Biomedical Imaging and Image Analysis

Lecture in Medical Informatics Course

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The theme

- Images are of central importance in medical diagnosis
- There has been a dramatic development in medical imaging during the last few decades
- In this lecture we will briefly describe different ways of
  - Lecture 1: Creating
  - Lecture 2: Analyzing medical images
Medical imaging vs. microscopy

• There are two main types of medical images: Microscopic and macroscopic.

• The macroscopic images are typically taken in situ from the patient while microscopic images are based on small samples taken out of the patient.

• The term “Medical imaging” is typically limited to images of the patient and his/her organs on a macroscopic scale.
Medical imaging motivations

- Medical imaging is used to visualize and understand the patient
  - Anatomy
  - Physiology (function)
  - Discovering injuries or pathology

- Different imaging methods are better at one or the other aspect
Medical imaging modalities
Imaging motivations - microscopy

• Visual evaluation of tissue samples in a microscope is usually the final basis for diagnosis of all cancers and many other diseases

• Used to be all optical
  Is rapidly becoming digital
  Also a rapid development of new microscopy imaging techniques
Microscopic imaging modalities

- Brightfield light microscopy
  - The classical microscopy
- Fluorescent microscopy
  - Used for research
  - Several versions:
    - Full field
    - Confocal
    - Two-photon
    - STED
- Electron Microscopy
  - The highest resolution but complex and tedious
Microscopic images

- Brightfield microscopy
- Fluorescent microscopy
- Tissue microarray
- Electron microscopy
Medical imaging

- Using different parts of the electromagnetic spectrum
  - PET – hard gamma rays, 511keV
  - X-ray images, CT
  - Visible light
  - Heat images, thermography
  - Radio waves from nuclear spinn, MRT
  - The electric activity of the body, EEG
- Sound waves, ultrasound
Classical X-ray projection, gives a 2D shadow image
X-rays: Röntgen – the inventor

Wilhelm Conrad Roentgen

If one holds the hand between the discharge apparatus and the screen, one sees the darker shadows of the bones within the much fainter shadow picture of the hand itself. Roentgen
X-ray technology trends

• Since about 100 years X-ray imaging through analogue electronic technology and photography

• Since about 30 years with digital technology

• Digital technology is rapidly taking over – in this field as in most other
Fluoroscopy vs radiography

**Fluoroscopy** – transillumination,
- Creates a live image of the patient
- Can support real time diagnosis
- Shows dynamics
- Can control certain invasive diagnostic procedures
- Gives a relative high dose also to the medical doctor

**Radiography** – X-ray photography
- Creates a frozen permanent image
- Can be interpreted without rush
- Gives medical and legal documentation
Fluoroscopy

- Fluoroscope, originally zinccadmiumsulphide screen, 7% efficiency
- Electro-optical image amplifiers with fluorescent screen (>10,000 x amplification)
- Image amplifier with TV-camera (tube or CCD)
- Digitally registering the image from the TV-camera
  - Digital fluoroscopy
  - Digital subtraction angiography
Blood vessels
- Angiography
Digital fluoroscopy
Radiography

- Original direct film exposure, gives the sharpest images but low efficiency, only used in special cases such as dental imaging
- Amplification screens converts X-rays to light, gain 100-10 000 x
- Can use secondary aperture, a grid to decrease scattered light and increase contrast
- The film can be replaced by image plates, gives a greater dynamic range and possibilities of directly digitizing and improving the image through image processing
Muscles and bones
Conventional vs digital, high-frequency amplified X-ray image

Film Chest X-ray

Digital Chest X-ray
Digital radiography, advantages

• Greater contrast range gives fewer retakes because of poor exposure
• Digital image handling gives fewer lost films and simplified archiving
• More environmentally friendly through less use of film and chemicals
• Easier to consult other experts over the network
Computed Tomography (CT) creates images of slices through the body.
How the tomograph functions
CT-functional principles

- In a large number of projection rays though the body the X-ray absorption is measured, this yields many density profiles.
- These can be reprojected into the slice through Radon's formula or through filtered back projection.
- CT gives good contrast resolution and very good geometric accuracy.
Computed tomography

CT gives anatomical information
CT image properties

- CT measures X-ray density in absolute units according to the Hounsfields scale:
  - -1000 for air
  - 0 for water
  - +1000 for bone
- Through different contrast windows in the display different tissues can be displayed optimally.
A modern CT can have 64 parallel channels

