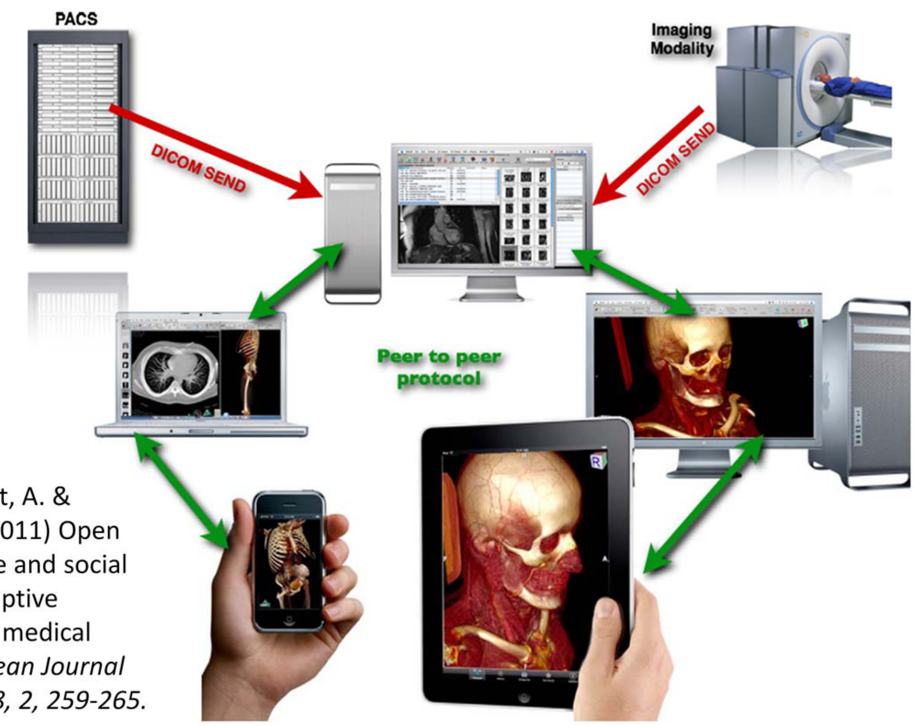
Slide 10-29 DICOM instances allowing the storage of meshes



Lemke, H. U. & Berliner, L. (2011) PACS for surgery and interventional radiology: Features of a Therapy Imaging and Model Management System (TIMMS). *European Journal of Radiology, 78, 2, 239-242.*

This is just an example: A special DICOM Supplement defines a way to store and communicate meshes as DICOM instances, allowing the storage of the meshes together with the images on a PACS server – meshes are important for computer assisted surgery (Lemke & Berliner, 2011).

Slide 10-30 Image distribution workflow



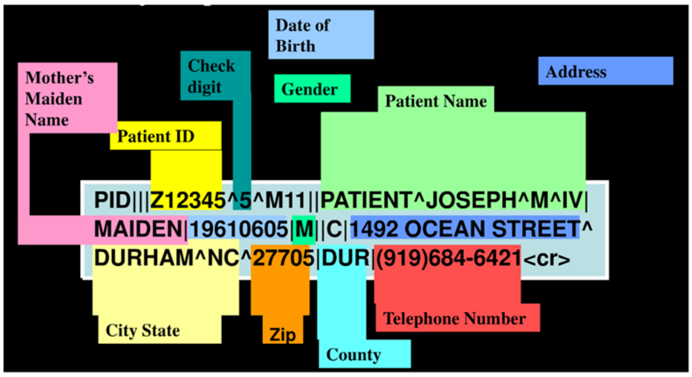
Ratib, O., Rosset, A. & Heuberger, J. (2011) Open Source software and social networks: Disruptive alternatives for medical imaging. *European Journal of Radiology, 78, 2, 259-265.*

In the last years many changes in computer and communication technology have pushed the limits of PACS beyond the traditional system architecture providing new perspectives and innovative approaches to a traditionally conservative medical community. Technologies such as the Web, wireless networking, Open Source software and recent emergence of cyber communities and social networks have imposed an accelerated pace in the progress of computer and technology infrastructure applicable to medical imaging applications.
In this slide we see some modern approaches: Industry has started to adopt OSIRIX as a base for new business models where they provide the support and integration of services as well as training and customization of generic platforms. Several certified versions for Europe and for FDA in the US have already appeared on the market recently. And finally, and probably most importantly, the academic community has started to regroup its efforts to support and promote Open Source initiatives in medical imaging and medical informatics (Ratib, Rosset & Heuberger, 2011).
OSIRIX software program and its source code are available under Open Source licensing agreement and can be downloaded free of charge at: http://www.osirix-viewer.com

Slide 10-31 HL7 Use Case: serum glucose lab result

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.

```
MSH|^~\&|GHH LAB|ELAB-3|GHH OE|BLDG4|200202150930||ORU^R01|CNTRL-3456|P|2.4<cr>
PID|||555-44-4444||EVERYWOMAN^EVE^E^^^^L|JONES|19620320|F|||153 FERNWOOD DR.^
^STATESVILLE^OH^35292||(206)3345232|(206)752-121||||AC555444444||67-A4335^OH^20030520<cr>
OBR|1|845439^GHH OE|1045813^GHH LAB|15545^GLUCOSE|||200202150730|||||||||
555-55-5555^PRIMARY^PATRICIA P^^^^MD^^|||||||||F||||||444-44-4444^HIPPOCRATES^HOWARD H^^^^MD<cr>
OBX|1|SN|1554-5^GLUCOSE^POST 12H CFST:MCNC:PT:SER/PLAS:QN||^182|mg/dl|70_105|H|||F<cr>
```



| - FIELD DELIMITER
^ - SUB FIELD DELIMITER
& - SUB-SUB FIELD DELIMITER
~ - SEPARATOR - REPEATING FIELDS
\- ESCAPE CHARACTER

Examples: http://www.ringholm.com/docs/04300_en.htm

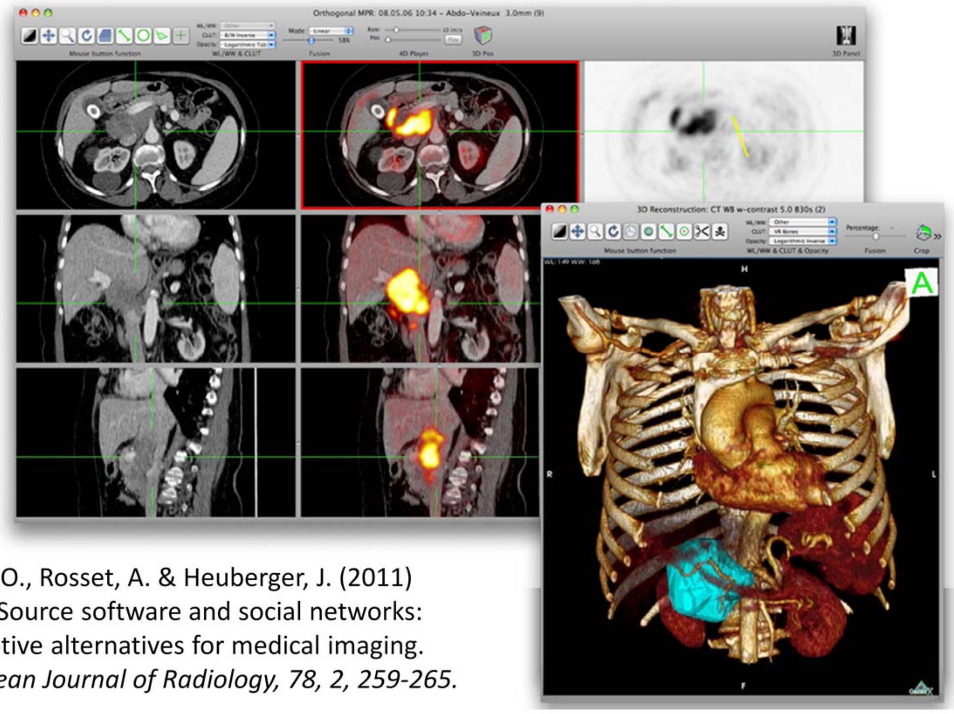
This slide show an example business use case related to a laboratory results message, as well as a V2.4 and a v3 representation. The v3 message is based upon the normative XML ITS 1.0 and schema from the May 2006 Informative Edition of HL7 v3. The use case is the completion of a serum glucose laboratory result of 182 mg/dL authored by Howard H. Hippocrates. The laboratory test was ordered by Patricia Primary for patient Eve E. Everywoman. The use case takes place in the US Realm. See more details via: http://www.ringholm.com/docs/04300_en.htm

Slide 10-32 PACS consoles and modern workplaces

Ratib, O., Rosset, A. & Heuberger, J. (2011) Open Source software and social networks: Disruptive alternatives for medical imaging. *European Journal of Radiology, 78, 2, 259-265.*

This slide shows a PACS console and a typical PACS-Viewer, which runs meanwhile on standard platforms such as Mac or Windows.