- Typical specifications;
  - 64 x 0.625mm acquisition
  - 0.34mm x 0.34mm x 0.34mm isotropic resolution
  - 0.4 second rotation time
  - Up to 24 Lp/cm ultra-high spatial resolution
  - High resolution 768 and 1024 reconstruction matrices
  - Reconstruction up to 40 images per second
CT examples
Magnetic Resonance Tomography (MRT)

Based on magnetic pulse sequences in a strong magnetic field

Different pulse sequences gives different contrast

The orientation of the slices can be chosen freely through manipulation of the magnetic fields
Magnetic Resonance Imaging

MRI gives anatomical information
Magnetic Resonance Imaging

MRI the main parts of the machine
How MRT works

• Nuclei with odd number of protons/neutrons has spin

• The spin vector can be aligned to a (very) strong magnetic field

• Can be disturbed by a radio signal in resonance with the spin frequency, the so-called Larmor frequency

• When the atoms return to rest position they become radio transmitters which can be detected by sensitive receivers

• Through control of field gradients and pulse sequences one can determine which atoms are activated and listened to respectively and thus images can be created in 2D and 3D
Some fundamental MR-concepts

- MR-images can be weighted to show two time constants giving different contrast:

- $T_1$ is the time constant that determines how fast the spin $M_Z$ returns to equilibrium, it is called spin lattice relaxation time
  $$M_Z = M_0 \left(1 - e^{-t/T_1}\right)$$

- $T_2$ is the time constant that determines the return to equilibrium for the transversal magnetisation $M_{XY}$, it is called spin-spin relaxation time
  $$M_{XY} = M_{XY_0} e^{-t/T_2}$$
MRT image properties

- Very good contrast resolution for soft tissue
- Very flexible, different pulse sequences gives different contrast
- Usually not possible to determine the signal levels in absolute terms
- Poor geometric precision
- No known harmful effects
- Still under strong development
3.0T High Resolution Neuro

High res 3D inflow angio using SENSE and CHARM
Matrix 512
Thk 0.6 mm
Scan time 05:00 min

Left: High res IR TSE
Matrix 512
Thk 4.0 mm

Right: High res T2W TSE
Matrix 512
0.5 x 0.5 x 1.0 mm

High res 3D T1W TFE
SENSE factor 3
MPR’s
0.65 x 0.65 x 0.65 mm
250 slices
Scan time 05:10 min
Muscles and bones (joints)
Microscopic resolution for orthopedics

- 0.078 mm in-plane resolution of wrist
- Observe clear delineation of fine structures such as the vessel walls
- Technical details:
  - T1 FLASH
  - TR 591 ms,
  - TE 7.5 ms,
  - TA 6:09 min,
  - SL 3 mm,
  - slices 19,
  - matrix 1024,
  - FoV 80 mm.
Whole body MR imaging
Neurological

Multiple sclerosis
Angiography
The heart
MRT technologies

• The image properties are influenced by many factors:
• Radio antenna coils can be adapted to anatomy and pathology
  – Closer coil gives better image
• Different pulse sequences gives different contrast, resolution, signal noise and registration times
• Triggering by heart beat, blood motion and breathing can increase the resolution
• Contrast media can enhance certain structures
• With functional MR, fMRI activity in the brain can be registered and imaged
MRT technologies

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Functional imaging

SHOWS WHERE THE BRAIN IS PARTICULARLY ACTIVE
Functional imaging - how it works
MR diffusion tensor imaging

- Showing the connections of "fibers" in the brain
Brain fiber visualization by Anders Brun CMIV/CBA
For further studies about MRT

- A good description of the MRI technology at: http://www.cis.rit.edu/htbooks/mri/inside.htm
- A good popular description at:
- A leading research group in MR and other medical image visualisation, CMIV:
  - http://www.cmiv.liu.se
Positron Emission Tomography (PET)

PET shows the concentration and distribution of positron emitting tracer substances in the patient. These images are functional, not anatomical, i.e. they show physiological parameters.
PET – functional principle
PET functional principles

- A positron emitting compound is injected into the body (must be produced in an accelerator)
- The positrons will, within a couple of mm, collide with an electron and create two co-linear 511keV gamma rays
- These are detected by two detectors located in opposite locations in rings around the person and based on this one can figure out where the event took place
- Re-projection based on the tomographic principle
Positron Emission Tomography

PET gives functional information
Positron Emission Tomografi: accelerator for creating the radioactive tracer substances
The properties of PET images

- Gives functional images with rather good resolution at least 1 cm
- Glucose can be labelled with C11 and this makes it possible to see where in the brain “fuel” is needed i.e. where the brain is working
- Very specific substances can be labelled so PET has many applications in pharmaceutical research
- The need for an accelerator and a chemical lab which can handle high speed synthesis of radioactive compounds makes the technology very expensive
PET in Uppsala

- The PET-research in Uppsala is in the international front-line
- In 2001 the university PET-centre was sold to Amersham-Biosciences and Imanet AB was created
- Amersham-Biosciences was bought by GE Medical a few years later
- Now the PET-centre medical activity is back at Uppsala university hospital
- Will get the first PET-MR system in Sweden next year
Typical result from PCA image enhancement of PET images
HV NK1-receptor tracer GLD

Pasha Razifar PhD thesis work at IMANET AB and CBA
Single Photon Emission Computed Tomography (SPECT)

SPECT is similar to PET and shows the concentration and distribution of a radioactive tracer in the patient. The images are functional, not anatomical.
Scintigraphy - SPECT camera
SPECT functional principles

- A radioactive tracer is injected into the body
- With a matrix of detectors arranged above the body the location of the radioactive disintegrations is approximately determined
- The detector can be moved into different positions, which makes tomographic reconstruction possible
- Alternatively a collimator with slanted holes can be used - ectomography
Single Photon Emission Tomography

SPECT gives functional information
The SPECT image properties

- SPECT gives a functional image with relatively low resolution, some cm
- The images are intrinsically 3D
- The radioactive compounds can be obtained from long lived mother isotopes which is much cheaper than accelerators
- Dynamic processes can be studied through long registrations
Ultrasound, US

- Based on the sonar, acoustic echo principle. Sound with high frequency, typically a few MHz is sent into the body and the echoes are studied.
- Can with a small, compact equipment give dynamic images in 2D or 3D.
- The images has problems with coherent noise, specle, and with non-lineararities in the sound propagation.
Ultrasound equipment
Ultrasound, best at showing soft tissue
Heart
Ultrasound images of a heart

Sharp images of structures in a moving heart
Ultrasound for fetal examinations
3D rendering of dynamic Ultrasound
Ultrasound can show flow through Doppler technology.
Digital image analysis

- Most modern medical imaging devices are digital
- This creates opportunities for also using digital image processing techniques to help interpret the images
- Actually digital techniques are necessary even for being able to handle some types of images
Advantages of digital technology

• Can create images with greater contrast range with less radiation
• Can handle the images more efficiently through PACS – Picture Archiving and Communication Systems
• Can create completely new types of images
  – Slice images, computer tomography
  – Three dimensional volume images
  – Images of new physiological aspects e.g. oxygen consumption or flow
• Can visualize the images in new ways, 3D
• Can extract quantitative information from the images
Man vs computer

• Man is superior when it comes to recognising and interpreting patterns

• The computer is superior when it comes to
  – Store
  – Transport
  – Present
  – Count and measure

• The computer can make the images better for human visual analysis
PACS – the computer as an administrative tool

• Large amounts of images are registered daily at a modern hospital. Administration and storage of these requires great resources

• A Picture Archiving and Communication System, PACS, can make this more rational

• Requires high capacity storage units and networks. Typically several TB needs to be handled and stored.

• Sectra-Imtec in Linköping is a leading company in this field
Digital image enhancement

- When the images are available in digital format the computer can be used to help presenting them optimally
- In order to enhance the images they are filtered
  - point-wise
  - through neighbourhood filters
  - or in the spectral domain
FIGURE 3.3 Some basic gray-level transformation functions used for image enhancement.
Example of simple greyscale transforms: Contrast inverted mammograms

**FIGURE 3.4**
(a) Original digital mammogram. (b) Negative image obtained using the negative transformation in Eq. (3.2-1). (Courtesy of G.E. Medical Systems.)
Contrast-enhancement with non-linear greyscale-transform
Image subtraction
image with contrast – image without

**FIGURE 3.29**
Enhancement by image subtraction.
(a) Mask image.
(b) An image (taken after injection of contrast medium into the bloodstream) with mask subtracted out.
Spatial filtering