Slide 10-33 Multimodal imaging techniques: Hybrid PET-CT



Ratib, O., Rosset, A. & Heuberger, J. (2011)
Open Source software and social networks:
Disruptive alternatives for medical imaging.
European Journal of Radiology, 78, 2, 259-265.

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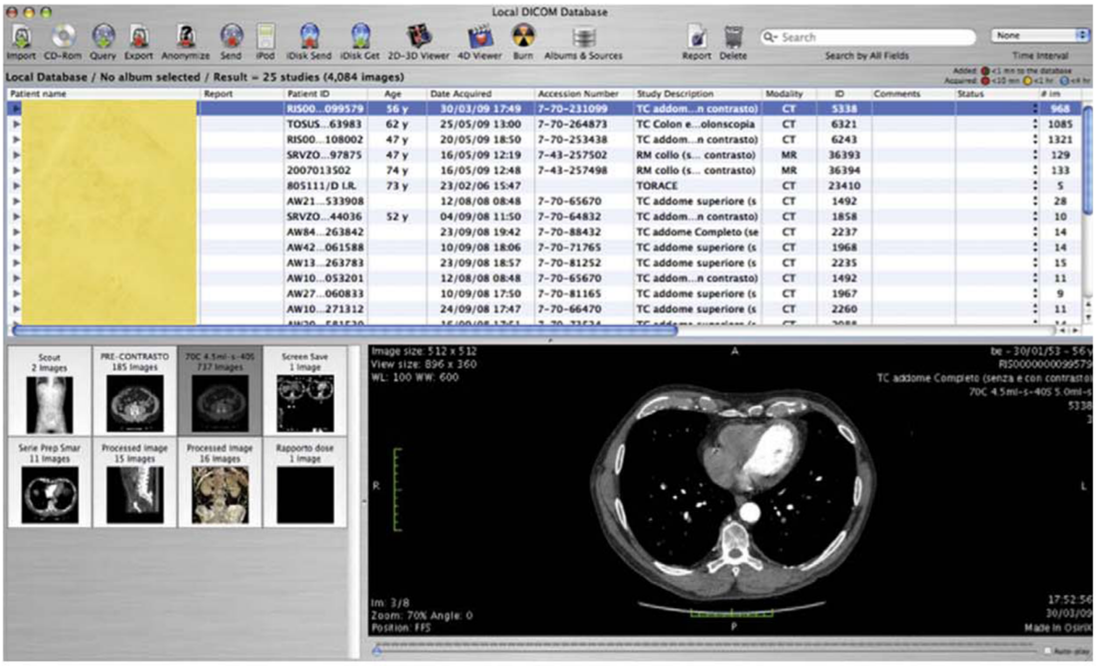
In this slide we see advanced image display and analysis tools adapted to multimodality imaging techniques such as hybrid PET-CT images showing multi-planar reformatting of fused images (back window) as well as volume rendering and segmentation of tumor outline from PET images (front window).
Development of commercial systems driven by medical imaging manufacturers lags behind the increasing demand for such advanced processing tools. Industry usually follows research and clinical validation slowly and requires several years before releasing new products on the market. The certification processes within the medical area are long lasting and costly; therefore each vendor tries to sell their available products as long as possible.
Although Open Source and free software is becoming more widely adopted in the medical community it is still rare that a hospital (especially a public one) adopt these to their daily routine. Private hospitals are more open for advanced technologies in general as they have usually a shorter decision chain in the hospital management.
Open Source would not only provide a cost effective alternative, but, because they are being developed by a community of developers from the field, the software tools can be customized to match the needs and specific usage in clinical setups outside radiology. Also Open Source have less restrictions on providing new innovative and challenging viewing and analysis tools that respond to users demands even before industry and commercial vendors identify these new trends as potential source of revenue (Ratib, Rosset & Heuberger, 2011).

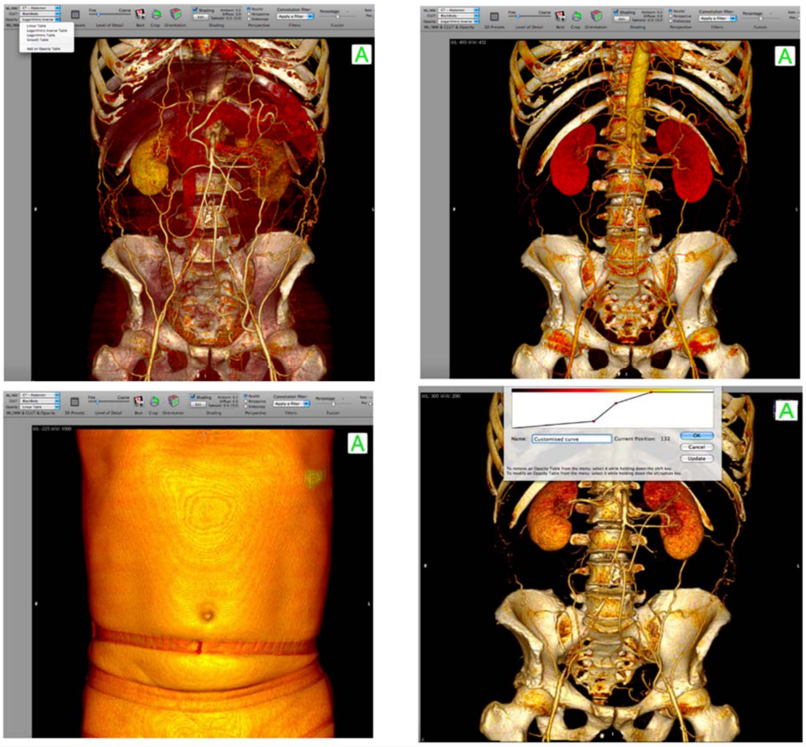
Slide 10-34 Example: OsiriX integrated RIS–PACS interface



Faggioni, L., Neri, E., Castellana, C., Caramella, D. & Bartolozzi, C. (2011) The future of PACS in healthcare enterprises. *European Journal of Radiology, 78, 2, 253-258.*

This slide shows an OsiriX integrated RIS–PACS interface: a query list for retrieval from PACS and image list for a given PACS-retrieved examination. Note: The Radiological Information System (RIS) is often part of the general Hospital Information System (HIS).
The increasing availability of such integrated RIS–PACS solutions for image reading and reporting of medical imaging examinations has fuelled the development of integrated tools for digital image processing. This evolution represents a further step towards total integration of all instruments needed for interpretation and reporting of diagnostic imaging examinations in a health service environment, i.e. at a universal clinical workplace. Technical problems have been faced, especially in early times, due to stringent hardware and software requirements for accomplishing such tasks (Faggioni et al., 2011).
More information about the open-source software OsiriX can be found here: http://www.osirix-viewer.com

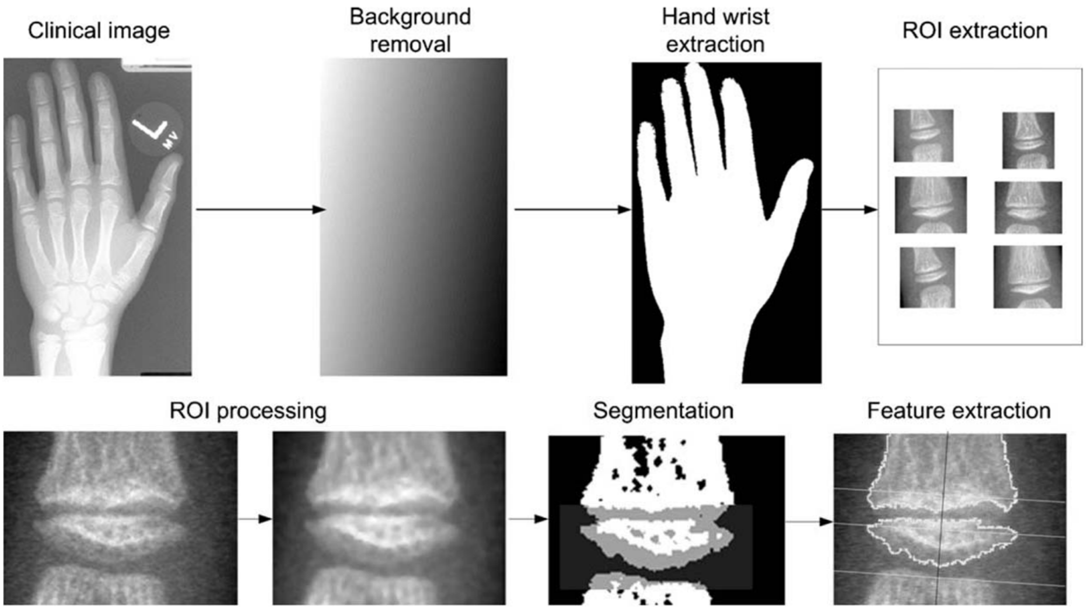
Slide 10-35 Example: Application of VR in medical imaging



Faggioni et al. (2011)

Radiologists were ever since the drivers in imaging technologies and they constantly are adopting advanced technologies into routine. Here an example of the application of Virtual Reality in medical imaging (Faggioni et al., 2011).

Slide 10-36 Bone age assessment DSS workflow

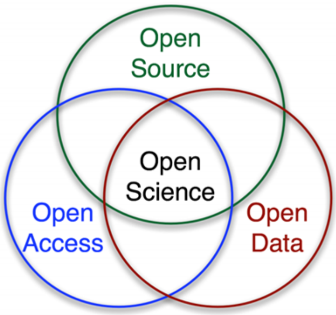


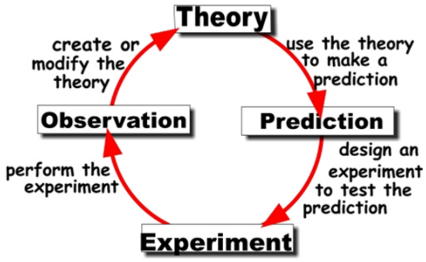
Piętka, E., Kawa, J., Spinczyk, D., Badura, P., Więcławek, W., Czajkowska, J. & Rudzki, M. (2011) Role of radiologists in CAD life-cycle. *European Journal of Radiology, 78, 2, 225-233.*

Meanwhile many preprocessing and imaging processing techniques are integrated in the radiological workplace as can be seen here on the example of a workflow of the automated assessment of the skeletal maturity. Regions that may deliver false positives are excluded from the analysis. Due to the individual variability, some landmarks may be pointed in order to precisely define the size of the Region of Interest (RoI). Typically, two types of RoIs are defined: The first one, usually of a rectangular shape, shrinks the area to be searched and permits robust segmentation procedures. These regions are pointed by radiologists as areas of a strong discriminative power that feature significant changes during the development of the process to be described. As an example, distal, middle, and proximal regions in the phalanges have been pointed by radiologist as areas very sensitive to the development of the skeletal system. 'The more distal the better' is their opinion. Another region pointed by radiologists includes the carpal bones. They happen to be good indicators at the early stage of the skeletal development. The other type of the RoIs is related to anatomical structures. If an abnormal tissue is searched within a certain structure (lung, liver, brain, etc.), this structure has to be segmented in the first place. The required accuracy of the delineation depends on a possible location of the pathological tissue within this structure. If the tissue is attached to the border and, in addition, its pixel (voxel) intensity is similar to the intensity of the neighbourhood, a problem dependent procedure has to be developed in order to delineate the structure (Piętka et al., 2011).

Open …

Open …





License	Apache	BSD/MIT	GPL	LGPL	MPL/CDDL	CPL/EPL
Reciprocity	No	No	Yes	Maybe	No	No
Modification release	No	No	Yes	Yes	Yes	Yes
Patent	Yes	No	No	No	Yes	Yes
Jurisdiction	Silent	Silent	Silent	Silent	California	New York
Freedom	PR	Free	PR	PR	Free	PR

Braun, M. L. & Ong, C. S. 2014. Open Science in Machine Learning. Implementing Reproducible Research, 343.

Holzinger, A. 2010. Process Guide for Students for Interdisciplinary Work in Computer Science/Informatics. Second Edition, Norderstedt, BoD.

GPL = General Public License (alos GNU)

The rights of the developer to redistribute a modified product. A comparison of open source software licenses listed as “with strong communities” on
http://opensource.org/licenses/category. The reciprocity term of GPL states that
if derivative works from a GPLed licensed software are distributed in binary form, then the
recipient of the binary form must also be given the source code of the derivative work licensed under the same GPL license. Other important questions are whether the source code
to modifications must be released (Modification release); whether it provides an explicit license of patents covering the code (Patent); the legal jurisdiction the license falls under
(Jurisdiction); freedom to adapt licence terms (Freedom) (PR = Permission Required from
license drafter). Apache: License used by the Apache web server; BSD: License under which
the BSD Unix variant is released; MIT: developed by the MIT; GPL/LGPL: (lesser) GNU
General Public License; MPL: License used by the Mozilla web browser; CDDL: Common
Development and Distribution License developed by Sun Microsystems based on the MPL;
CPL: Common Public License published by IBM; EPL: Eclipse Public License used by the
Eclipse Foundation, derived from the CPL.

The foundations of Science:

To replicate an experiment or study, either by the same researcher or by someone else working independently. Reproducibility is one of the main principles of the scientific method.

The values obtained from distinct experimental trials are said to be commensurate if they are obtained according to the same reproducible experimental description and procedure. The basic idea can be seen in Aristotle's dictum that there is no scientific knowledge of the individual, where the word used for individual in Greek had the connotation of the idiosyncratic, or wholly isolated occurrence. Thus all knowledge, all science, necessarily involves the formation of general concepts and the invocation of their corresponding symbols in language (cf. Turner). Aristotle′s conception about the knowledge of the individual being considered unscientific is due to lack of the field of statistics in his time, so he could not appeal to statistical averaging by the individual.

A particular experimentally obtained value is said to be reproducible if there is a high degree of agreement between measurements or observations conducted on replicate specimens in different locations by different people—that is, if the experimental value is found to have a high precision

Slide 10-38 Open Source: Legal and regulatory constraints

open source ≠ FDA CE

- 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)

In Slide 10-33 we have discussed the advantages of Open Source software.
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.

Slide 10-39 Future outlook

- 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) Search tools will be integrated within the clinical workplace to provide a quick **overview first,** and then zoom and filter on demand …
- 4) Integrated ML will enable **knowledge discovery with the doctor-in-the-loop …**