**FIGURE 3.1** A $3 \times 3$ neighborhood about a point $(x, y)$ in an image.

Image $f(x, y)$
Mean filtering

Linear quadratic mean filter with increasing size
3, 5, 9, 15, 35
Noise reducing filtering

Original image  3x3 mean filter  3x3 medianfilter
Laplace filter 3x3

\[
\begin{array}{ccc}
0 & 1 & 0 \\
1 & -4 & 1 \\
0 & 1 & 0 \\
\end{array}
\quad
\begin{array}{ccc}
1 & 1 & 1 \\
1 & -8 & 1 \\
1 & 1 & 1 \\
\end{array}
\quad
\begin{array}{ccc}
0 & -1 & 0 \\
-1 & 4 & -1 \\
-1 & 8 & -1 \\
\end{array}
\quad
\begin{array}{ccc}
0 & -1 & 0 \\
-1 & -1 & -1 \\
-1 & -1 & -1 \\
\end{array}
\]

FIGURE 3.39
(a) Filter mask used to implement the digital Laplacian, as defined in Eq. (3.7-4).
(b) Mask used to implement an extension of this equation that includes the diagonal neighbors. (c) and (d) Two other implementations of the Laplacian.
Edge sharpening filter
Image filtering example

a) Whole body image
b) Laplace filtered
c) Sum a and b
d) Sobel filtered a
e) 5x5 mean of a
f) c*e
g) a+f
h) Greyscale transf. of g
Image enhancement with the Context Vision method (adaptive neighborhood filtering)
Context Vision filtering of MR
Medical image analysis: CAD - Computer Aided Diagnosis

- To filter an image so that it becomes significantly better for visual analysis is difficult, the visual system is very adaptive and can handle rather poor images.
- To automatically find abnormalities in images is even harder, requires advanced image analysis.
- The technology is about to mature in this area.
Typical Mammography image
Typical Mammography image
Typical Mammography image

Automated detection of suspicious cancerous lesions
Quantitative Microscopy
BlobFinder

Special features
• z-stack input and enhancement slice by slice
• zooming
• slide-bar for object thresholding in real time (at configuration setup)

GUI by Amin Allalou
An MR camera gives a 3D image. Classical X-ray image handling works with 2D film. 3D images gives a whole stack of 2D images to be interpreted jointly.
Volume rendering

An imaginative light ray is sent through each pixel in the image plane. The colour and intensity is determined through the interaction between the ray and the volume elements in the volume in combination with different light sources.
Volume rendering methods

• Single modalities
  – Greylevel gradient shading
  – Maximum intensity projection (MIP)
  – Integrated projection

• Multiple modalities
  – Combined rendering
  – Implicit segmentation
  – Surface projection of cortical activity
Greylevel gradient shading

• A greylevel threshold is set and rays are sent into the volume until a volume element with a value greater than the threshold is encountered

• The intensity gradients at these positions are combined with the light sources to render the image

• Cutting planes can be used to remove parts of the volume to make other parts more visible
3D volume rendering used for CT

Much easier than for MR because of fixed Hounsfield units
Maximum intensity projection (MIP)

• Along each ray the maximal density/intensity value is determined

• This is particularly useful for small intense structures such as the vessels in angiography

• Can become complex if several vessels are crossing and overlapping each other
With special image analysis (based on greyscale connectivity) the different vessel can be separated.
Rotating MIP gives good 3D effect
Image Fusion

• Different modalities give complimentary information, anatomy and physiology respectively. There are therefore needs to fuse data from different modalities.

• Image fusion includes
  – spatial registration
  – combined visualisation
  – combined analysis
Reference

Choose starting parameters

Transform Study

Evaluate similarity (cost function)

Converged?

Yes

No

Choose new set of parameters
SPECT-MRI
Multimodal registration can also be combined with 3D visualization.
Surface projection of cortical activity
Stereo rendering
3D visualisation requires segmentation

- Small differences in the properties of different tissue types makes advanced segmentation methods necessary
- High demands of correct reproduction of small details in the anatomy
- Need for rapid interaction between man and the system
- Greate needs for research
Summary

- Humans are good at recognising patterns
- Computers are good at counting and measuring
- The 3D reality is hard to represent accurately in 2D images
- Computers can significantly improve and facilitate medical diagnostics
- So far mainly by producing new types of images
- In the future 3D visualisation and CAD will probably also have great importance
THE END

That's all, thanks for your attention!