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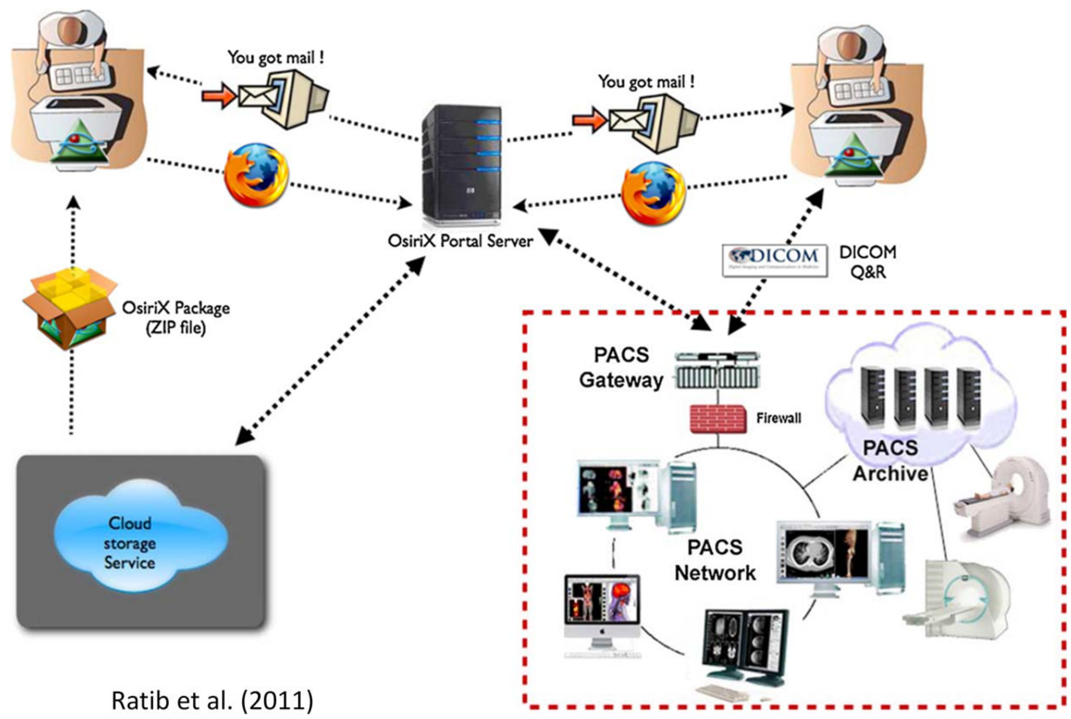
For sure the future hospital information systems will have three components
1) the world (even the hospital world) of tomorrow will be mobile
2) the data will be stored in the cloud as well as software-as-a-service will be used (Key problem: Privacy, Security, Safety and Data Protection).
3) Content Analytics will be integrated as tools within the clinical workplace

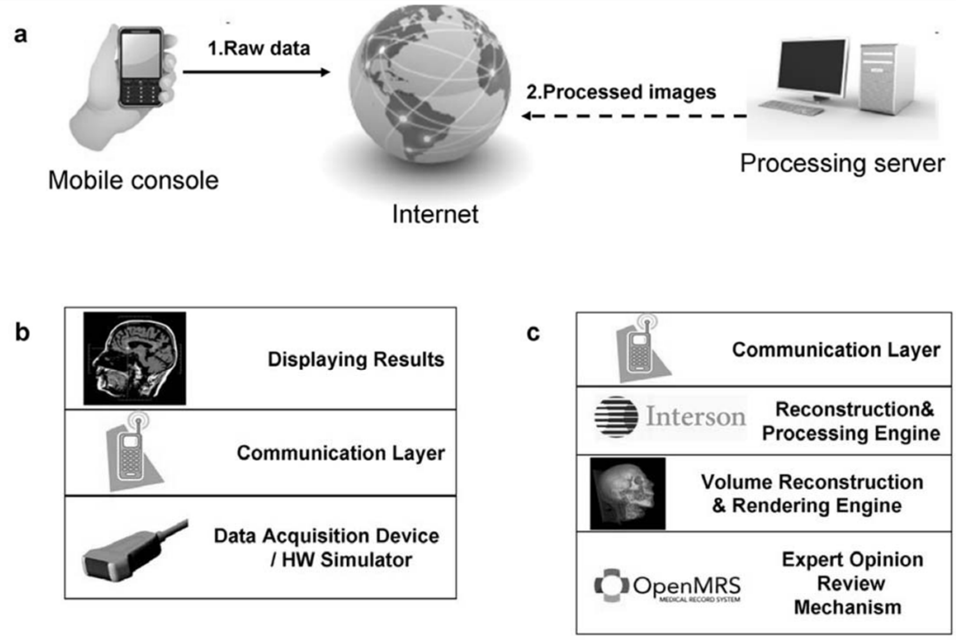
Slide 10-40 Future cloud computing solutions



Ratib et al. (2011)

Innovative solutions for rapid and robust transfer of very large data files are emerging and will probably change significantly the current limitations in the next few years. Online free file transfer providers such as yousendit (http://www.yousendit.com) have already become very popular for convenient transfer of large files, notifying the recipient by Email when the file is available for him to download. However, these public services lack the performance and security that would be required for transferring medical data. Examples are Open Source software solutions such as the Xebra software framework for Web-based distribution and visualization of medical imaging (http://www.hxti.com/technology/xebra.html). Major standardization efforts are being deployed as part of the IHE (Integrating the Healthcare Enterprise) initiative to develop new communication profiles and guidelines for exchanging medical data and images. The Cross-Document Sharing (XDS) an IHE profile for exchanging documents has led to an extension specific for medical images (XDS-i) that is more suitable for exchange of large medical imaging files. In compliance with DICOM standards an extension for image transfer called WADO (Web Access to DICOM Objects) isnowbeing adopted in replacement of traditional C-move (a DICOM service for moving data) allowing more flexibility and better performance. These emerging standard are already being adopted in large metropolitan or even national projects. A recent example of such deployments is the Canadian national diagnostic imaging repository (DI-r) which consolidates imaging results and provide a shared PACS application as part of the national interoperable electronic health record (Ratib, Rosset & Heuberger, 2011).

Slide 10-41 Future System Architecture: Cloud Ultrasound



Meir, A. & Rubinsky, B. (2009) Distributed Network, Wireless and Cloud Computing Enabled 3-D Ultrasound; a New Medical Technology Paradigm. *Plos One, 4, 11, e7974.*

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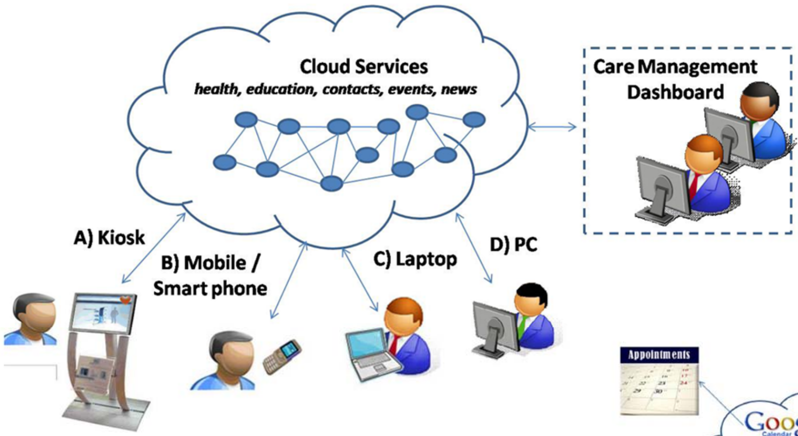
Cloud based computing follows the SaaS-Paradigm (Software as a Service) and offers a pay-per-use based virtual infrastructure, made dynamically scalable by the ability to spawn and destroy virtual machine instances on demand. This allows virtual servers to be created as needed to meet current demand and then scaled back when strain on the system is reduced, lowering resource usage and cost. In this example we see such an system architecture: (a) Overall system architecture includes the mobile console component and the remote processing server (Expert System) which performs the computation-extensive work. (b) Mobile Console Architecture. The console has one or more data acquisition devices, a communication module and a display capability. (c) Server Architecture. Contains a communication module, a processing engine, a visualization engine and an expert assessment mechanism (Mohammed, Servos & Fiaidhi, 2011).
The usefulness of mobile computing applications in the medical domain is commonly accepted. Such systems are able to facilitate efficient and effective patient care information input and access at the point of patient care resulting in an improvement of the quality of services (Holzinger et al., 2011). Problems include issues of usability, privacy and security.

Slide 10-42 Future: Software as a Service (SaaS)



Botts, N., Thoms, B., Noamani, A. & Horan, T. A. (2010) Cloud Computing Architectures for the Underserved: Public Health Cyberinfrastructures through a Network of HealthATMs. *43rd International Conference on System Sciences (HICSS). 1-10.*

This image illustrates the delivery of health data and information from a cloud computing environment (Botts et al., 2010).
The main problems involved are legal ones: Privacy, Security, Safety and Data Protection (Weippl, Holzinger & Tjoa, 2006).

Example : k-Anonymization of Medical Data

87 % of the population in the USA can be uniquely re-identified by Zip-Code, Gender and date of birth

Hospital Patient Data

Birthdate	Sex	Zipcode	Disease
1/21/76	Male	53715	Flu
4/13/86	Female	53715	Hepatitis
2/28/76	Male	53703	Brochitis
1/21/76	Male	53703	Broken Arm
4/13/86	Female	53706	Sprained Ankle
2/28/76	Female	53706	Hang Nail

Voter Registration Data

Name	Birthdate	Sex	Zipcode
Andre	1/21/76	Male	53715
Beth	1/10/81	Female	55410
Carol	10/1/44	Female	90210
Dan	2/21/84	Male	02174
Ellen	4/19/72	Female	02237

Sweeney, L. 2002. Achieving k-anonymity privacy protection using generalization and suppression. International Journal of Uncertainty, Fuzziness and Knowledge-Based Systems, 10, (05), 571-588.

The amount of patient-related data produced in today's clinical setting poses many challenges with respect to collection, storage and responsible use. For example, in research and public health care analysis data must be anonymized before transfer, for which the k-anonymity measure was introduced and successively enhanced by further criteria. As k-anonymity is an NP-hard problem, modern approaches make use of approximation as well as heuristics based methods. This talk will give a short introduction into anonymization and its criteria followed by an overview of methods & state-of-the-art algorithms to tackle the problem. I will demonstrate currently available tools and outline their strengths and weaknesses, before concluding the session by contemplating an interactive machine learning (iML) approach to the problem.

Anonymization of Patient Data

- **K-Anonymity** … not fully protected against attribute disclosure
- **L-Diversity** … extension requiring that the values of all confidential attributes within a group of *k* sets contain at least *l* clearly distinct values
- **t-Closeness** … extension requiring that the distribution of the confidential attribute within a group of *k* records is similar to the confidential attribute in the whole data set
- More in the upcoming 11th lecture !

K-Anonymity … eg. If the values of confidential attributes are very similar in a group of k records which overlap quasi-identifier values
L-diversity …

T-closeness … at most distance t between both distributions

Thank you!

My DEDICATION is to make data valuable … 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
- **CellProfiler** = open source modular image analysis software developed at the Broad Institute; algorithms for image analysis; 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
- **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
- **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
- **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

Some useful links

- http://www.gimias.org/download/sampledata (some useful sample 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 (Medical Image Database)
- http://www.incits.org (International Committee for Information Technology Standards)
- http://medical.nema.org (about DICOM)
- http://www.aycan.de/main/lp/dicom-bilder-zum-download.html (DICOM examples for download)
- http://www.ringholm.com/docs/04300_en.htm (HL7 Message Examples)
- http://www.openehr.org (Open HER – good UML examples)
- http://www.sparxsystems.com/uml-tutorial.html (UML 2.0 Tutorial)
- http://www.agilemodeling.com/essays/umlDiagrams.htm (Excellent description of UML diagrams)
- http://www.wfmc.org (Workflow Management Coalition)

Appendix: Open Source in medical imaging

http://www.idoimaging.com

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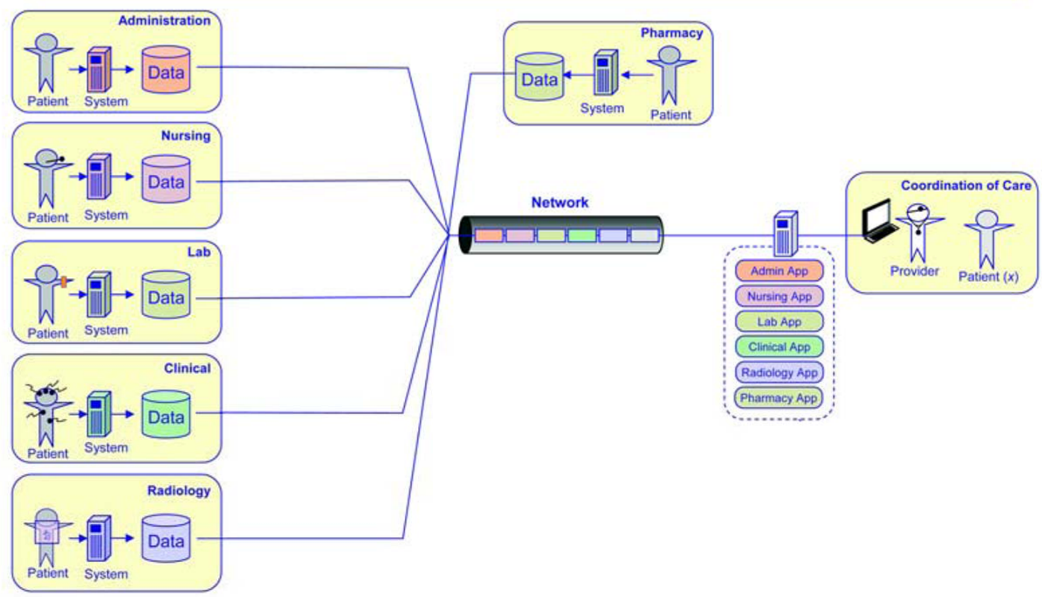
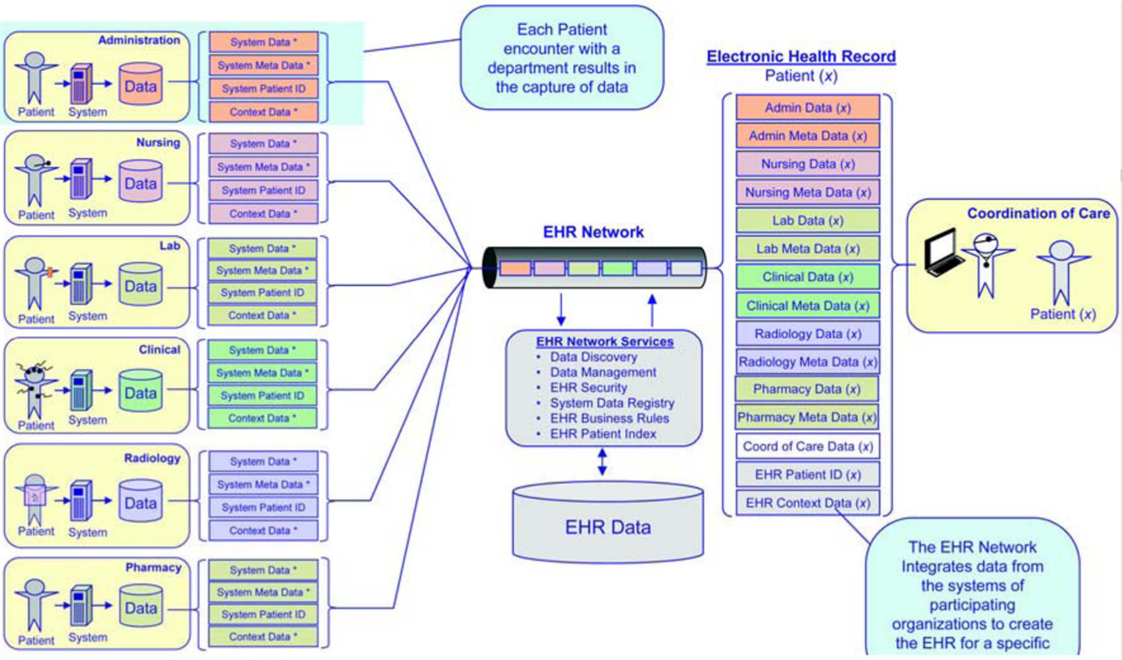
Numerous Open Source initiatives in medicine leading to innovative and cost effective information systems supporting electronic patient record applications and medical imaging and PACS have emerged in the recent years. Recent reports showed that adoption of computerized medical records and medical informatics in medicine have significantly lagged behind expectations due to three major barriers: excessive cost, the transience of vendors, and

Appendix: Electronic Health Records (1)



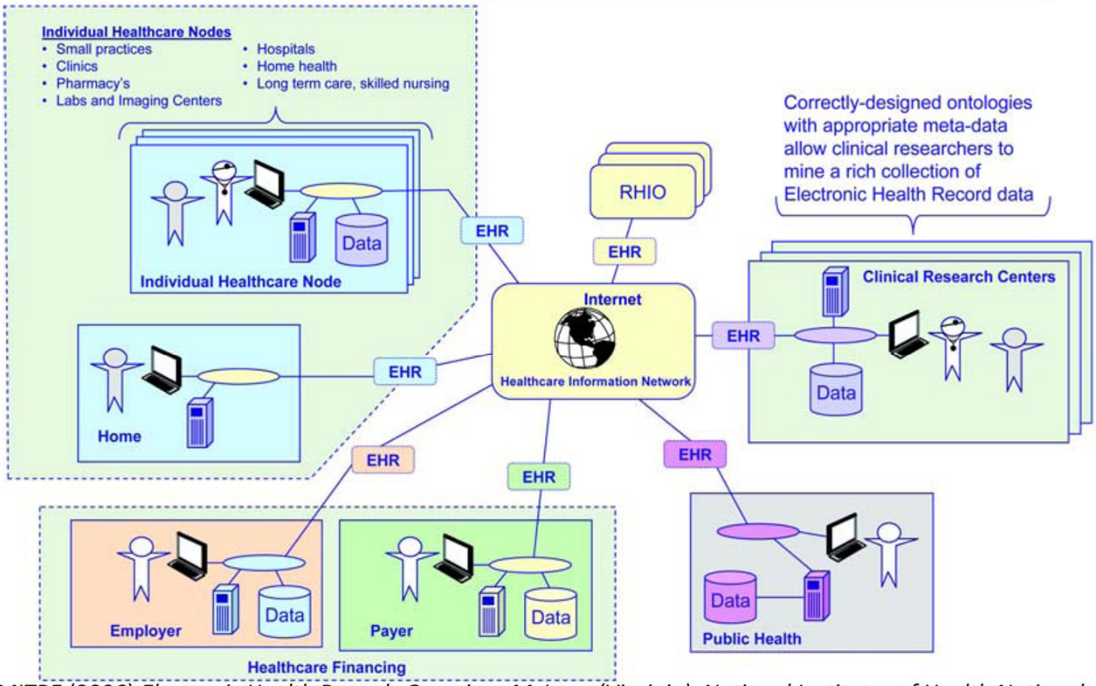
MITRE (2006) *Electronic Health Records Overview. McLean (Virginia), National Institutes of Health National Center for Research Resources.*

Appendix: Electronic Health Records (2)



MITRE (2006) *Electronic Health Records Overview. McLean (Virginia), National Institutes of Health National Center for Research Resources.*

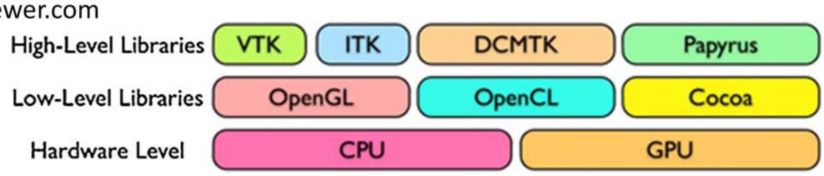
Appendix: Electronic Health Records (3)



MITRE (2006) *Electronic Health Records Overview. McLean (Virginia), National Institutes of Health National Center for Research Resources.*

Appendix: OsiriX Open Source component architecture

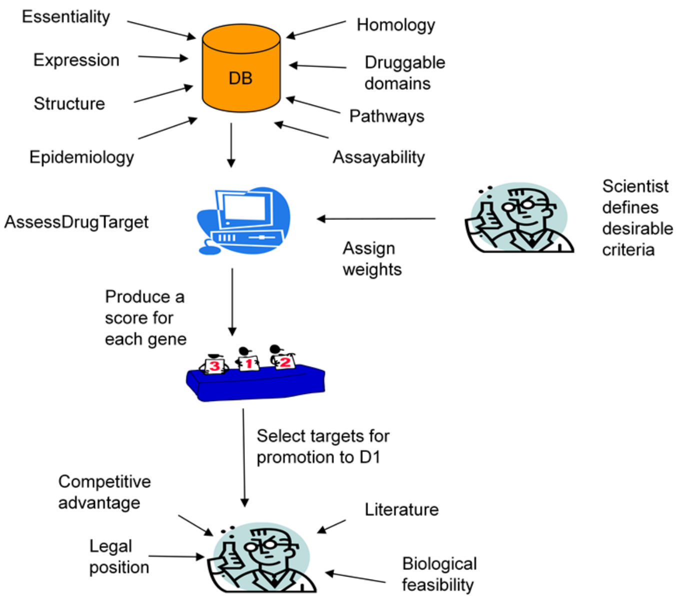
http://www.osirix-viewer.com



Rosset, A., Spadola, L. & Ratib, O. (2004) OsiriX: an open-source software for navigating in multidimensional DICOM images. *Journal of Digital Imaging, 17,* ***3, 205-216.***

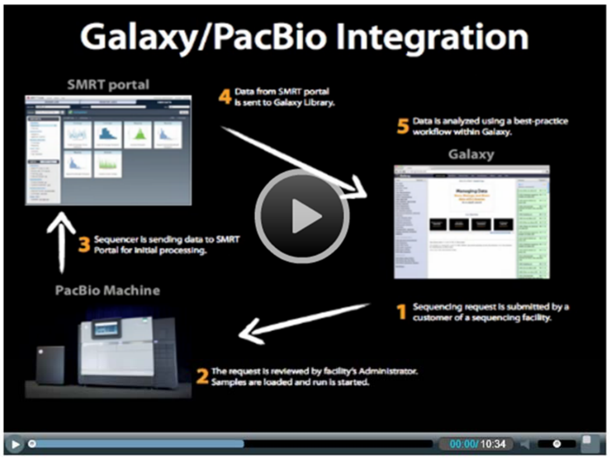
Advanced image processing and analysis tools are being added to the program everyday. Developers from all around the world
have contributed to the extension of OSIRIX by adding innovative and specialized image processing features. Furthermore, the OSIRIX
software architecture allows for separate processing modules to be added to the program as plug-ins. Such plug-ins will be
imbedded in the program when it is launched but they do not have to be integrated in the core of the main program. These external
plug-ins could also be components that are not shared as Open Source software but could be protected as binary modules or even
sold as commercial extensions to the OSIRIX platform.

Example: Drug Target Identification



Hasan, S., Daugelat, S., Rao, P. S. S. & Schreiber, M. (2006) Prioritizing genomic drug targets in pathogens: application to Mycobacterium tuberculosis. *PLoS Computational Biology, 2, 6, e61.*

Bioinformatics Workflow Management System



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

Goecks, J., Nekrutenko, A., Taylor, J. & Team, T. G. (2010) Galaxy: a comprehensive approach for supporting accessible, reproducible, and transparent computational research in the life sciences. *Genome Biology, 11, 8, R86.*

Blankenberg, D., Kuster, G. V., Coraor, N., Ananda, G., Lazarus, R., Mangan, M., Nekrutenko, A. & Taylor, J. (2010) Galaxy: A Web-Based Genome Analysis Tool for Experimentalists. *Current Protocols in Molecular Biology. John Wiley & Sons, Inc.*

Quality – Quality – Quality

- Experts consider health IT key for improving efficiency and quality of health care processes.
- Please, carefully determine between:
- Quality of Systems

  and
- Quality of Data
- Quality of Information
- Quality of Knowledge
- Quality of Action

Chaudhry, B., Wang, J., Wu, S. Y., Maglione, M., Mojica, W., Roth, E., Morton, S. C. & Shekelle, P. G. (2006) Systematic review: Impact of health information technology on quality, efficiency, and costs of medical care. *Annals of Internal Medicine, 144,* ***10, 742-752.***

PACS R&D Progress and R&D Topics

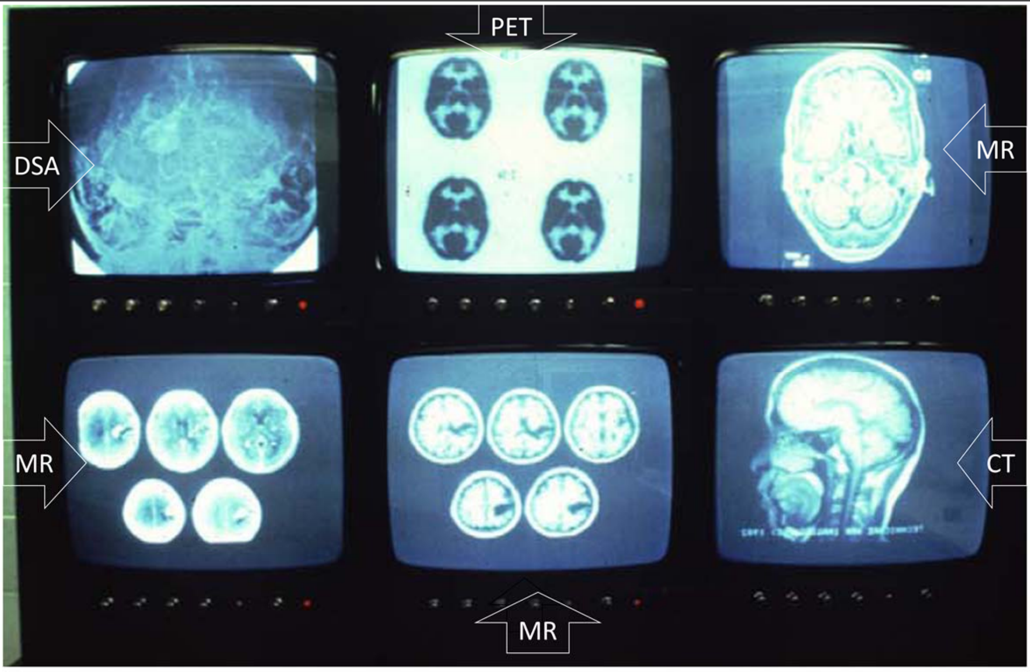
Decade	R&D progress	R&D topics
1980s	Medical imaging technology development	CR, MRI, CT, US, DR, WS, storage, networks
Late 1980s	Imaging systems integration	PACS, ACR/NEMA, DICOM, high-speed networks
Early 1990s	Integration of HIS/RIS/PACS	DICOM, HL7, Intranet and Internet
Late 1990s – present	Workflow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

- 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;

Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

This historical review of PACS covers the PACS development in the USA during the past 28 years from 1982 to 2010. Many important events triggered the successful journey of PACS from its infancy to maturation. Among these are the dedication of key pioneers' contributions, the behind the scene heroes introducing the computed radiography, optical juke box, high-resolution multiple screen workstations, DICOM standard, IHE workflow profiles, resilient software operating system, high-speed communication networks, and the system integration concept.

1st PACS 1985: Multi modality images on 6 CRTs



Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

MR = Magnetic Resonance
CT = Computed Tomography
PET = Positron emission tomography
DSA = Digital subtraction angiography

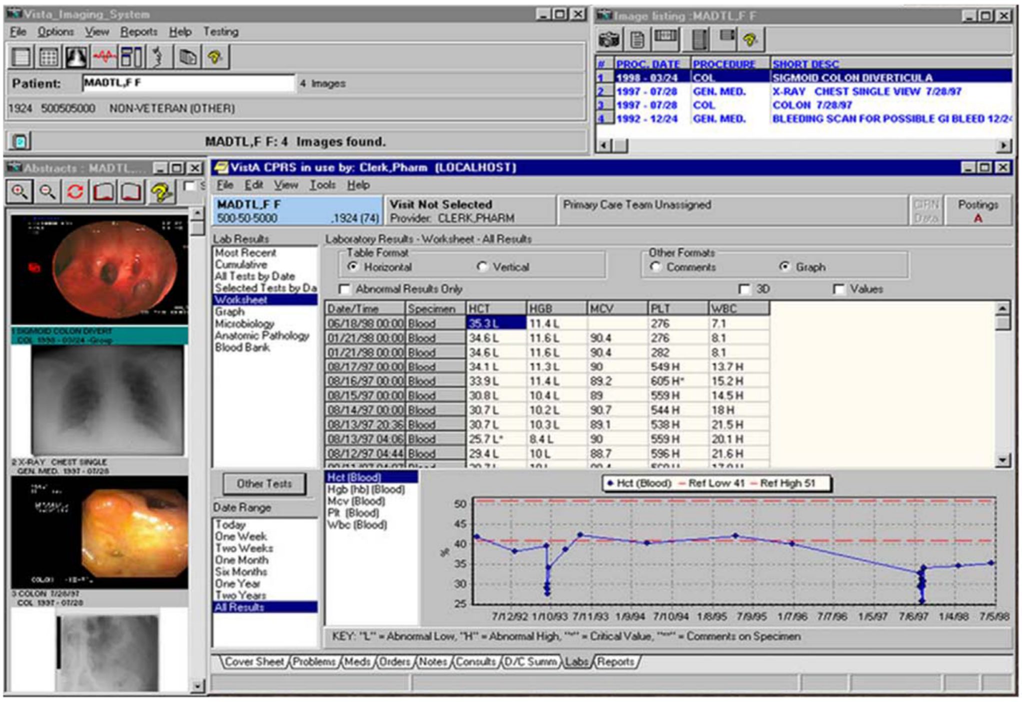
Pros/Cons of six PACS implementation models

Method	Advantages	Disadvantages
1. Home-grown system	Built to specifications, state-of-the-art technology, continuously upgrading, not dependent on a single manufacturer	Difficult to assemble a team, one-of-a-kind system, difficult to service and maintain
2. Two-team effort	Specifications written for a certain clinical environment, implementation delegated to the manufacturer	Specifications over ambitious, underestimate technical and operational difficulty, manufacturer lacks clinical experience, expensive
3. Turnkey	Lower cost, easier maintenance	Too general, not state-of-the-art technology
4. Partnership	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	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
5. ASP	Minimize initial capital cost, may accelerate potential return on investment, no risk in technology obsolescence, provide flexible growth, no space requirement in data center	More expensive over 2–4-year time frame comparing to a capital purchase, customer has no ownership in equipment
6. Open source	Healthcare provider purchases its computer and communication equipment, use open source software, good for special PACS application server, lower cost	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

ASP = application service provider model

Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

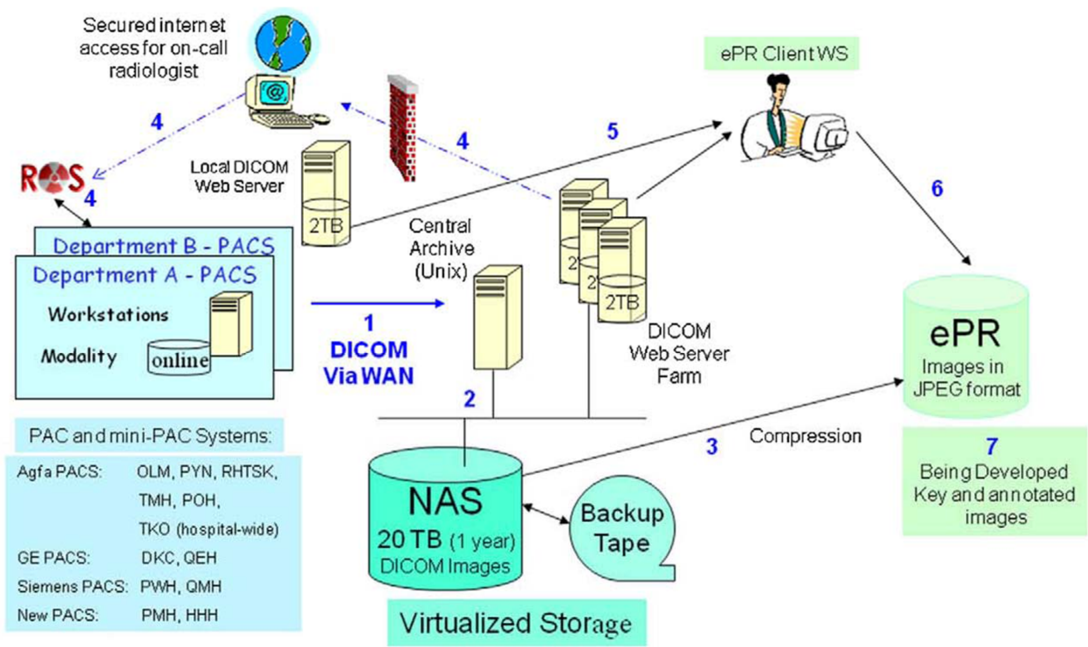
Example: Images within the EPR



Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

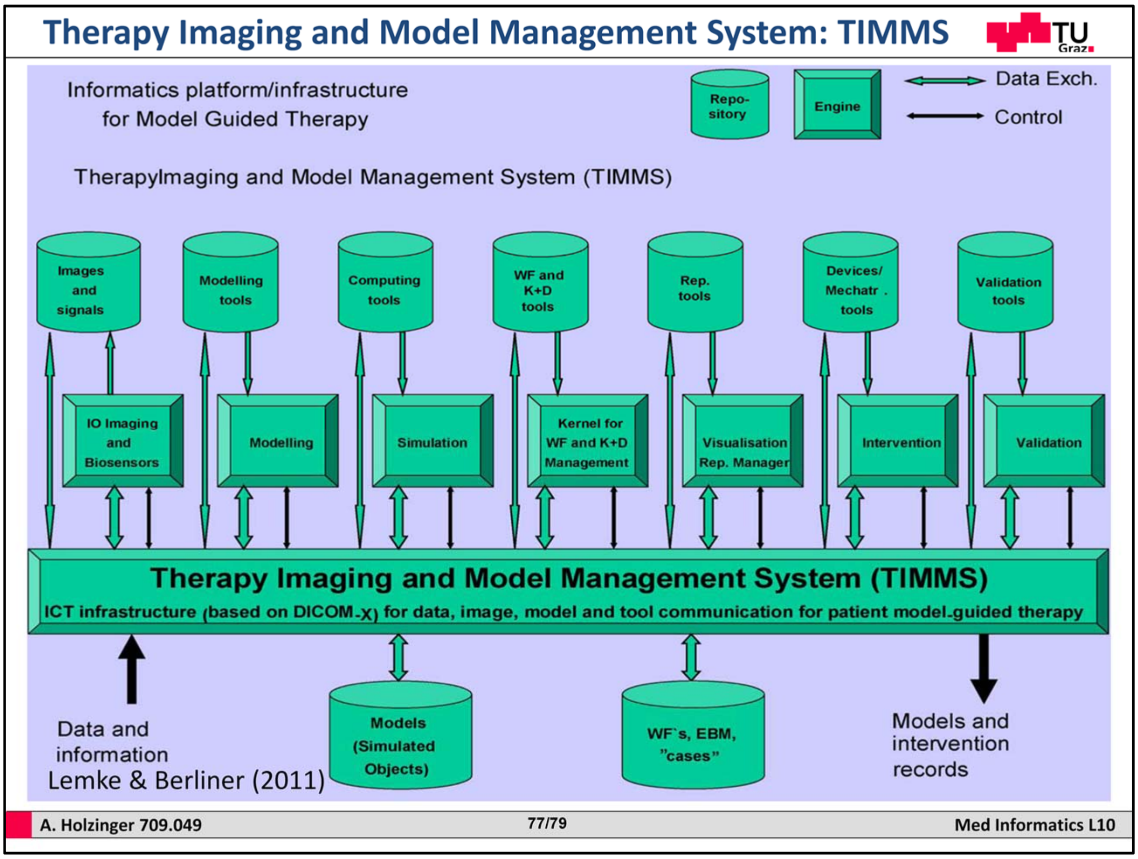
(a) VistA Imaging displays the patient record with images. Courtesy of Drs. H. Rutherford and R. Dayhoff; (b) the Hong Kong Hospital Authority (HKHA) central archive,
ePR with image integration and workflow steps. This design was based on the existing HKHA clinical information systems (CMS) (courtesy of Dr. Cheung et al.).

Ex.: The Hong Kong Hospital Clinical Information System



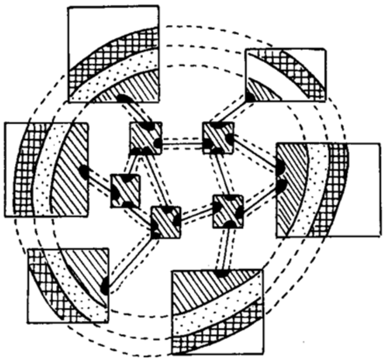
Huang, H. K. (2011) Short history of PACS (USA). *European Journal of Radiology, 78, 2, 163-176.*

(a) VistA Imaging displays the patient record with images. Courtesy of Drs. H. Rutherford and R. Dayhoff; (b) the Hong Kong Hospital Authority (HKHA) central archive,
ePR with image integration and workflow steps. This design was based on the existing HKHA clinical information systems (CMS) (courtesy of Dr. Cheung et al.).

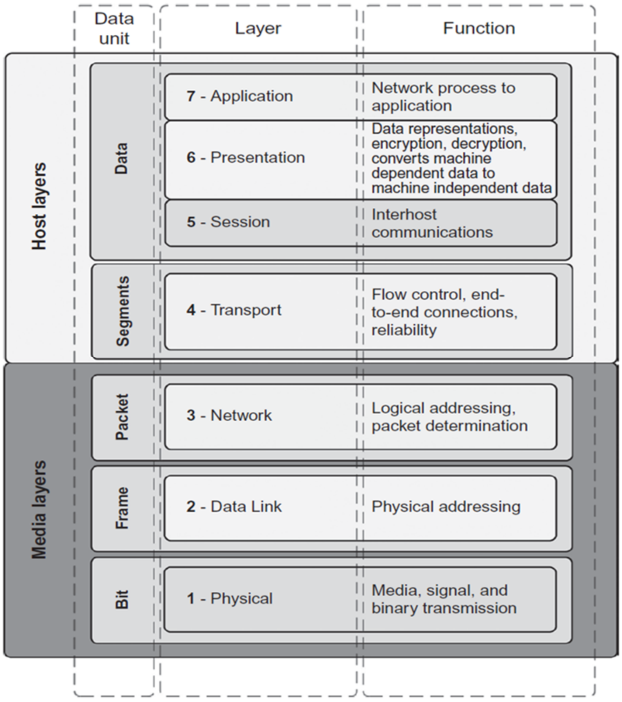


This illustrates a meta-architecture concept of a high level SAS modular structure. The high level modules are abstracted from specific, recently developed CAS/IGT systems. Most R&D and commercial SAS systems are limited to propriety implementations of some of these functionalities. A central position is occupied by the "Kernel for workflow and knowledge and decision management". It provides the strategic intelligence for preoperative
planning and intraoperative execution. Often, this module (or parts of it) is integrated into other engines. Modular, scalable and distributableTIMMScomponents act synergistically to provide functionality and utility that exceed the sum of their parts. These components include:
1. Seven "engines" – or software modules that can be executed on an appropriate computing machine – that work independently
and dependently to account for all facets of complex medical and surgical procedures.
The seven engines are:
1. intraoperative imaging and biosensors engine,
2. modelling engine,
3. simulation engine,
4. Kernel for workflow and knowledge and decision management
engine,
5. visualization representation manager engine,
6. intervention engine, and
7. validation engine.
2. Associated repositories – integrated hardware and software
structure that stores and makes available data and/or data processing
tools – linked to each of the seven engines.
3. Additional repositories which are provided for:
1. models (models are defined as simulated objects and may
represent patient-specific information, implants, etc.) and
2. references such as workflow models, evidence-based medical
data, case-based medical data.
An ICT infrastructure enables intercommunication and interactivity among all TIMMS or S-PACS components. The engines, tools, repositories, ICT infrastructure and data sources – including the operative team – are linked through a distributed network, providing full functionality of TIMMS, including planning, guidance,
learning, and data mining and processing.

ISO/OSI Layer Model (ISO 7498) Communication Standards



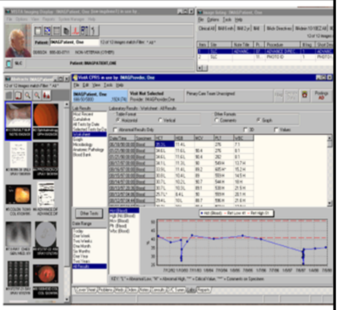
Zimmermann, H. (1980) OSI reference model-The ISO model of architecture for open systems interconnection. *IEEE Transactions on Communications, 28,* ***4, 425-432.***

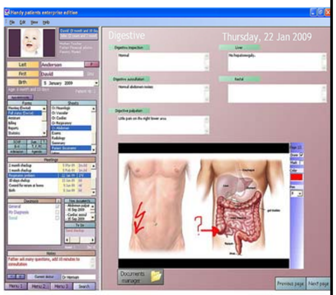


Paulsen, K. (2011) Networked Storage. *Moving Media Storage Technologies. Boston, Focal Press, 429-467.*

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





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